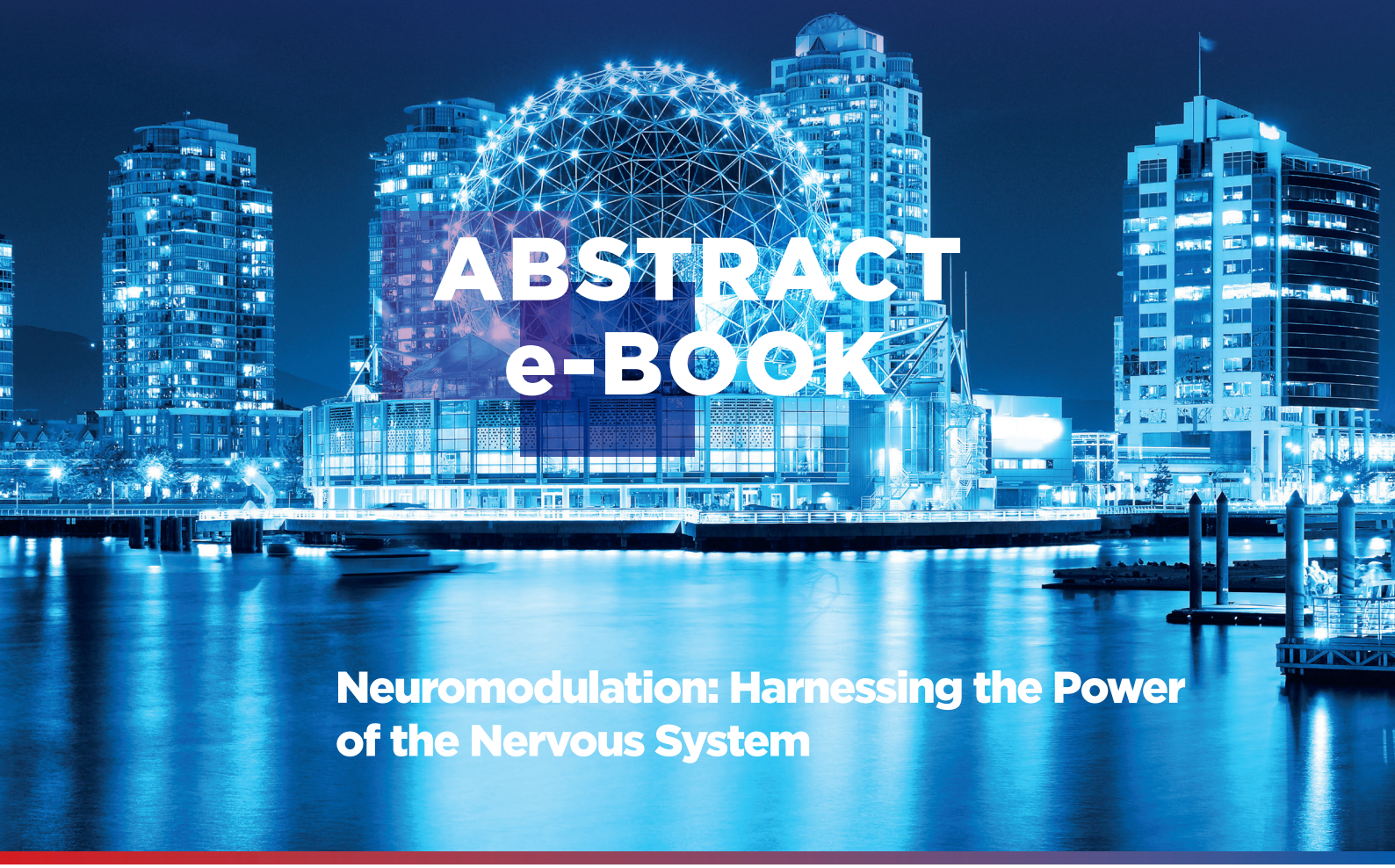
INS 2024

16TH WORLD CONGRESS OF THE INTERNATIONAL NEUROMODULATION SOCIETY

11-16 MAY, 2024

VANCOUVER, CANADA



ABSTRACT e-BOOK

Neuromodulation: Harnessing the Power of the Nervous System

ins International Neuromodulation Society

ins-congress.com

Pre-Conference Abstracts

Oral Abstracts

O001

Oral Presentations
ORAL POSTER PRESENTATIONS FIVE BEST ABSTRACTS
13-05-2024 12:00 - 13:00

LONG TERM SPINAL CORD STIMULATION INDUCES STRUCTURAL CHANGES OF THE NOCICEPTIVE SYSTEM IN AN ANIMAL MODEL FOR PAINFUL DIABETIC PERIPHERAL NEUROPATHY

Thomas De Geus, MSc[1,2], Glenn Franken, PhD[1,2], Jan Van Zundert, PhD[1], Bert Joosten, PhD[1,2]
[1]Maastrichtuniversity, Anaesthesiology, Maastricht, Netherlands, [2]Maastrichtuniversity, Department Of Translational Neuroscience, Maastricht, Netherlands

Introduction: Clinical studies indicate a decline in the initial large efficacy of spinal cord stimulation (SCS) for painful diabetic peripheral neuropathy (PDPN) (1,2). Furthermore, preclinical studies suggest that long-term SCS can alleviate baseline mechanical hypersensitivity and enhance hind paw blood flow in PDPN rats (3). We therefore aim to study possible structural changes in the nociceptive network induced by SCS in an animal model of PDPN. First, we hypothesize that long-term SCS promotes nerve fiber growth in the hind paws of PDPN rats. Second, we hypothesize that long-term SCS restores this central inflammatory balance, involving microglia and astrocytes, in PDPN animals.

Materials / Methods: Diabetes was induced in male Sprague Dawley rats (n=36) through streptozotocin injection. Four weeks after streptozotocin injection SCS-leads were implanted in the hypersensitive rats (n=13) at spinal levels L2-L5. Effects on mechanical hypersensitivity of 4-week, 12-hour daily Conventional (con)-SCS (50Hz) (n=5) and Sham-SCS (n=4) after 1, 2, 3, and 4 weeks of stimulation and 24 hours post-stimulation was measured using the Von Frey (VF) test, assessing the paw withdrawal threshold (PWT). Hind paw skin tissue, collected after the final VF-test, was immuno-stained for PGP9.5 (all small fibers) or CRGP (specific nociceptive and vasodilatory fibers) and the intra-epidermal nerve fiber density (IENFD) was calculated. Additionally, spinal cord was collected and extracted for protein expression using western blotting with antibodies for P2X4, p-p38-MAPK, GFAP, and BDNF. IENFD and protein levels of Con- and Sham-SCS groups were compared using t-tests.

Results: PWT significantly increased after 1, 3, and 4 weeks of Con-SCS but not Sham-SCS. Furthermore, 24 hours post stimulation, long-term Con-SCS-treated PDPN animals exhibited significantly increased PWT compared to baseline. Concurrently, IENFD of PGP9.5 fibers in hind paw skin tissue significantly increased in Con-SCS animals compared to Sham-SCS. Protein analysis showed that pro-BDNF expression was significantly decreased in long-term Con-SCS-treated animals compared to Sham-SCS animals. No significant difference was observed in IENFD of CGRP-ergic fibers or protein levels of central inflammatory response markers: GFAP, p-p38MAPK, P2X4, between the two groups.

Discussion: Our findings confirm that long-term Con-SCS reduces baseline mechanical hypersensitivity in PDPN rats, aligning with previous research (3). Furthermore, we show that long-term Con-SCS induces structural changes both in peripheral- (hind paw) and central- (spinal cord) nervous system. These changes may be related to and explain the reduced efficacy of long-term Con-SCS in PDPN patients.

Conclusions: Long-term Con-SCS alleviates baseline mechanical hypersensitivity and induces structural changes to the nociceptive network in PDPN rats.

Supplemental Data:

References: 1 Slangen R, Schaper NC, Faber CG, Joosten EA, Dirksen CD, Van Dongen RT, Kessels AG, Van Kleef M. Spinal cord stimulation and pain relief in painful diabetic peripheral neuropathy: a prospective two-center randomized controlled trial. Diabetes Care. 2014 Nov;37(11):3016–24. . DOI:10.2337/DC14-0684 2 Van Beek M, Geurts JW, Slangen R, Schaper NC,

Faber CG, Joosten EA, Dirksen CD, Van Dongen RT, Van Kuijk SMJ, Van Kleef M. Severity of Neuropathy Is Associated With Long-term Spinal Cord Stimulation Outcome in Painful Diabetic Peripheral Neuropathy: Five-Year Follow-up of a Prospective Two-Center Clinical Trial. Diabetes Care. 2018 Jan;41(1):32–8. . DOI:10.2337/DC17-0983 3 van Beek M, Hermes D, Honig WM, Linderoth B, van Kuijk SMJ, van Kleef M, Joosten EA. Long-Term Spinal Cord Stimulation Alleviates Mechanical Hypersensitivity and Increases Peripheral Cutaneous Blood Perfusion in Experimental Painful Diabetic Polyneuropathy. Neuromodulation. 2018;21(5):472–9. . DOI:10.1111/ner.12757

Acknowledgements:

Learning Objectives: 1. Study the effects of long term SCS in an animal model for PDPN on nerve fiber growth in the hind paw skin. Outcome: Long term conventional SCS increases the intra epidermal nerve fiber density of PGP9.5 stained fibers. This indicates that long term Con SCS induces small nerve fiber sprouting in the hind paw skin. 2. Study the effects of long term SCS in an animal model for PDPN on the inflammatory balance in the spinal dorsal horn. Outcome: Protein analysis showed that pro-BDNF expression was significantly decreased in long-term Con-SCS-treated animals compared to Sham-SCS animals. This indicates that Con-SCS might reduce the inflammatory response in the spinal dorsal horn. 3. Reproduce the behavioural finding that long term conventional SCS results in a decreased baseline hypersensitivity in PDPN animals. Outcome: Our findings confirm that long-term Con-SCS reduces baseline mechanical hypersensitivity in PDPN rats.

Financial Disclosures: Bert Joosten Name of Company: Medtronic Role: Education / Research Level of Compensation: $20,001 - $100,000 USD This study was supported by Medtronic, which provided a research grant (contract number ERP-2020-12545) to Prof. Dr. E.A. Joosten. Medtronic was not involved in the analysis and interpretation of the data or in writing the manuscript.

Disclosure: No significant relationships.

O002

Oral Presentations
ORAL POSTER PRESENTATIONS FIVE BEST ABSTRACTS
13-05-2024 12:00 - 13:00

DECIPHERING THE ANATOMICAL AND FUNCTIONAL ORGANIZATION OF CARDIAC FIBERS IN THE PORCINE CERVICAL VAGUS NERVE FOR SPATIALLY SELECTIVE CARDIAC EFFERENT NEUROMODULATION

Nicole Thompson, PhD[1], Enrico Ravagli, PhD[1], Svetlana Mastitskaya, PhD[1], Ronald Challita, MD[2], Joseph Hadaya, MD[2], Francesco Iacoviello, PhD[3], Ahmad Shah Idil, BSc (Hons)[1], Paul Shearing, PhD[3], Olujimi Ajijola, MD, PhD[2], Jeffrey Ardell, PhD[4], Kalyanam Shivkumar, MD, PhD[5], David Holder, PhD[1], Kirill Aristovich, PhD[1]
[1]University College London, Medical Physics And Biomedical Engineering, London, United Kingdom, [2]University of California Los Angeles, Los Angeles, United States of America, [3]University College London, Electrochemical Innovations Lab, Chemical Engineering, London, United Kingdom, [4]University of California, Los Angeles, Ucla Cardiac Arrhythmia Center And Ucla Neurocardiology Research Program Of Excellence, Los Angeles, United States of America, [5]UCLA, Ucla Cardiac Arrhythmia Center & Ep Programs, Los Angeles, United States of America

Introduction: Spatially selective vagus nerve stimulation (sVNS) offers a promising solution to mitigate the off-target effects associated with traditional VNS. This could serve as a precise method for addressing chronic heart failure by specifically targeting efferent cardiac fibers. It could enhance therapeutic outcomes by avoiding off-target effects and eliminating the need for time-consuming titration. Recent studies have demonstrated the independent modulation of breathing rate, heart rate (HR), and laryngeal contraction through sVNS[1]. However, the spatial organization of afferent and efferent cardiac-related fibers within the vagus nerve remains unexplored.

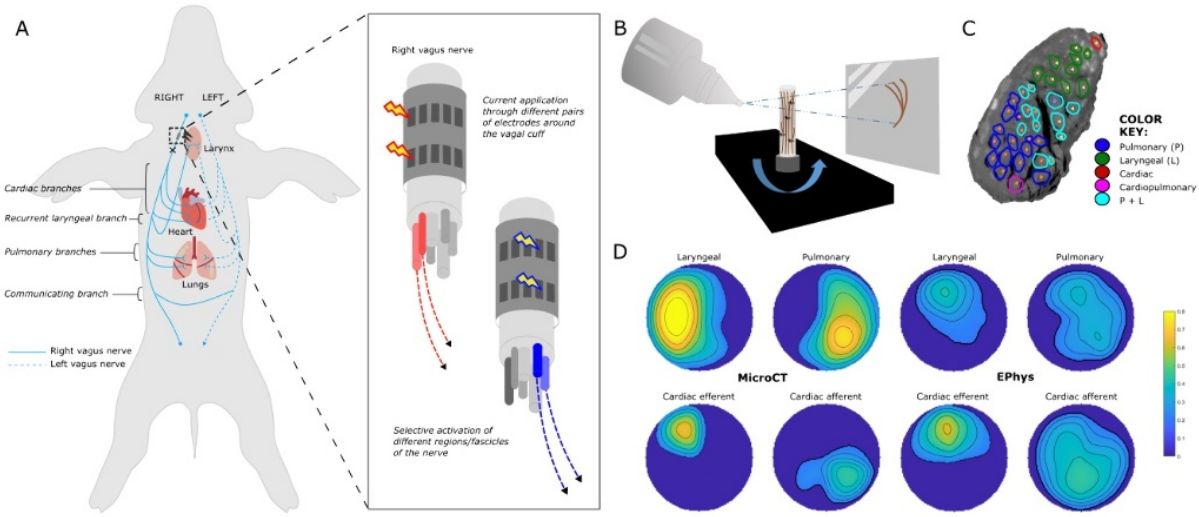
Materials / Methods: In 10 anaesthetised pigs a 28-electrode array (2 rings x 14 electrodes 3mm apart) was surgically inserted on the right mid-cervical vagus nerve. Current was applied to one pair of electrodes in the same radial position while recording any evoked cardiac, pulmonary or laryngeal responses. This was repeated for all pairs in turn and repeated after vagotomy, distal to the cuff, to identify afferent fibers. These functional studies were correlated with contrast-enhanced microCT scanning of the nerve resected post-mortem from above the nodose ganglion to all thoracic branches (n=5). Computerised segmentation permitted tracing of the connected organ and fiber direction. Centers of mass (CoMs) of functional regions identified by both methods were co-registered.

Results: Four significantly separated regions were identified: laryngeal, pulmonary, and cardiac efferent and afferent. Stimulation of the cardiac regions pre- (efferent) and post- (afferent) vagotomy elicited a HR decrease of -7.8±3.4% and increase of 10.2±5.3% (n=6) which was sustained after left vagotomy, respectively. There was significant spatial separation of the cardiac afferent and efferent CoMs (179±55° microCT, $p<0.05$ and 200±137°, $p<0.05$ sVNS, mean±1SD) at the mid-cervical level, with no significant difference between the two techniques. Of the 29.2±2.2 fascicles, 47% were identified as afferent/sensory, 36% motor/efferent, and 17% containing mixed fibers.

Discussion: Significant separation between afferent and efferent cardiac-related regions occurred in all animals, localized to roughly the opposite sides of the nerve, in close proximity to the pulmonary and laryngeal regions, respectively. This corresponded with the roughly equitable spread of afferent and efferent fibers as well as with recent findings of cardiopulmonary convergent neurons and circuits.

Conclusions: Separate localization of cardiac afferent and efferent regions was identified. We demonstrated the ability to selectively elicit therapeutic-related efferent effects without affecting afferent-related reflexes. This paves the way for more targeted neuromodulation to enhance precision and efficacy of VNS therapy in treating heart failure, myocardial infarction and other conditions by reducing off-target effects and eliminating the need for

titration.



Supplemental Data:

References: 1. Thompson N, Ravagli E, Mastitskaya S, Iacoviello F, Stathopoulou T-R, Perkins J, Shearing P R, Aristovich K and Holder D 2023 Organotopic organization of the porcine mid-cervical vagus nerve *Front Neurosci* **17**

Acknowledgements: National Institutes of Health grant 3OT2OD026545.

Learning Objectives: 1. Improve understanding of the anatomical organisation of the vagus nerve to allow for further developments in targeted vagal neuromodulation. 2. Promote use and application of VNS/sVNS to treatment beyond epilepsy and depression, to heart failure, asthma and other immune disorders to ultimately enhance efficacy of treatments worldwide. 3. Familiarise and improve understanding of sVNS and microCT imaging techniques for adoption in other studies.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O003

Oral Presentations
ORAL POSTER PRESENTATIONS FIVE BEST ABSTRACTS
13-05-2024 12:00 - 13:00

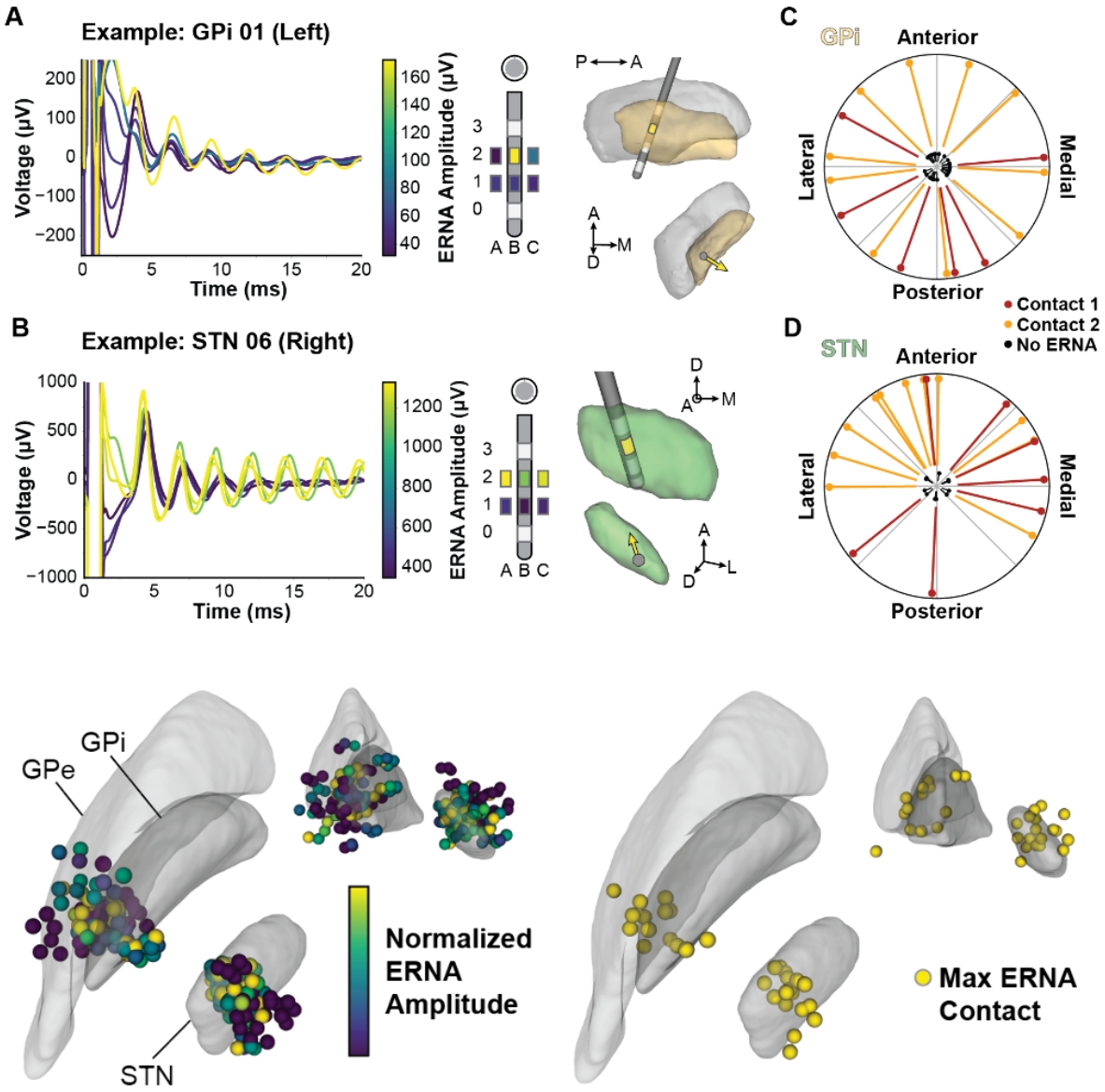
SPATIO-DIRECTIONAL TUNING OF EVOKED RESONANT NEURAL ACTIVITY WITH DEEP BRAIN STIMULATION IN PARKINSON'S DISEASE

Kara Johnson, PhD[1,2], Jackson Cagle, PhD[1,2], Justin Hilliard, MD[2,3], Kelly Foote, MD[2,3], Coralie De Hemptinne, PhD[1,2]
[1]University of Florida, Neurology, Gainesville, United States of America, [2]University of Florida, Norman Fixel Institute For Neurological Diseases, Gainesville, United States of America, [3]University of Florida, Neurosurgery, Gainesville, United States of America

Introduction: Objective markers of therapeutic deep brain stimulation (DBS) for Parkinson's disease (PD) are needed to tailor stimulation on a patient-specific basis and to fully leverage directional stimulation capabilities. Evoked resonant neural activity (ERNA) elicited by DBS in the subthalamic nucleus (STN) region or the pallidum (globus pallidus internus (GPi)/externus (GPe)) may be useful to guide targeting or stimulation parameter selection [1, 2]. However, it is unclear where ERNA is precisely localized or whether ERNA could be used to determine the optimal stimulation direction. We aimed to determine how ERNA varies when stimulating in different directions within the pallidum and the STN region in patients with PD.

Materials / Methods: Intraoperative recordings were acquired in 36 subjects (38 hemispheres; 17 GPi and 21 STN) who underwent DBS implantation surgery with directional leads for the treatment of PD. Local field potentials were recorded and referenced to a scalp corkscrew electrode. High-frequency stimulation (135 Hz) was delivered in bursts of 10 pulses repeated twice per second 10-20 times from each contact sequentially while recording from the other contacts. Offline, the recordings were bipolar referenced, and each burst was aligned to the last pulse to average the evoked responses. The evoked response amplitudes were quantified and compared across subjects and stimulating contacts. The contacts and their directional orientations were localized in each patient's postoperative CT and transformed to a common atlas space.

Results: ERNA was observed in 16/17 pallidum and 18/21 STN. The ERNA amplitudes varied depending on the stimulating contact (Figure 1A-B). The maximum ERNA contact was oriented approximately postero-lateral in 62.5% of pallidal leads and approximately antero-medial in 72.2% of STN leads (Figure 1C-D). In the pallidum, the contacts with maximum ERNA were clustered around the posterior GPi/GPe border, while in the STN, ERNA amplitudes were highest within the STN (Figure 2). Contacts located medial or dorsal to the STN did not elicit
ERNA.



Discussion: ERNA was present in the majority of subjects and may be localized to the posterior GPi/GPe border and within the STN. This localization suggests ERNA may involve modulation of pallido-STN pathways, which may be sensitive to specific stimulation directions. Future studies will investigate whether directional ERNA is correlated with postoperative stimulation parameters and clinical outcomes.

Conclusions: ERNA may be tuned to specific stimulation directions and neuroanatomical structures, which suggests it could provide spatial context to guide DBS targeting or stimulation parameter selection for PD.

Supplemental Data:

References: 1. Sinclair NC, McDermott HJ, Bulluss KJ, Fallon JB, Perera T, Xu SS, et al. Subthalamic nucleus deep brain stimulation evokes resonant neural activity. Annals of Neurology. 2018;83:1027–1031. 2. Johnson KA, Cagle JN, Lopes JL, Wong JK, Okun MS, Gunduz A, et al. Globus pallidus internus deep brain stimulation evokes resonant neural activity in Parkinson's disease. Brain Communications. 2023;5:fcad025.

Acknowledgements:

Learning Objectives: 1. Understand the features of ERNA elicited by DBS in the STN and the pallidum. 2. Understand the orientations and neuroanatomical locations where the maximum ERNA was elicited in the STN and the pallidum. 3. Understand the potential clinical applications of ERNA for DBS for PD.

Financial Disclosures: Kelly D. Foote: Medtronic - Education/Research: Fellowship funding and donation of DBS hardware to the institution for NIH sponsored research ($20,000 to $100,000). Boston Scientific - Education/Research: Fellowship funding and donation of DBS hardware to the institution for NIH sponsored research ($20,000 to $100,000).

Disclosure: No significant relationships.

O004

Oral Presentations
ORAL POSTER PRESENTATIONS FIVE BEST ABSTRACTS
13-05-2024 12:00 - 13:00

STIMULATION-INDUCED GAMMA ENTRAINMENT DIFFERS FROM LEVODOPA-INDUCED NARROWBAND OSCILLATIONS IN PATIENTS WITH PARKINSON'S DISEASE

Maria Olaru, MSc[1], Amelia Hahn, BSc (Hons)[1], Stephanie Cernera, PhD[1], Wolf-Julian Neumann, MD[2], Philip Starr, MD, PhD[3]
[1]UNIVERSITY OF CALIFORNIA - SAN FRANCISCO, Neurological Surgery, SAN FRANCISCO, United States of America, [2]Charité – Universitätsmedizin Berlin, Neurology, Berlin, Germany, [3]University of California San Fransisco, Neurosurgery, San Fransisco, United States of America

Introduction: Levodopa-induced narrowband gamma (NBG) oscillations (65-90 Hz) invasively recorded from the cortex have been linked to dyskinesia in human subjects with Parkinson's disease[1]. Cortical stimulation-induced NBG, known as entrained NBG, has also been observed at one-half of the stimulation frequency at the subthalamic nucleus in human subjects with Parkinson's disease[1][2][3]. Although entraining NBG oscillations with transcranial alternating current stimulation suggests that this electrophysiological signal has the potential to be beneficial, the relationship between levodopa-induced and entrained NBG via deep brain stimulation has not yet been studied. Here, we examine the relationship between levodopa-induced narrowband gamma and entrained narrowband gamma, and whether these oscillations may differ with respect to dyskinesia monitoring.

Materials / Methods: Prior to the onset of stimulation, we recorded over 50 hours of multisite recordings in three hemispheres of three subjects with Parkinson's disease implanted with investigational Medtronic RC+S. We also recorded over 40 hours of stimulation amplitude increases up to clinically therapeutic settings from these subjects. Each subject wore either Personal KinetiGraph® or Apple watches which recorded continuous dyskinesia scores. For each subject, we computed power spectra in 60-second intervals **(Figure 1A)** and spectrograms for the electrode recording site on the precentral gyrus and visually inspected the signal for NBG at one-half stimulation frequency across stimulation amplitudes **(Figure 2A)**. Next, we correlated fluctuations in NBG power at one-half stimulation frequency (1:2 entrainment) to trends in wearable dyskinesia scores with Pearson's correlations.

Results: We found that entrained gamma does not depend on the presence or absence of levodopa-induced oscillations **(Figure 1B)**. We also found that smaller differences in levodopa-induced peak gamma frequency and one-half stimulation frequency may result in entrainment at a lower stimulation amplitude **(Figure 2B)**. Lastly, we found that entrained gamma was not correlated to dyskinesia scores in our subject with a clinical history of dyskinesia as assessed by the Unified Parkinson's Disease Rating Scale (r=0.001, P-value=0.992, **Figure 3**).

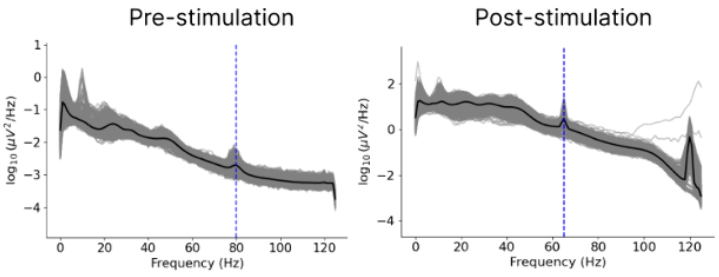
Discussion: The distinct occurrence of levodopa and stimulation-induced narrowband gamma hint that the underlying mechanisms and functional relevance may differ across these oscillations. The relationship between levodopa-induced NBG frequency and stimulation amplitude is largely in line with the neural circuit model used by Sermon et al. to predict entrainment[4].

Conclusions: Entrained gamma is distinct from levodopa-induced gamma and may be a clinically therapeutic electrophysiological marker.

Supplemental Data:

Figure 1. Gamma entrainment occurs regardless of levodopa-induced narrowband gamma oscillations

A. Example subject with levodopa-induced NBG entrains



B. Relationship of levodopa-induced and entrained NBG

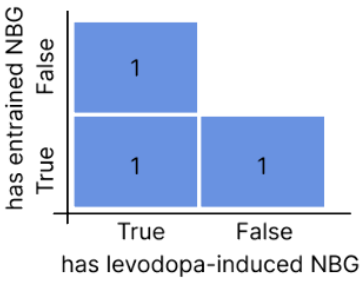
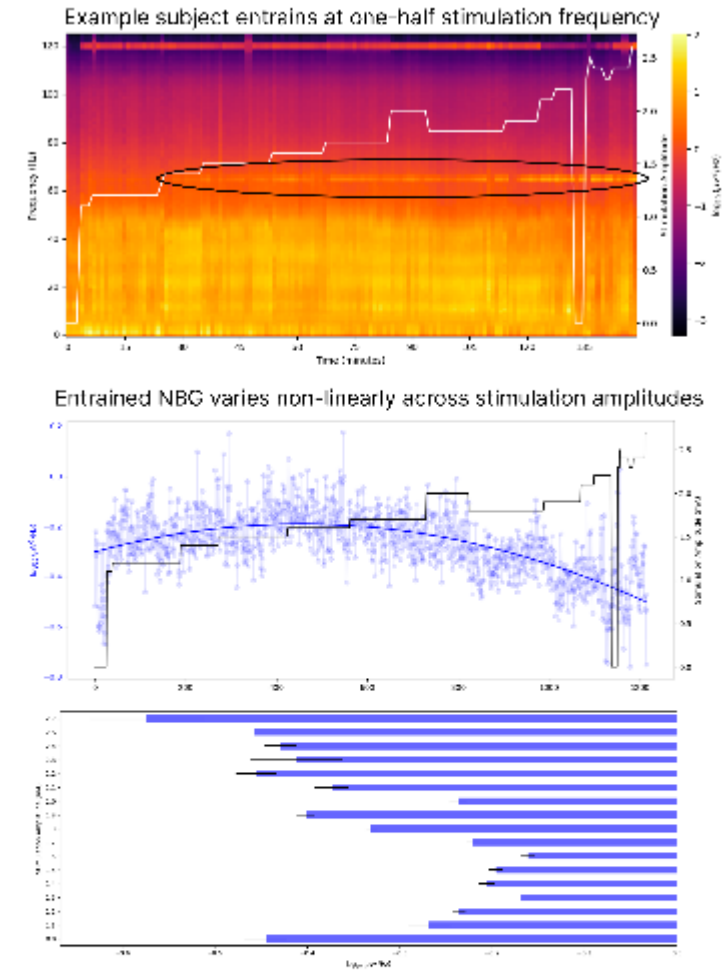


Figure 2. Relationship between levodopa-induced NBG peak frequency and onset of entrainment

A. Example subject during the NBG entrainment wash-in



B. Relationship of levodopa-induced NBG oscillations to entrainment onset

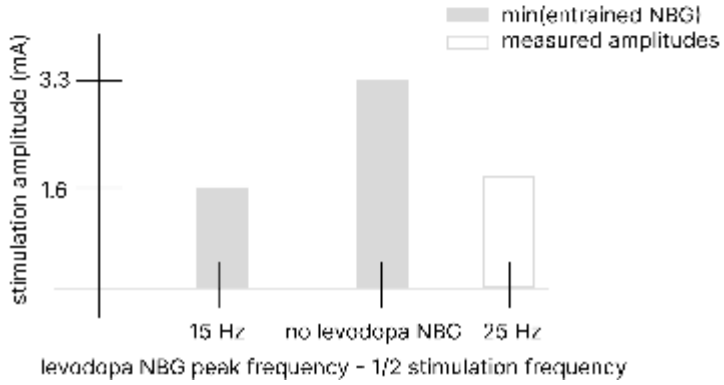
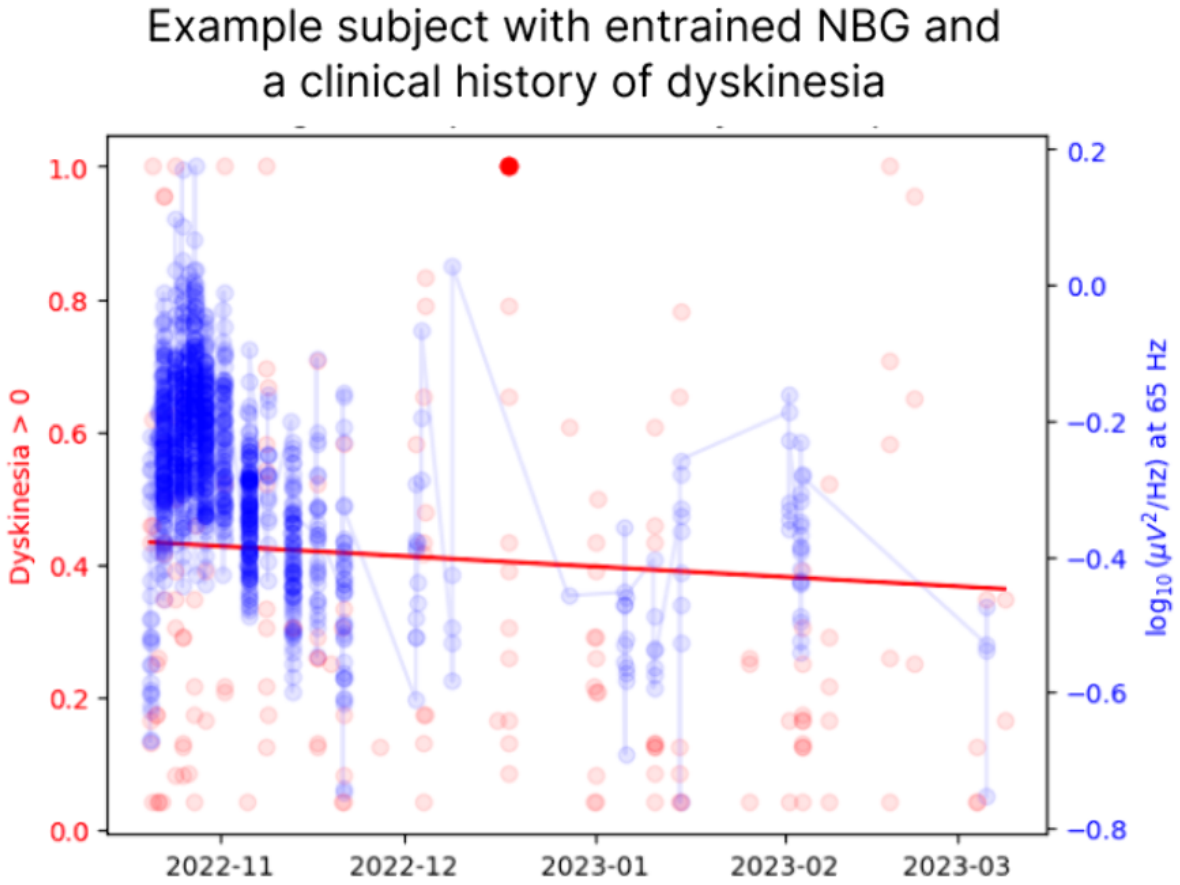


Figure 3. Entrained NBG is not a correlate of dyskinesia scores



References: 1. Swann, N. C. et al. Gamma Oscillations in the Hyperkinetic State Detected with Chronic Human Brain Recordings in Parkinson's Disease. J. Neurosci. 36, 6445–6458 (2016). 2. Gilron, R. et al. Long-term wireless streaming of neural recordings for circuit discovery and adaptive stimulation in individuals with Parkinson's disease. Nature Biotechnology vol. 39 1078–1085 Preprint at https://doi.org/10.1038/s41587-021-00897-5 (2021). 3. Swann, N. C. et al. Adaptive deep brain stimulation for Parkinson's disease using motor cortex sensing. J. Neural Eng. 15, 046006 (2018). 4. Sermon, J. J. et al. Sub-harmonic entrainment of cortical gamma oscillations to deep brain stimulation in Parkinson's disease: Model based predictions and validation in three human subjects. Brain Stimul. 16, 1412–1424 (2023).

Acknowledgements: None

Learning Objectives: (1) To differentiate levodopa-induced and deep brain stimulation entrained gamma oscillations in their occurrence (2) To understand the relationship between levodopa-induced narrowband gamma peak frequency and entrained gamma wash-in as a function of stimulation amplitude
(3) To understand whether narrowband gamma has the potential to serve as a clinically therapeutic electrophysiological signal

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O005

Oral Presentations
ORAL POSTER PRESENTATIONS FIVE BEST ABSTRACTS
13-05-2024 12:00 - 13:00

USING SOMATOSENSORY EVOKED POTENTIALS TO LOCALIZE SENSORIMOTOR FUNCTIONAL REGIONS IN THE CEREBELLAR DENTATE NUCLEUS IN CHRONIC POST-STROKE HEMIPARETIC PATIENTS

Prateek Dullur, BSc[1], Brett Campbell, PhD[2], Jakov Tiefenbach, MD[1], Carmen Toth, BSc[1], Andre Machado, MD[1,2], Kenneth Baker, PhD[1,2]
[1]Cleveland Clinic Lerner Research Institute, Department Of Neurosciences, Cleveland, United States of America, [2]Cleveland Clinic Neurological Institute, Center For Neurological Restoration, Cleveland, United States of America

Introduction: Stroke is a severely debilitating condition that can lead to long-term impairment to quality of life. Our group is investigating whether electrical stimulation of the cerebellar dentate nucleus (DN) can modulate excitability of sensorimotor cortical regions to promote functional reorganization and motor recovery for patients with chronic, post-stroke motor deficits [1]. Here, we investigated whether somatosensory evoked potentials (SSEPs) elicited by median nerve stimulation were reflected in local field potential (LFP) recordings from the DN. Our translational goal was to evaluate whether SSEPs may help to delineate the sensorimotor sub-region of the DN and help identify therapeutic stimulation targets.

Materials / Methods: We analyzed 10 patients who underwent unilateral DBS lead implantation in the DN contralateral to the stroke-affected cerebral hemisphere as part of a Phase I clinical trial. Median nerve SSEPs were recorded intraoperatively from the DBS lead (Boston Scientific Vercise™ standard) and from electroencephalography (EEG). EEG was re-referenced to Afz while LFPs were created through adjacent-bipolar re-referencing. SSEPs were filtered, split into time-locked segments, and artifact and baseline corrected. SSEP components were quantified via latency, amplitude z-scoring, and normalization across each lead. Observed activity was mapped to anatomical locations in the DN via MRI segmentation and lead reconstruction.

Results: Cortical SSEPs were identified in all patients, however their morphology was variable across patients (possibly due to stroke heterogeneity). Short-latency (<45 ms) and long-latency (45 ms – 100 ms) SSEP components were identified in the DN of 8 of 10 patients. SSEP activity was localized to specific contacts based on amplitude of response and phase reversals, which indicate possible somatosensory generator sites within the DN.

Discussion: To the best of our knowledge, this is the first study to examine properties of SSEPs from electrophysiological recordings of the DN in humans. Our findings support a localized effect and point to patient-specific DN somatotopy. Given the varied pathways for sensory transduction (i.e., dorsal column ascending volley and spinocerebellar pathway), and the complexity of subsequent cortical interactions, identifying characteristics of the DN SSEP may offer insight into the cerebellar role in this sensory pathway, especially in stroke.

Conclusions: These findings provide further support for the functional somatotopy of the DN [2, 3, 4] in humans. Moreover, the results support the potential use of SSEPs as a tool to localize sensorimotor regions within the DN. Incorporating these findings into existing DBS paradigms may have the potential to improve therapeutic benefits of DBS for treating stroke and restoring neurological function.

Supplemental Data:

References: 1. Baker, Kenneth B., Ela B. Plow, Sean Nagel, Anson B. Rosenfeldt, Raghavan Gopalakrishnan, Cynthia Clark, Alexandria Wyant, et al. “Cerebellar Deep Brain Stimulation for Chronic Post-Stroke Motor Rehabilitation: A Phase I Trial.” *Nature Medicine* 29, no. 9 (September

2023): 2366–74. https://doi.org/10.1038/s41591-023-02507-0. 2. Dum, Richard P., and Peter L. Strick. “An Unfolded Map of the Cerebellar Dentate Nucleus and Its Projections to the Cerebral Cortex.” *Journal of Neurophysiology* 89, no. 1 (January 1, 2003): 634–39. https://doi.org/10.1152/jn.00626.2002. 3. Strick, Peter L., Richard P. Dum, and Julie A. Fiez. “Cerebellum and Nonmotor Function.” *Annual Review of Neuroscience* 32, no. 1 (June 1, 2009): 413–34. https://doi.org/10.1146/annurev.neuro.31.060407.125606. 4. Voogd, Jan. “What We Do Not Know about Cerebellar Systems Neuroscience.” *Frontiers in Systems Neuroscience* 8 (December 18, 2014). https://doi.org/10.3389/fnsys.2014.00227. 5. Nowacki, Andreas, David Zhang, Jonathan Wermelinger, Pablo Abel Alvarez Abut, Jan Rosner, Claudio Pollo, and Kathleen Seidel. “Directional Recordings of Somatosensory Evoked Potentials from the Sensory Thalamus in Chronic Poststroke Pain Patients.” *Clinical Neurophysiology* 151 (July 2023): 50–58. https://doi.org/10.1016/j.clinph.2023.03.359. 6. Trenado, Carlos, Saskia Elben, Lena Friggemann, Sonja Gruhn, Stefan Jun Groiss, Jan Vesper, Alfons Schnitzler, and Lars Wojtecki. “Long-Latency Somatosensory Evoked Potentials of the Subthalamic Nucleus in Patients with Parkinson’s Disease.” Edited by Robert Chen. *PLOS ONE* 12, no. 1 (January 12, 2017): e0168151. https://doi.org/10.1371/journal.pone.0168151. 7. Trenado, Carlos, Saskia Elben, Lena Friggemann, Stefan Jun Groiss, Jan Vesper, Alfons Schnitzler, and Lars Wojtecki. “Intraoperative Localization of the Subthalamic Nucleus Using Long-Latency Somatosensory Evoked Potentials.” *Neuromodulation: Technology at the Neural Interface* 21, no. 6 (August 2018): 582–87. https://doi.org/10.1111/ner.12727.

Acknowledgements: We thank all study participants who devoted time to our research and trusted us with their health in a clinical trial that involved an experimental neurological intervention. We thank all research personnel who dedicated time and effort to the success of the clinical trial including physical and occupational therapists, nurses in the neurological units of Cleveland Clinic, colleagues and caregivers in the Anesthesiology Institute of Cleveland Clinic, all nurses and caregivers in the operating rooms as well as colleagues in the Cerebrovascular Center and Department of Physical Medicine and Rehabilitation at Cleveland Clinic, Department of Neurology at University Hospitals of Cleveland and Department of Physical Medicine and Rehabilitation at MetroHealth who helped us identify potential candidates for the study. We thank M. Pierre (at Enspire DBS) for support regarding the investigational device exemption and regulatory compliance throughout the study. This study was supported by the National Institutes of Health Brain Research Through Advancing Innovative Neurotechnologies Initiative under grant number UH3NS100543 (to Dr. Andre Machado and Dr. Kenneth Baker) as well as by Enspire DBS, a spin-off company of Cleveland Clinic.

Learning Objectives: 1. To better understand the role of the dentate nucleus in sensory processing in humans. 2. To understand the somatotopic organization of sensory processing in the dentate nucleus and its relationship to scalp-EEG-derived cerebral cortical evoked activation. 3. To explore the feasibility of using somatosensory evoked potentials as a way to identify therapeutic stimulation locations within the dentate nucleus in promoting functional recovery from stroke.

Financial Disclosures: Dr. Andre Machado serves as Chief Medical Officer and Chair of the Scientific Advisory Board for Enspire DBS Therapy and is paid with stock options. As the inventor, Dr. Machado will receive portions of commercialization and/or Cleveland Clinic Foundation stock revenue and payments through Cleveland Clinic Foundation with fees deducted. Dr. Kenneth Baker serves on the Scientific Advisory Board and is paid with stock options. Enspire DBS Therapy partially sponsored the study and had access to the safety, feasibility and secondary outcome measures. The company had no role in the drafting or editing of this abstract.

Disclosure: No significant relationships.

O006

Oral Presentations
NEUROMODULATION – MECHANISM(S) OF ACTION
13-05-2024 16:30 - 18:20

NEUROMODULATION USING ULTRA LOW FREQUENCY CURRENT WAVEFORMS ATTENUATES ACTIVITY OF THALAMIC NEURONES IN A RODENT NEUROPATHIC PAIN MODEL

Martyn Jones, PhD[1,2], Liam Matthews, BSc (Hons)[3,4], Scott Lempka, Associate Professor[3,4,5], Nishant Verma, PhD[6], James Harris, PhD[7]
[1]King's College London, Wolfson Sensory, Pain, And Regeneration Centre, London, United Kingdom, [2]King's College London, Zenith Neurotech Ltd., London, United Kingdom, [3]University of Michigan, Department Of Biomedical Engineering, Ann Arbor, United States of America, [4]University of Michigan, Biointerfaces Institute, Ann Arbor, United States of America, [5]University of Michigan, Department Of Anesthesiology, Ann Arbor, United States of America, [6]Presidio Medical, Science & Technology, South San Francisco, United States of America, [7]Presidio Medical, South San Francisco, United States of America

Introduction: Chronic intractable pain is a major cause of disability with an enduring clinical reliance on opioid analgesics, despite the negative side effects associated with their use. Electrical neuromodulation is an alternative approach for treating chronic pain. It has been long established that conduction of action potentials in nerves can be blocked by direct current (DC). Largely, this technique has not been used clinically as sustained application of DC delivered via traditional materials can cause tissue damage. We have developed an ultra-low frequency (ULF™) biphasic current waveform that consists of long duration pulses to safely emulate the effects of DC on neural tissue. Here, we studied the supraspinal effects of ULF™ therapy in the ventral thalamus, a region important for relaying pain-related signals in the brain.

Materials / Methods: We studied the impact of ULF™ (Presidio Medical Inc., South San Francisco, California, USA) current on signal conduction from sensory afferents by recording spontaneous activity of cells in the ventromedial posterolateral nucleus (VPL) in the thalamus while applying ULF™ current at the T9/T10 vertebral level, epidurally in rodents. We used a semi-chronic spinal nerve ligation model of neuropathic pain, in which the injury was induced and allowed to develop for several days before thalamic neural recordings were made and ULF™ current was applied.

Results: Spinal epidurally-applied ULF™ current reduced the activity of VPL neurones in a dose-dependent manner. At 200, 400 and 600 µA, ULF™ current significantly reduced firing in 4/14 (29%), 10/19 (53%) and 9/17 (53%) cells, respectively. During application of ULF™ therapy, the mean firing rate of cells tested at 200, 400 and 600 µA ULF™ was reduced by 16±7%, 25±12% and 35±10% of the baseline pathological activity, respectively.

Discussion: In this model, many neurones in the VPL develop sustained activity driven by afferent input from damaged sensory fibres. Here, we demonstrated a progressive effect of ULF™: increases in ULF™ current amplitude resulted in further decreases in ectopic activity. These results are mirrored by our previous work where we showed that ULF™ current can inhibit conduction of action potentials in dorsal root filaments of normal and neuropathic models in a tuneable and reversible manner[1].

Conclusions: Our interpretation of these findings is that ULF™ current can reduce activity of cells in the thalamus by modulating conduction of sensory afferent signals via ascending spinal pathways. These findings indicate the potential for spinal epidural ULF™ current as a novel analgesic strategy.

Supplemental Data:

References: [1]Jones, Martyn G., Evan R. Rogers, James P. Harris, Andrew Sullivan, D. Michael Ackermann, Marc Russo, Scott F. Lempka, and Stephen B. McMahon. “Neuromodulation Using Ultra Low Frequency Current Waveform Reversibly Blocks Axonal Conduction and Chronic Pain.” Science

Translational Medicine 13, no. 608 (August 25, 2021): eabg9890.
https://doi.org/10.1126/scitranslmed.abg9890.

Acknowledgements: The support of Presidio Medical for this project is gratefully acknowledged.

Learning Objectives: 1 – Provide basic scientific principles regarding ULF^{TM} therapy for inhibition 2 – Describe the rodent pain model and importance of thalamus in pain processing 3 – Educate audience regarding the inhibition of pain via ULF^{TM} therapy

Financial Disclosures: Martyn G. Jones - Sponsored Research > 100k USD Liam A. Matthews - Sponsored Research > 100k USD Scott Lempka - Role: Stock Options, Consultant/ Advisory Board, and Sponsored Research > 100k USD Nishant Verma - Role: Company Employee James P. Harris - Role: Company Employee

Disclosure: No significant relationships.

O007

Oral Presentations
NEUROMODULATION – MECHANISM(S) OF ACTION
13-05-2024 16:30 - 18:20

10 KHZ SPINAL CORD STIMULATION IMPROVES METRICS OF SPINAL SENSORY PROCESSING IN A RODENT MODEL OF DIABETES

Kwan Yeop Lee, PhD, Dong Wang, PhD, Dongchul Lee, PhD, Zack Kagan, PhD, Kerry Bradley, MSc
Nevro Corp, Redwood City, United States of America

Introduction: To explore why clinical 10 kHz spinal cord stimulation (10 kHz SCS) might improve neurological function in patients with painful diabetic neuropathy (PDN), we studied the electrophysiological and histological effects of 10kHz SCS using short-term streptozotocin (STZ)-induced diabetic rats.

Materials / Methods: We established four testing groups: Naïve controls, STZ controls, STZ+Sham SCS, and STZ+10kHz SCS. After intraperitoneal injection (60 mg/kg) of STZ caused the rats to become hyperglycemic, SCS electrodes were implanted in the dorsal epidural space over the L5-L6 spinal segments in the STZ+Sham SCS and STZ+10kHz SCS groups and were stimulated for 14 days. At termination, animals were anesthetized and the electrophysiologic response of dorsal horn neurons (receptive field size, vibration, radiant warmth) of the ipsilateral hindpaw was measured. Tissue from the plantar paw surface was obtained post-euthanization for intraepidermal nerve fiber density measurements.

Results: For the following groups [Naïve (N_{rats}=3, $n_{neurons}$=16), STZ Control (N_{rats}=3, $n_{neurons}$=17), STZ+ShamSCS (N_{rats}=3, $n_{neurons}$=15), STZ+10kHzSCS (N_{rats}=3, $n_{neurons}$=18)], the Naïve and STZ+10kHzSCS groups had significantly smaller RFs than the STZ Control and STZ+ShamSCS groups ($p < 0.01$ and $p < 0.05$ respectively), while the Naïve and STZ+10kHzSCS groups were not significantly different. In response to a 1 Hz vibration frequency, Naïve and STZ+10kHzSCS groups had higher peak power spectral density (PSD) of DH firing than STZ+ShamSCS ($p < 0.01$), and PSD for the STZ+10kHzSCS group was statistically higher than for the STZ Control group ($p < 0.05$); Naïve and STZ+10kHzSCS groups were not statistically different. Response of DH neurons showed no significant differences between groups during the thermal stimulation, but the post-stimulus firing rates for the STZ+10kHzSCS group were significantly higher compared to STZ Control and STZ+ShamSCS ($p < 0.01$). Single-factor ANOVA indicated significant differences in IENFD between groups ($F(3, 31) = 5.23$, $p<0.01$) , and post hoc Tukey tests revealed that the Naïve group had significantly higher cutaneous nerve fiber density than the STZ+ShamSCS and STZ+10kHzSCS groups ($p < 0.05$). No other groups were observed to show significant differences.

Discussion: These data suggest that 10 kHz SCS amplified the DH response to large fiber (vibration) and small fiber (warm) signals and normalized the receptive field of the paw (acuity) in PDN rats, but did not demonstrate increased relative cutaneous nerve fiber density.

Conclusions: We hypothesize that 10 kHz SCS in the central nervous system may compensate for the reduced functionality seen in the peripheral sensory systems, thus restoring sensation, and possibly modifying the prognosis of the disease.

Supplemental Data:

References: None

Acknowledgements: This study was supported by Nevro Corp.

Learning Objectives: 1. 10kHz SCS may improve somato sensation in PDN patients. 2. 10kHz SCS may improve thermal sensation in PDN patients.

Financial Disclosures: All of the authors are employees of Nevro Corp.

Disclosure: No significant relationships.

O008

Oral Presentations
NEUROMODULATION – MECHANISM(S) OF ACTION
13-05-2024 16:30 - 18:20

10KHZ SPINAL CORD STIMULATION ALLEVIATES MECHANICAL HYPERSENSITIVITY IN A RAT MODEL OF TYPE 2 DIABETES

Dong Wang, PhD, Kwan Yeop Lee, PhD, Zachary Kagan, PhD, Dongchul Lee, PhD, Kerry Bradley, MSc
Nevro Corp, Redwood City, United States of America

Introduction: Painful diabetic neuropathy (PDN) is a serious complication of diabetes and occurs in approximately 20% of patients with diabetes mellitus. In the largest randomized controlled clinical trial of spinal cord stimulation (SCS) for PDN, 10kHz SCS was shown to significantly reduce pain, weight, and HbA1c, and restore neurological status, including foot protective sensation (Petersen et al 2023). In this study, we aimed to observe the behavioral and neural effects of 10kHz SCS on PDN using type 2 diabetes animal model - the Zucker diabetic fatty (ZDF) rat, heretofore an unstudied model in SCS.

Materials / Methods: Male ZDF rats were fed with a high-energy diet to induce programmed and consistent development of type 2 diabetes. We established four testing groups: Lean controls, ZDF controls, ZDF+Sham SCS (ZDF rats with implanted-but-unstimulated epidural spinal electrode), and ZDF+10kHz SCS (ZDF rats with implanted-and-stimulated epidural spinal electrode).

Results: ZDF rats became hyperglycemic (>270 mg/dl) after 8-9 weeks of high-energy diet feeding and this symptom lasted throughout the 63 days experiment. The ZDF rats also showed a significantly reduced body weight in compared to Lean control rats. In behavioral assessments, we observed that, compared to own-baseline values, ZDF controls, and ZDF+ShamSCS, 14 days of continuous (24h/day) low intensity (30% of motor threshold) 10kHz SCS significantly increased von Frey paw withdrawal thresholds, and these results were durable through 42 days of 10kHz SCS.

Discussion: Previous preclinical investigations used the streptozotocin (STZ)-injection model, which creates neuropathic conditions in the short-term that have been shown to be improved with SCS. The STZ model is generally believed to mostly mimic a type 1 diabetic condition. Here we demonstrate for the first time that 10 kHz SCS reduces mechanical hypersensitivity in a type 2 diabetes rodent model, which may provide better translational confirmation of clinical outcomes of 10kHz SCS in PDN.

Conclusions: Our results suggest that 10kHz SCS resulted in behavioral outcomes reflective of pain reduction in the type 2 diabetes animal model. These findings provide supporting evidence for large-scale randomized clinical trial data of 10kHz SCS and underscore the conclusion that 10kHz SCS can effectively treat patients with refractory PDN.

Supplemental Data:

References: Peterson et al. Long-term efficacy of high-frequency (10 kHz) spinal cord stimulation for the treatment of painful diabetic neuropathy: 24-Month results of a randomized controlled trial. Diabetes Res Clin Pract. 2023 Sep:203:110865.

Acknowledgements: The support of Nevro Corp for this project is gratefully acknowledged.

Learning Objectives: 1. Establish and validate the PDN in the rat model of type 2 diabetes. 2. Evaluate the effect of 10kHz spinal cord stimulation (10kHz SCS) on mechanical hypersensitivity in type 2 diabetic animals. 3. Explore the neural mechanism of 10kHz SCS-mediated pain relief in PDN animals.

Financial Disclosures: D.W, K.Y.L, Z.K, D.C.L, and K.B are full-time employees at Nevro Corporation.

Disclosure: Full-time employee at Nevro Corporation.

O009

Oral Presentations
NEUROMODULATION – MECHANISM(S) OF ACTION
13-05-2024 16:30 - 18:20

TRANSCRIPTOMICS OF THE L5-DRG IN EARLY AND LATE STAGES OF A SPARED NERVE INJURY MODEL AFTER A DIFFERENTIAL TARGETED MULTIPLEXED SCS PROGRAM

David Cedeño, PhD[1], Sandra Rodriguez-Zas, PhD[2], David Platt, MSc[3], Joseph Williams, PhD[3], Bruce Southey, PhD[2], Elena Romanova, PhD[2], Jonatahn Sweedler, PhD[2], Ricardo Vallejo, MD, PhD[1]
[1]SGX Medical LLC, Bloomington, United States of America, [2]University of Illinois at Urbana Champaign, Champaign, United States of America, [3]Illinois Wesleyan University, Blooomington, United States of America

Introduction: The effect of spinal cord stimulation (SCS) on the transcriptomics of neural tissues in animal models of neuropathic pain have been studied.[1] Despite differences in models and experimental designs, studies agreed that SCS regulates biological processes (BPs) related to neuroinflammation and synaptic transmission. Previous work has used the spared nerve injury (SNI) model in which SCS was applied early after SNI.[2] This current study evaluated the effect of SCS using a differential target multiplexed program (DTMP) on the transcriptomics of the L5-dorsal root ganglion (DRG) ipsilateral to injury when applied at different timepoints in the evolution of the SNI pain model.

Materials / Methods: Adult male rats were randomized to 12 experimental groups (Table 1). The SNI model was implemented at the beginning of the study in the SNI and SCS groups according to the literature[3]. Animals in the SCS group were implanted with a quadrupolar lead 7 days before the start of continuous DTMP (2-day, 50 Hz base, 3x300 Hz prime, 40% motor threshold). Mechanical sensitivity using a von Frey anesthesiometer was assessed before SNI, and then once a week (except during post-surgical recovery) until the study endpoint (9d, 30d, 44d, or 65d). Animals in corresponding groups were assessed in parallel. At the end of each endpoint, tissues were dissected and stored frozen. RNA from the L5-DRG ipsilateral to injury was sequenced.[4] RNA counts used to compare expression levels as SCS/SNI and SNI/Naïve. Significant (FDR-P < 0.05) differentially expressed genes (DEGs) in both comparisons were selected. Enrichment analyses of Gene Ontology (GO) BPs (FDR-P < 0.05)[5] among significant DEGs were run for each study endpoint.

Table 1. Experimental groups separated into 4 study endpoints. DTMP refers to SCS treatment initiated 2-day before the end of each study endpoint (9-day, 30-day, 44-day, and 65-day).

9d			30d			44d			65d		
Naïve	SNI	DTMP	Naïve	SNI	DTMP	Naïve	SNI	DTMP	Naïve	SNI	DTMP

Results: Continuous DTMP significantly relieved mechanical hypersensitivity at all timepoints (Figure 1). 579 significant DEGs were identified in SNI/Naïve and SCS/Naïve comparisons. BPs that are significantly enriched in these DEGs and common among timepoints include inflammatory response, immune response, regulation of cell activation and signaling. Figure 2 shows fold changes of those DEGs at each timepoint. A back-regulating effect of SCS is more pronounced at the earliest timepoint, which contrasts with the effects of SCS when the model becomes more chronic.

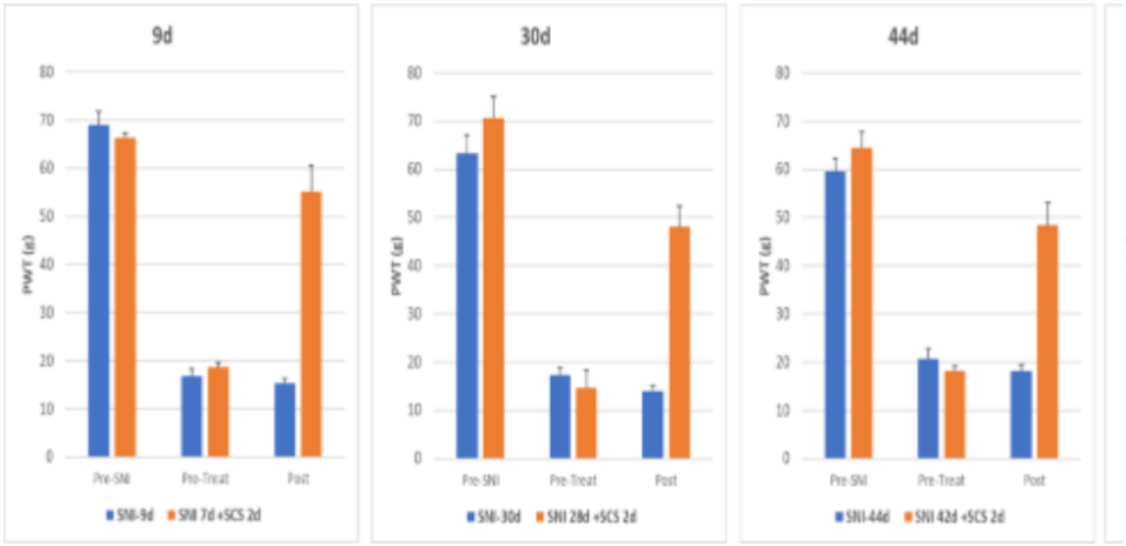


Figure 1. Mean paw withdrawal thresholds (PWT) for SNI and SCS (SNI + SCS) groups at every endpoint. Pre-SNI: before SNI surgery, pre-Treat: before SCS, Post: after 2-day SCS. Error bars are SEM for N = 4-7. All SNI vs SCS are significantly different after treatment at all endpoints ($P < 0.001$). Significance evaluated using two-way ANOVA followed by Holm-Sidak corrections for mutiple comparisons.

Figure 2. Heat maps of significant DEGs (N = 579) arranged in 4 sets after sorting them in terms of FC = SNI/Naïve at every endpoint. Both SNI/Naïve and SCS/SNI comparisons (FCs) are shown for each timepoint in each heat map set. Top row set: sorted by SNI/Naïve at 65d (N = 205); Second row set: sorted by SNI/Naïve at 44d (N = 268); Third row set: sorted by SNI/Naïve at 30d (N = 189); Botton row set: sorted by SNI/Naïve at 9d (N = 195).

Discussion: This is the first study of the effect of SCS in the L5-DRG transcriptome at different timepoints in the evolution of the SNI model of neuropathic pain, showing a robust effect SCS on a pain model.

Conclusions: These preliminary results suggest that the effect of SCS may be different at early stages of the development of chronic pain.

Supplemental Data:

References: 1. Cedeño DL, Kelley CA, Chakravarthy K, Vallejo R. Modulation of Glia-Mediated Processes by Spinal Cord Stimulation in Animal Models of Neuropathic Pain. Front Pain Res (Lausanne). 2021 Jul 14;2:702906. 2. Vallejo R, Tilley DM, Cedeño DL, Kelley CA, DeMaegd M, Benyamin R. Genomics of the effect of spinal cord stimulation on an animal model of neuropathic pain. Neuromodulation. 2016 Aug;19(6):576-86. 3. Decosterd I, Woolf CJ. Spared nerve injury: an animal model of persistent peripheral neuropathic pain. Pain. 2000 Aug;87(2):149-158. 4. Rymut HE, Rund LA, Southey BR, Johnson RW, Sweedler JV, Rodriguez-Zas SL. Prefrontal cortex response to prenatal insult and postnatal opioid exposure. Genes (Basel). 2022 Jul 30;13(8):1371 5. Liao Y, Wang J, Jaehnig EJ, Shi Z, Zhang B. WebGestalt 2019: gene set analysis toolkit with revamped UIs and APIs. Nucleic Acids Res. 2019 Jul 2;47(W1):W199-W205.

Acknowledgements: The support of SGX Medical, Illinois Wesleyan University and a US NIH/NIDA award P30 DA018310 (to Jonathan V. Sweedler) is gratefully acknowledged.

Learning Objectives: 1. Understand the evolution of the transcriptomics of the L5-DRG in the SNI model of neuropathic as the model becomes chronic. 2. Interpret the effect of SCS on the transcriptomics of the L5-DRG at various stages of the SNI model. 3. Learn methodological aspects of the study of a mechanism of action using molecular biology tools.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O010

Oral Presentations
NEUROMODULATION – MECHANISM(S) OF ACTION
13-05-2024 16:30 - 18:20

EVOKED COMPOUND ACTION POTENTIAL-CONTROLLED CLOSED-LOOP SPINAL CORD STIMULATION REDUCES NEUROPATHIC PAIN IN RATS

Eline Versantvoort, MSc[1], Birte Dietz, PhD[2], Dave Mugan, BSc (Hons)[2], Quoc Vuong, PhD[3], Ilona Obara, PhD MSc[1]
[1]Newcastle University, School Of Pharmacy And Translational And Clinical Research Institute, Newcastle upon Tyne, United Kingdom, [2]Saluda Medical, Harrogate, United Kingdom, [3]Newcastle University, Biosciences Institute And School Of Psychology, Newcastle upon Tyne, United Kingdom

Introduction: The evoked compound action potential (ECAP) represents a measure of dorsal column fiber activation that approximates the onset of SCS-induced sensations[1]. In humans, ECAP-controlled closed-loop (CL)-SCS provides effective analgesia[2]. Therefore, ECAPs may provide an objective surrogate to identify sensation threshold and optimize SCS dose for CL-SCS in preclinical models. This study extends our previous work[3] by assessing, for the first time, the efficacy of ECAP-controlled CL-SCS in reducing mechanical and cold hypersensitivity in freely behaving rats subjected to an experimental model of neuropathic pain.

Materials / Methods: Neuropathic pain was induced in Sprague-Dawley rats (200-300 g; n = 6-7) using the spared nerve injury (SNI) model. A custom-made six-contact lead was implanted epidurally covering T11-L3, as confirmed by computed tomography (**Fig. 1A**). A specially designed multi-channel system was used to record ECAPs and to apply ECAP-controlled CL-SCS for 30 min at 50 Hz 200 µs. Stimulation and recording were performed in freely behaving animals. Sensitivity to mechanical and cold stimuli were assessed to determine analgesic effects from ECAP-controlled CL-SCS. All protocols were approved by the UK Home Office.

Results: Through constant and controlled activation of dorsal column fibers (**Fig. 1B,C**), ECAP-controlled CL-SCS provided a significant reduction of mechanical hypersensitivity after 15 and 30 min of stimulation in SNI, SCS-ON animals when compared to SNI animals that did not receive lead implantation (SNI; *p*s < 0.001) and to SNI animals receiving no stimulation (SNI, SCS-OFF; *p*s < 0.001; **Fig. 2A**). In addition, cold hypersensitivity was significantly reduced in SNI, SCS-ON animals compared to SNI, SCS-OFF animals during stimulation (15 min: $p = 0.004$; 30 min: $p = 0.007$; **Fig.**

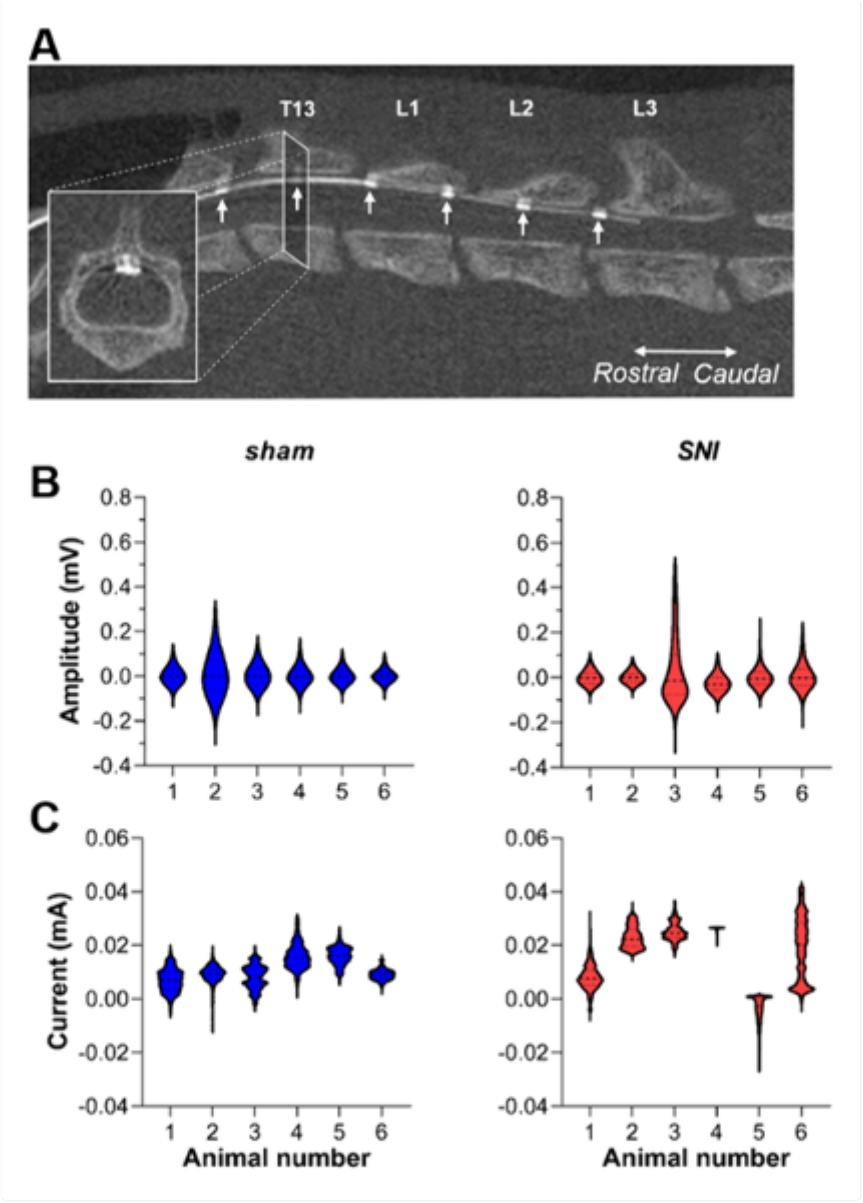


Figure 1. (A) CT image confirming epidural implantation of the lead and position of the channels. Arrows indicate the 6 channels. **(B, C)** ECAP-controlled CL-SCS allows for constant and controlled activation of dorsal column fibers by keeping the ECAP amplitude (mV) constant through real-time adjustments of stimulation current (mA). **(B)** Frequency distributions of the difference between measured and target ECAP amplitude for each animal. **(C)** Frequency distributions of the difference between measured current and ECAPT for each animal.

2B).

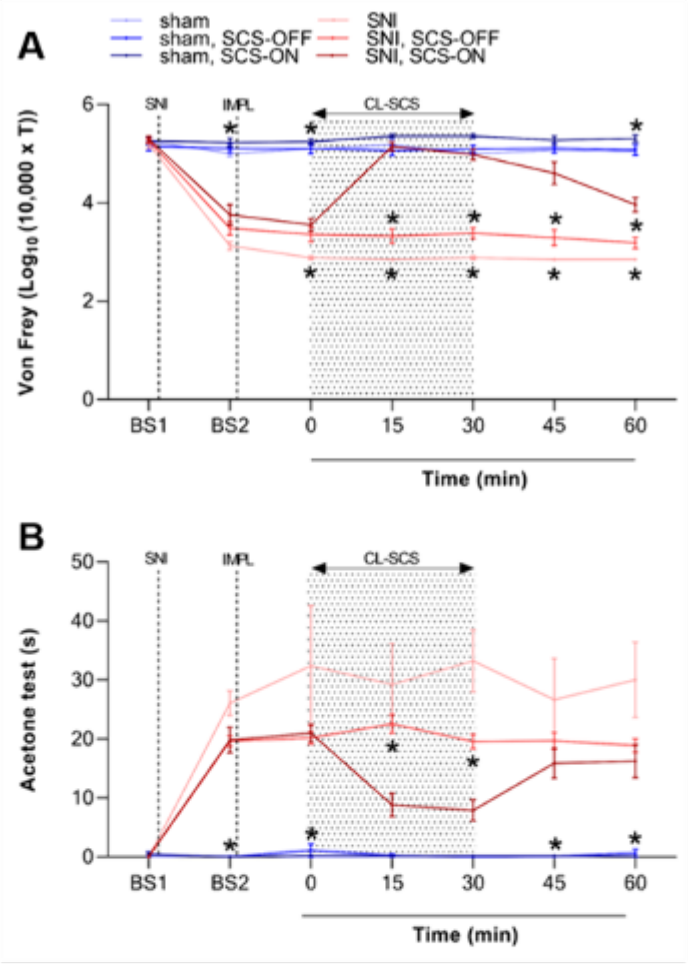


Figure 2. The effect of CL-SCS on mechanical **(A)** and cold **(B)** hypersensitivity was assessed using the von Frey and acetone tests in sham and SNI animals. **(A)** Mean log10 thresholds (T, in grams) and **(B)** paw withdrawal latencies before SNI surgery (BS1), before lead implantation (BS2), and at 0, 15, 30, 45 and 60 min after the onset of CL-SCS delivery. The dotted lines represent spared nerve injury (SNI) surgery and lead implantation (IMPL). The texture background represents the time that CL-SCS was delivered. Data are presented as mean ± SEM, n = 6-7. $p < 0.05$ (corrected for multiple comparisons) was used as the significance level (two-way ANOVA, t-test). * denotes significance compared to SNI, SCS-ON. Sham animals received no SNI surgery and no lead implantation (sham), or no stimulation (sham, SCS-OFF) or were subjected to CL-SCS (sham, SCS-ON). SNI animals received SNI surgery and no lead implantation (SNI), or no stimulation (SNI, SCS-OFF) or were subjected to CL-SCS (SNI, SCS-ON).

Discussion: This is the first study that successfully implemented ECAP-based SCS dose in ECAP-controlled CL-SCS in animals subjected to an experimental model of neuropathic pain. This approach resulted in significant reductions in mechanical and cold hypersensitivity induced by the nerve injury, which is comparable to the reduction in pain intensity reported in neuropathic pain patients[2].

Conclusions: The use of CL control combined with ECAP recordings can improve SCS models in rats. These models can further elucidate the mechanisms of SCS action, and allow for better translation of findings between animals and humans.

Supplemental Data:

References: 1. Gmel GE, Santos Escapa R, Parker JL, Mugan D, Al-Kaisy A, et al. The Effect of Spinal Cord Stimulation Frequency on the Neural Response and Perceived Sensation in Patients With Chronic Pain. *Front Neurosci* 15, 625835 (2021). 2. Mekhail N, Levy RM, Deer TR, Kapural L, Li S, Amirdelfan K, et al. Durability of Clinical and Quality-of-Life Outcomes of Closed-Loop Spinal Cord Stimulation for Chronic Back and Leg Pain: A Secondary Analysis of the Evoke Randomized Clinical Trial. *JAMA Neurol.* 79, 251–260 (2022). 3. Dietz BE, Mugan D, Vuong QC, Obara I. Electrically Evoked Compound Action Potentials in Spinal Cord Stimulation: Implications for Preclinical Research Models. *Neuromodulation* 25, 64–74 (2022).

Acknowledgements: Funding and equipment were provided by Saluda Medical.

Learning Objectives: 1. Be able to describe characteristics of ECAP-controlled CL-SCS approach in freely behaving SNI rats. 2. Be able to interpret experimental outcomes showing that ECAP-controlled CL-SCS produces analgesia in neuropathic rats. 3. Be able to identify the translational values of preclinical SCS models implementing CL-SCS.

Financial Disclosures: Birte Elisabeth Dietz ($20,001 - $100,000 USD; stock options) and Dave Mugan (> $100,000 USD; stock options) are employed by Saluda Medical. Ilona Obara has received travel and research grants from Saluda Medical (> $100,000 USD). None of the authors have a commercial interest in the material presented here. There are no other relationships that might lead to a conflict of interest in the current study.

Disclosure: No significant relationships.

O011

Oral Presentations
NEUROMODULATION – MECHANISM(S) OF ACTION
13-05-2024 16:30 - 18:20

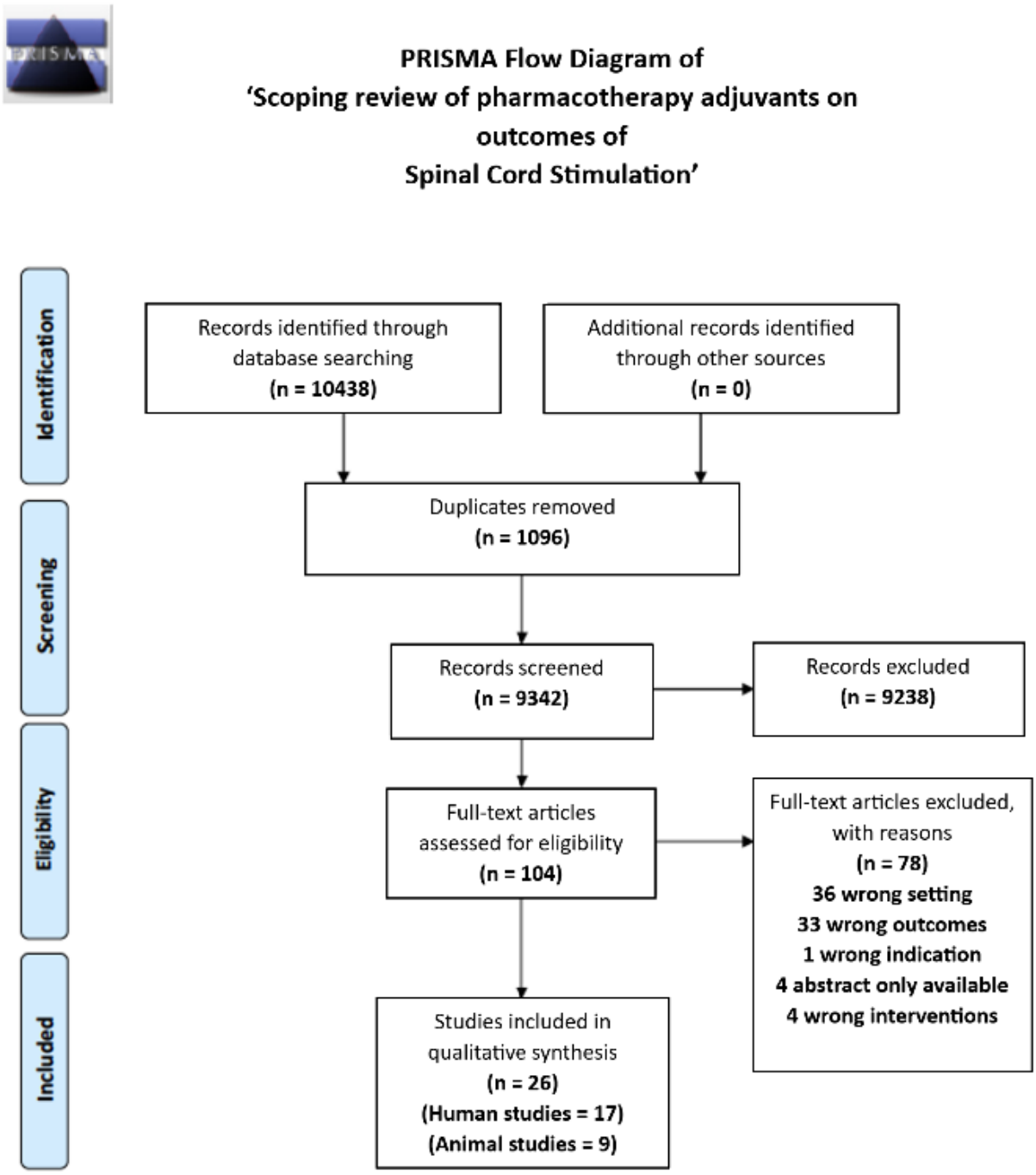
ADJUVANT PHARMACOTHERAPY WITH SPINAL CORD STIMULATION – A HELP OR A HINDRANCE?: A SCOPING REVIEW

Yilin Zhang, MDCM Candidate[1], Sachin Sahni, MD[2], Olivia Chung, Health Science Student[3], Pranab Kumar, MD[2], Bengt Linderoth, MD, PhD[4], Anuj Bhatia, MD[5]
[1]McGill University, Faculty Of Medicine, Montreal, Canada, [2]University of Toronto and Toronto Western Hospital, Department Of Anesthesia And Pain Medicine, Toronto, Canada, [3]McMaster University, Bachelor Of Health Sciences Honors, Hamilton, Canada, [4]Karolinska Institutet, Tomtebodavägen, Department Of Clinical Neuroscience, Stockholm, Sweden, [5]University Health Network, Department Of Anesthesia, Toronto Western Hospital, Toronto, Canada

Introduction: Spinal cord stimulation (SCS) can ameliorate neuropathic pain. The analgesic benefit from SCS may be altered by the use of adjuvant analgesic medications by patients who receive SCS implants. We undertook a scoping review to scan and summarize the evidence for modulation of SCS therapy by adjuvant pharmacotherapy.

Materials / Methods: A literature review of SCS studies on humans and animals was performed by using medical databases including MEDLINE, EMBASE, CINAHL, Cochrane CENTRAL and Google Scholar from inception until April 19, 2023. Data extraction and analysis was done on the effect of pharmacotherapy on SCS or DRGS outcome, measured through various methods such as pain questionnaires, opioid usage, and extraction

rates.

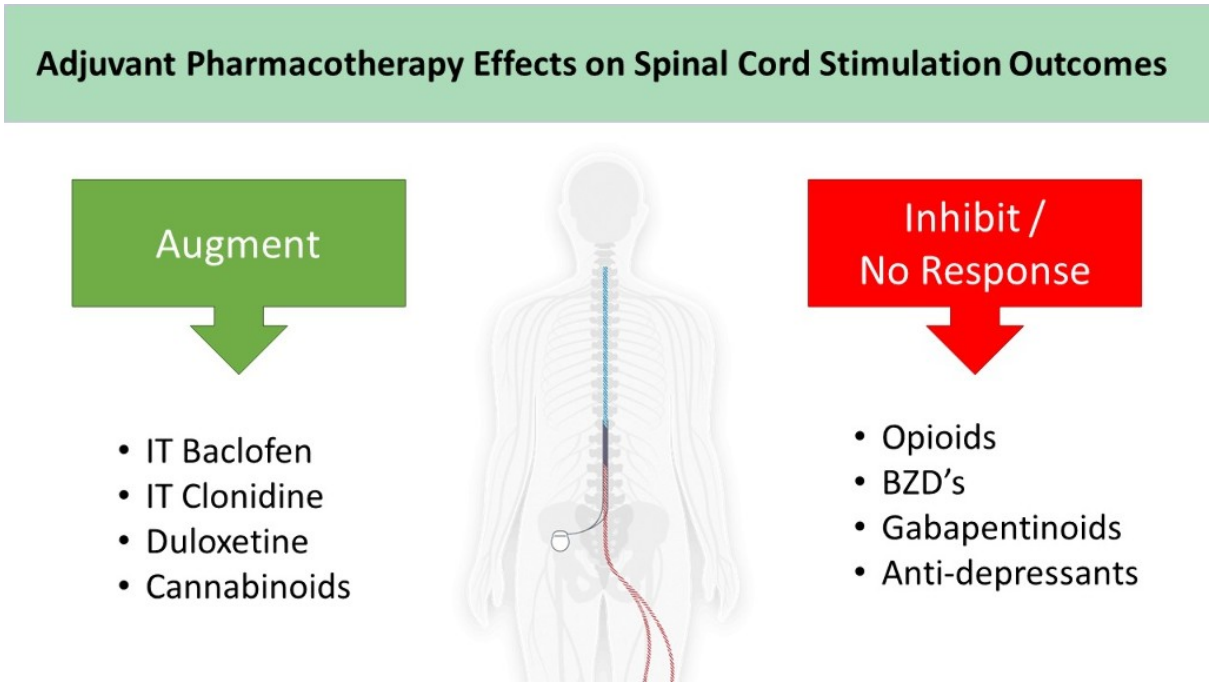


Results: 26 studies, 17 on humans and 9 on animals, were identified. In human studies, SCS non-responders with neuropathic pain reported substantial improvement with administration of intrathecal baclofen, clonidine and ketamine. The suppressive effect of SCS on mechanical hypersensitivity was enhanced with antidepressants, especially shown with sub-effective doses of intrathecal milnacipran. Gabapentinoids did not augment the analgesic benefit from SCS nor was there a reduction in opioid use. Patients who eliminated opioid use or who were opioid naïve had superior clinical outcomes with SCS compared to those who continued opioids or had high preoperative opioid usage. In animal studies, SCS augmentation was seen with intrathecal GABA, baclofen, and clonidine. In one study, intrathecal ketamine enhanced pain-relieving effect of SCS on tactile hypersensitivity and play a role in converting SCS non-responders to responders.

Discussion: This scoping review is the first of its kind to broadly examine the effects of adjuvant pharmacotherapy on the outcomes of SCS. Another recent systematic review with fewer studies included showed similar findings to our scoping review in which gabapentinoids and duloxetine were associated with improved quality of life but not in other pain measurement outcomes, and saw limited evidence in antidepressants enhancing SCS outcomes.

Conclusions: This review suggests adjunctive pharmacotherapy may have a role in enhancing analgesic benefits from SCS therapy. Further prospective comparative studies are required to establish the impact of adjuvant pharmacotherapy on SCS for pain.

Supplemental Data:



References: 1.Deer TR, Mekhail N, Provenzano D et al. Neuromodulation 2014;17:515–550. 2.Grider JS, Manchikanti L, et al. Pain Physician. 2016;19:E33–54. 3.Sawynok J, Reid A. Pain 2001;93:51–9. 4.Eisenach JC, Hood DD, Curry R. Anesth Analg. 1998;87:591–6. 5.Hassenbusch SJ, Gunes S, Wachsman S, Willis KD. Pain Med. 2002;3:85–91.

Acknowledgements: none

Learning Objectives: 1. I would like to acquire a deeper and more comprehensive understanding of various neuromodulation techniques, including spinal cord stimulation, peripheral nerve stimulation, and intrathecal drug delivery, to effectively evaluate their clinical applications, mechanisms, and patient suitability in chronic pain management. 2. I wish to stay updated on the latest advancements in neuromodulation through participation in scientific sessions, workshops, and presentations in order to learn more about emerging technologies that could enhance future patient outcomes in pain management. 3. I strive to establish connections and foster relationships with leading experts, practitioners, and like-minded medical students in the fields of anesthesiology and pain clinic. Especially as a current medical student, I hope to gain insights into career pathways, training opportunities, and potential mentorship within the realm of pain management and neuromodulation.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O012

Oral Presentations
NEUROMODULATION – MECHANISM(S) OF ACTION
13-05-2024 16:30 - 18:20

CORTICAL LOW-FREQUENCY NETWORK ACTIVITY DURING SPINAL CORD STIMULATION IN PATIENTS WITH NEUROPATHIC PAIN

Britta Kretzschmar, MD[1], Andre Rupp, PhD[2], Mohammad Mehdi Hajiabadi, MD[1], Sandro M. Krieg, MD[1], Rezvan Ahmadi, MD[1]
[1]Heidelberg University Hospital, Neurosurgery, Heidelberg, Germany, [2]Heidelberg University Hospital, Neurology, Heidelberg, Germany

Introduction: While spinal cord stimulation (SCS) is widely employed for managing refractory neuropathic pain, the underlying mechanisms remain incompletely understood. Specifically, it is not well known how SCS affects brain centers and influences pain processing. Objective markers to assess therapy efficacy are currently unavailable. Hence, this study focuses on investigating the cortical functional network activity of the nociceptive system in patients with refractory neuropathic pain undergoing SCS therapy.

Materials / Methods: We included four patients suffering from neuropathic pain after successful implantation of a closed-loop SCS system. We used a 64-channel electroencephalograph (EEG) to record brain activity. During the recording, we applied 40 noxious laser pulses to both the affected dermatome and its corresponding control site. We recorded laser-evoked potentials while low-frequency SCS was active and when it was turned off. To perform source-specific time-frequency analysis, we employed a Hilbert transform projected onto the cortical surface. Additionally, we conducted coherence analyses of the functional network system, which included the secondary somatosensory cortex, the anterior insula, and the anterior cingulate cortex (ACC).

Results: Preliminary temporal-spectral data revealed an increase in theta power in the somatosensory cortex, insula and prefrontal cortex when the stimulator was turned off. Interestingly, a notable suppression, especially in prefrontal regions, was observed during low-frequency SCS. Moreover, coherence analysis in the theta-frequency range demonstrated reduced interaction between the anterior insula and ACC during SCS in contrast to the condition when the neurostimulator was inactive.

Discussion: Our findings underscore the modulation of the cortical pain-associated network during SCS in the theta-frequency range and provide insights into the functional dynamics of brain regions. It seems to be that the anterior insula and ACC are crucial targets during neuromodulatory pain therapy.

Conclusions: These methods seem to have the potential to serve as objective markers assessing therapy outcomes in SCS and might play a significant role in advancing the development of innovative stimulation paradigms in SCS in the future.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1. Functional connectivity analyses reveal distinct cortical network activity during SCS and when the stimulator is turned off. 2. SCS affects supraspinal pain processing, especially interaction between the anterior insular and the anterior cingulate cortex, in patients with neuropathic pain. 3. Cortical aspects, such as plasticity in chronic pain states, must be considered in SCS therapy, particularly for nonresponders.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O013

Oral Presentations
NEUROMODULATION – MECHANISM(S) OF ACTION
13-05-2024 16:30 - 18:20

COMPUTATIONAL MODELING OF EVOKED COMPOUND ACTION POTENTIALS DURING EPIDURAL SPINAL CORD STIMULATION IN A SWINE MODEL

Meagan Brucker-Hahn, MSBmE[1], Megan Settell, PhD[2], Justin Chin, BSc[3], Daniel Lust, N/A[3], Aniruddha Upadhye, MS[3], Renil Contractor, MS[3], Andrew Crofton, PhD[4], Mingming Zhang, PhD[5], Igor Lavrov, MD, PhD[6], Andrew Shoffstall, PhD[3], Kip Ludwig, PhD[2], Scott Lempka, Associate Professor[1]
[1]University of Michigan, Biomedical Engineering, Ann Arbor, United States of America, [2]Wisconsin Institute for Translational Neuroengineering, Madison, United States of America, [3]Case Western Reserve University, Biomedical Engineering, Cleveland, United States of America, [4]Case Western Reserve University, Anatomy, Cleveland, United States of America, [5]Abbott Neuromodulation, Plano, United States of America, [6]Mayo Clinic, Neurology And Biomedical Engineering, Rochester, United States of America

Introduction: Spinal cord stimulation (SCS) is a neurostimulation therapy used to treat chronic pain. Recently, inactive contacts on implanted SCS electrode arrays have been used to record epidural spinal recordings (ESRs) containing evoked compound action potentials (ECAPs) generated in response to SCS. The ECAP may serve as a control signal in closed-loop paradigms [1] and may be used in the selection of optimal electrode placement and parameters [2]. To improve the efficacy of ECAP-guided SCS, we utilized a computational modeling approach to investigate how anatomical and technical factors affect SCS-induced ECAPs and the corresponding ESRs.

Materials / Methods: We used averaged measurements from an experimental dataset containing magnetic resonance imaging (MRI), computed tomography (CT) scans, and ESRs during SCS from seven swine to develop a generalized swine finite element method model. Our model included a lower-thoracic spinal cord and surrounding tissues, two staggered SCS electrode arrays, and multicompartment cable models of axons distributed throughout the spinal cord. To compute ECAPs, we first calculated the electric potentials generated by SCS throughout our model. Next, we applied the extracellular potentials to the axon models and assessed the response to stimulation. Finally, we calculated the voltages at the recording electrodes.

Results: We generated model ECAPs using charge-balanced biphasic, bipolar stimulation on the proximal contacts of the caudal electrode array. We calculated recordings on all non-stimulating contacts. Using both symmetric and asymmetric waveforms, model ESRs were characteristically similar to experimental ESRs. Our model ECAPs propagated along the leads with conduction velocities and morphologies akin to the experimental recordings. As the distance between the stimulating and recording electrodes increased, the width of the ECAP increased and the ECAP amplitude decreased. The ECAP waveform also showed a dependence on the location of the stimulating and recording electrodes with respect to vertebral bone.

Discussion: Our model reproduced trends from experimental ESRs. Combining the results of our model and the experimental dataset, we can improve our understanding of the biological response to SCS and use these results to inform optimal stimulation and recording strategies for ECAP-based SCS.

Conclusions: The results of this study provide a mechanistic understanding of how various factors affect the composition of ECAP recordings and will help optimize the utility of ESRs in SCS.

Supplemental Data:

References: [1] Mekhail, N., Levy, R. M., Deer, T. R., Kapural, L., Li, S., Amirdelfan, K., Hunter, C. W., Rosen, S. M., Costandi, S. J., Falowski, S. M., Burgher, A. H., Pope, J. E., Gilmore, C. A.,

Qureshi, F. A., Staats, P. S., Scowcroft, J., Carlson, J., Kim, C. K., Yang, M. I., … Soliday, N. (2020). Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial. *The Lancet Neurology*, *19*(2), 123–134. https://doi.org/10.1016/S1474-4422(19)30414-4 [2] Verma, N., Romanauski, B., Lam, D., Lujan, L., Blanz, S., Ludwig, K., Lempka, S., Shoffstall, A., Knudson, B., Nishiyama, Y., Hao, J., Park, H.-J. J., Ross, E., Lavrov, I., & Zhang, M. (2023). Characterization and applications of evoked responses during epidural electrical stimulation. *Bioelectronic Medicine*, *9*(1). https://doi.org/10.1186/s42234-023-00106-5

Acknowledgements: Abbott Neuromodulation, the Rackham Merit Fellowship Program at the University of Michigan, and Advanced Research Computing at the University of Michigan.

Learning Objectives: Participants will be able to: 1. Describe the origins of evoked compound action potentials (ECAPs) during spinal cord stimulation 2. Explain how ECAP recordings can be used to improve the efficacy of SCS 3. Understand how various anatomical and technical factors affect the characteristics of the epidural ECAP recordings

Financial Disclosures: Mingming Zhang a) Aviation Medical b) Stock options c) $5,001 - $20,000 **Kip Ludwig** a) Neuronoff, Inc. b) Co-founder, equity holder, scientific advisory board member, consultant c) $501 - $5000 a) NeuroOne Medical Inc. b) Scientific board member and stock interests c) $20,001 - $100,000 a) Abbott b) Scientific advisory board member c) $501 - $5,000 a) Cala Health b) Scientific advisory board member c) $501 - $5,000 a) Blackfynn b) Scientific advisory board member c) $501 - $5,000 a) Battelle b) Scientific advisory board member c) $501 - $5,000 a) Presidio Medical b) Scientific advisory board member c) $501 - $5,000 a) Alfred Mann Foundation b) Consultant c) $501 - $5,000 a) CVRx b) Consultant c) $501 - $5,000 **Andrew Shoffstall** a) Neuronoff, Inc. b) CSO / Stockholder / Consultant c) $20,001 - $100,000 **Scott Lempka** a) Abbott Neuromodulation b) Consultant / Advisory Board c) $501 - 5,000 a) CereGate b) Consultant / Advisory Board and Stockholder c) $1 - $500 a) Hologram Consultants, LLC b) Stockholder Stock Value >5% c) $1 - $500 a) Neuronoff, Inc. b) Stockholder c) $1 - $500 a) Presidio Medical, Inc. b) Consultant / Advisory Board and Stockholder c) $1 - $500

Disclosure: No significant relationships.

O014

Oral Presentations
NEUROMODULATION – MECHANISM(S) OF ACTION
13-05-2024 16:30 - 18:20

5 HZ LOW-FREQUENCY STIMULATION OF VENTROLATERAL PERIAQUEDUCTAL GRAY MODULATES THE DESCENDING SEROTONERGIC SYSTEM

Hyun Ho Jung, MD, PhD
Yonsei University, Neurosurgery, Seoul, Korea, Republic of

Introduction: Neuropathic pain is a type of chronic pain, which entails severe prolonged sensory dysfunctions caused by a lesion of the somatosensory system. Many of those suffering from the condition do not experience significant improvement with existing medications, resulting in various side effects. In this study, Sprague-Dawley male rats were used and long-term deep brain stimulation (DBS) of the ventrolateral periaqueductal gray (vlPAG) was conducted in a rat model of spared nerve injury (SNI).

Materials / Methods: SNI models with adult male Sprague-Dawley rats were prepared, and on postoperative day 14, electrodes were introduced to the vl PAG (AP:-7.8mm, ML:-0.5mm, DV:-0.52mm). Three days after implantation, stimulation was turned on for 9 hours (200us, 200uA, 5Hz). During stimulation, the behavioral test (von Frey test) was done every 3 hours. To evaluate serotonergic system change, rostral ventromedial medulla (RVM), and spinal dorsal horn were harvested for western blot study. The whole brain section was done for the immunohistochemical stain to evaluate c-fos and NeuN.

Results: We found that 5 Hz DBS effectively modulated mechanical allodynia and induced neuronal activation in the RVM, restoring the impaired descending serotonergic system. At the spinal level, glial cells were still activated but only the 5-HT1a receptor in the spinal cord was activated, implying its inhibitory role in mechanical allodynia

Discussion: In the present study, we aimed to uncover a variable role of endogenous serotonergic pain modulation in chronic pain and 5-HT receptor subtypes in the spinal cord. We found that extremely low frequency (5 Hz) stimulation of vlPAG remarkably contributed to rescuing pain hypersensitivity in the peripheral neuropathic pain and only spinal 5-HT1a receptor expression was increased following long-term stimulation.

Conclusions: This study demonstrated that the malfunctioned descending serotonergic system in the peripheral nerve injury can be modulated with extremely low frequency (5 Hz) stimulation and suggested an inhibitory role of serotonergic transmission to the spinal cord. It remarkably improved neuropathic behaviors, and the persistent stimulation induced a greater analgesic effect with increasingly immediate effects as the stimulation continued.

Supplemental Data:

References: 1) Hentall I, Kurle P, White T. Correlations between serotonin level and single-cell firing in the rat's nucleus raphe magnus. Neuroscience 1999;95:1081-8. 2) Hentall ID, Luca CC, Widerstrom-Noga E, Vitores A, Fisher LD, Martinez-Arizala A, Jagid JR. The midbrain central gray best suppresses chronic pain with electrical stimulation at very low pulse rates in two human cases. Brain Res 2016;1632:119-26.

Acknowledgements: This work was supported by grants from the Basic Science Research Program through the National Research Foundation of Korea [2021R1I1A1A0104775012], Korea Medical Device Development Fund [RS-2022-00141392], Korea Drug Development Fund [KDDF2118217617-22], a faculty research grant of Yonsei University College of Medicine for 2012 [6-2012-0038].

Learning Objectives: 1. very low frequency (5Hz) stimulation of ventrolateral periaqueductal gray (vlPAG) attenuates neuropathic pain behavior 2. By stimulating vlPAG, RVM serotonergic descending inhibitory pathway could be modulated 3. 5-HT1a receptors in the spinal dorsal horn were increased by vlPAG DBS

Financial Disclosures: no significant relationships

Disclosure: No significant relationships.

O015

Oral Presentations
NEUROMODULATION – MECHANISM(S) OF ACTION
13-05-2024 16:30 - 18:20

TRANS-SPINAL LOW-INTENSITY FOCUSED ULTRASOUND NEUROMODULATION FOR THE TREATMENT OF CHRONIC PAIN

Weiguo Song, PhD[1], Naveen Jayaprakash, PhD[1], Nafiseh Saleknezhad, MD[1], Chris Puleo, PhD[2], Yousef Al-Abed, PhD[1], John Martin, PhD[3], Stavros Zanos, PhD[1]
[1]Feinstein Institute for biomedicine research, new york, United States of America, [2]General Electric Research, Niskayuna, United States of America, [3]city college of new york, new york, United States of America

Introduction: Chronic pain is a leading cause of disability and psychiatric disease. Pain medications often have limited efficacy and cause adverse effects [1]. Device-based methods, including electrical stimulation of nerves, spinal cord or brain have been tested, but evidence for clinical efficacy is conflicting [2,3]. Noninvasive focused ultrasound stimulation (FUS) has favorable spatiotemporal resolution and penetration depth [4]; recently, it has been used to target peripheral nerves dorsal root ganglia for pain treatment [5]. Few studies have tested FUS in the spinal cord [6,7]. We hypothesized that trans-spinal(tsFUS) delivered early after chronic constriction injury (CCI) could suppress the development of chronic pain.

Materials / Methods: tsFUS was delivered at spinal level L5 in rats either healthy or with CCI. In healthy rats (n=35), spinal reflexes (H-reflex, flexor reflex, withdrawal reflex) were measured before, during, and after 1 min-long tsFUS; Expression of *c-fos* was determined in IHC sections at spinal level L5 and at level T9 (as control) from tsFUS(n=3) and sham (n=3). In CCI rats, 3 daily, 1 min-long sessions of either tsFUS (n=6) or sham stimulation (n=6) were delivered, starting 3 days after CCI; Von Frey threshold was measured before and after CCI at 1, 3, 10 and 17 days from the final tsFUS session.

Results: In healthy rats, tsFUS suppresses the H-reflex, augments homosynaptic depression of the H-reflex, and reduces windup activity associated with slow, C-afferent fibers. The latency of withdrawal from hotplate was increased after tsFUS. These changes cannot be explained by thermal effects of tsFUS and are not associated with loss of spinal neurons. c-fos shows more expression at L5 than at T9 spinal neurons after tsFUS at L5. In CCI rats, injury results in significant reduction in Von Frey threshold . tsFUS-treated animals have higher pain threshold compared to sham-treated animals at 1, 3, 10, and 17 days following the final tsFUS session.

Discussion: Effects of tsFUS on the spinal circuit could be a combination of thermal and mechanical mechanisms. The reduction of H-reflex could represent suppression of presynaptic, synaptic, and/or postsynaptic elements of the monosynaptic circuit. tsFUS suppress pain might be through the inhibit the development of the spinal plasticity.

Conclusions: tsFUS could reduce pain by controlling abnormal excitability of spinal neurons and by altering synaptic transmission. tsFUS delivered early after CCI, is effective at preventing the development of chronic pain. tsFUS shows clinical potential for pain control and may be applicable in other translational applications, such as spinal cord injury.

Supplemental Data:

References: 1. Varrassi, G., et al., Pharmacological treatment of chronic pain - the need for CHANGE. Curr Med Res Opin, 2010. **26**(5): p. 1231-45. DOI: 10.1185/03007991003689175 2. Long, D.M., et al., Electrical stimulation of the spinal cord and peripheral nerves for pain control. A 10-year experience. Appl Neurophysiol, 1981. **44**(4): p. 207-17. DOI: 10.1159/000102203 3. Yang, Y., et al., Efficacy of transcutaneous electrical nerve stimulation in people with pain after spinal cord injury: a meta-analysis. Spinal Cord, 2022. **60**(5): p. 375-381. DOI: 10.1038/s41393-022-00776-z 4. Kubanek,

J., Neuromodulation with transcranial focused ultrasound. Neurosurg Focus, 2018. **44**(2): p. E14. 5. Liss, A., et al., Low Intensity Focused Ultrasound Increases Duration of Anti-Nociceptive Responses in Female Common Peroneal Nerve Injury Rats. Neuromodulation, 2021. DOI: 10.1111/ner.13531 6. Song, W., et al., Trans-spinal Focused Ultrasound Suppresses Spinal Reflexes in Healthy Rats. Neuromodulation. 2023. S1094-7159(23)00649-9. DOI: 10.1016/j.neurom.2023.04.476 7. Liao, Y.H., et al., Effects of Noninvasive Low-Intensity Focus Ultrasound Neuromodulation on Spinal Cord Neurocircuits In Vivo. Evid Based Complement Alternat Med, 2021. **2021**: p. 8534466. DOI: 10.1155/2021/8534466

Acknowledgements:

Learning Objectives: 1. get updated techniqe to apply spinal neuromodulation 2. know the field interests 3. connect with researchers for potential collaboration

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O016

Oral Presentations
NEUROMODULATION – MECHANISM(S) OF ACTION
13-05-2024 16:30 - 18:20

SPINAL CORD STIMULATION THRESHOLDS DECREASE WITH HIGH KHZ STIMULATION FREQUENCY

Kerry Bradley, MSc, Kwan Yeop Lee, PhD, Dong Wang, PhD, Dongchul Lee, PhD, Zachary Kagan, PhD
Nevro Corp, Redwood City, United States of America

Introduction: Paresthesia-based spinal cord stimulation (SCS) depends upon dorsal column (DC) fiber activation to engage pain relieving neural mechanisms. It has recently been hypothesized that the paresthesia perception threshold from DC activation may be dependent upon the pattern of neural activation (Sagalajev et al 2022). To understand the effect on dorsal column neural traffic from higher SCS frequencies, we measured the preclinical motor threshold (MT), over a range of stimulation frequencies.

Materials / Methods: In sedated naïve and neuropathic model Sprague-Dawley rats, SCS was applied via a micro-sized, in-line quadripolar electrode array positioned epidurally over the L5-L6 dorsal spinal segments (innervating the left/right hind paw). We applied different frequencies (2Hz-10kHz) of SCS pulses at pulse widths (PW) of 30us and 80us, while palpating the lower extremities, monitoring for the MT while increasing the stimulation amplitude. MTs across frequency were compared using one-way ANOVA, with post-hoc Tukey HSD and Q-test to compare interfrequency MT differences.

Results: ANOVA revealed that the per-animal-normalized MT was statistically significantly different with varied frequency ($P = 0.03$); all frequencies were statistically identical except the MT at 5kHz was significantly lower than 2Hz and 10Hz ($P=0.02$).

Discussion: We observed that the SCS MT trended downward from 2Hz to 1kHz, and was significantly different by approximately 20% from 2Hz to 5kHz. If it is presumed that stimulation at lower frequencies characterizes the nominal pulse charge activation threshold for a neuron, then increasing the stimulation frequency likely reduces this threshold, possibly increased ‘temporal summation’ at the membrane level.

Conclusions: This suggests that, while the hypothetical pattern of DC activation may become less synchronized with higher frequencies, the overall clinical result of using higher frequency SCS is to increase the likelihood of generating activation at a given stimulation pulse charge, in contrast to the proposed hypothesis. Further research is needed to elucidate these phenomena.

Supplemental Data:

References: Sagalajev B, Zhang T, Abdollahi N, Yousefpour N, Medlock L, Al-Basha D, Ribeiro-da-Silva A, Esteller R, Ratte S, Prescott SA. Paresthesia during spinal cord stimulation depends on synchrony of dorsal column axon activation. bioRxiv. 2023:2023-01.

Acknowledgements: This work was sponsored by Nevro Corporation.

Learning Objectives: To understand the effect of frequency SCS activation thresholds To understand that high kHz frequency can activate neurons differently than low frequency, requiring less stimulation current amplitude To understand that this effect is observable for antidromic activation of axons

Financial Disclosures: Kerry Bradley, Nevro Corp, VP Scientific Affairs, Salary and stock Dongchul Lee, Nevro Corp, Director Theoretical Research, Salary and stock Dong Wang, Nevro Corp, Principal Research Scientist, Salary and stock Kwan Yeop Lee, Nevro Corp, Principal Research Scientist, Salary and stock Zachary B Kagan, Nevro Corp, Principal Research Scientist, Salary and stock

Disclosure: Kerry Bradley, Nevro Corp, VP Scientific Affairs, Salary and stock

O017

Oral Presentations
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 16:30 - 18:20

COMPARISON OF GPI-DBS AND STN-DBS IN PRIMARY MEIGE SYNDROME

Ruen Liu, PhD, Qingpei Hao, MD
Peking University People's Hospital, Beijing, China

Introduction: Primary Meige syndrome (PMS) is a rare form of dystonia, and comparative analysis of globus pallidus internal deep brain stimulation (GPi-DBS) and subthalamic nucleus deep brain stimulation (STN-DBS) has been lacking.

Materials / Methods: This prospective cohort study recruited 80 patients who underwent bilateral GPi-DBS and STN-DBS, respectively. Clinical assessments, including motor and non-motor domains, were evaluated at baseline and at 1 year and 3 years after neurostimulation.

Results: In the GPi-DBS group, the movement score of the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) improved from a mean (SE) of 13.8 (1.0) before surgery to 5.0 (0.7) (95% CI, -10.5 to -7.1; $P < 0.001$) at 3 years. Similarly, in the STN-DBS group, the mean (SE) score improved from 13.2 (0.8) to 3.5 (0.5) (95% CI, -10.3 to -8.1; $P < 0.001$) at 3 years. Significant changes in the overall quality of life were observed in the DBS groups rather than in sleep, depression and cognition.

Discussion: Consistent with previous literature, GPi-DBS reduced BFMDRS movement scores by 61% at 1 year and 65% at 3 years, STN-DBS reduced movement scores by 66% at 1 year and 71% at 3 years, in line with the range of improvements reported (53%~96%). And there were no significant differences between the groups. Otherwise, the most notable symptom improvement in all groups was blepharospasm, followed by oromandibular dystonia and speech/swallowing. Nevertheless, the cervical dystonia in the groups showed no significant improvement, which contradicts some previous reports. The therapeutic failure in cervical dystonia is possibly due to the complexity and heterogeneity of the dystonia itself, as well as the minor quantity and lower severity of cervical symptoms in our cohort.

Conclusions: Bilateral GPi-DBS and STN-DBS are effective and relatively safe treatments for patients with PMS, with similar clinical outcomes. More importantly, it is crucial to consider psychiatric abnormalities, particularly sleep disorders and depression, to develop a deeper understanding of the pathophysiology and treatment of psychiatric disorders. Psychological interventions play a momentous role in the overall neurosurgical management of PMS and should be embraced as an integral component.

Supplemental Data: no

References: None

Acknowledgements: We thank all the patients and their families involved in this study, as well as Huixin Liu (Statistics Office, Peking University People's Hospital), who provided guidance in statistical analysis.

Learning Objectives: To compare the efficacy, safety, and psychiatric features of GPi-DBS and STN-DBS in patients with PMS.

Financial Disclosures: No competing interests were reported.

Disclosure: No significant relationships.

O018

Oral Presentations
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 16:30 - 18:20

THE IMPACT OF IMPULSIVITY ON QUALITY OF LIFE IN PATIENTS UNDERGOING DEEP BRAIN STIMULATION: A MULTIPLE LINEAR REGRESSION MODELLING APPROACH

John Eraifej, MB ChB[1], Alex Fung, MBBS[1], Alexander Green, PhD FRCS(SN)[1], Simon Prangnell, DPsych[2]
[1]University of Oxford, Nuffield Department Of Clinical Neurosciences (ndcn), Medical Sciences Division, Oxford, United Kingdom, [2]Oxford University Hospitals NHS Trust, Psychological Medicine, Oxford, United Kingdom

Introduction: The prevalence of impulsive and compulsive behaviours (ICBs) in Parkinson's disease (PD) is approximately ten times that of the general population, leading to significant reduction in quality of life (QoL). The Questionnaire for Impulsive-Compulsive Disorders (ICDs) in Parkinson's Disease-Rating Scale (QUIP-RS) is a validated tool for quantification of ICBs in PD but the relative contribution of ICBs to patient QoL, adjusted for motor-symptom severity, has not yet been quantified. In this study, we quantify this contribution in PD patients undergoing deep brain stimulation as measured by the PD Questionnaire-39 (PDQ39).

Materials / Methods: In this prospective observational study, we assessed patients pre-operatively and at approximately 1-year follow-up post-operatively. Clinical scores included UPDRS III, QUIP-RS and PDQ39. Age, disease duration, sex and levodopa equivalent dose (LED) were also collected. Pre-operative scores were compared with post-operative scores using paired T-tests and the incidence of ICDs was compared using a Chi-squared test. Multiple linear regression was used to estimate PDQ39 using these clinical predictors. Analyses were completed in SPSS 28.

Results: 39 patients undergoing deep brain stimulation for PD were included. Mean age was 60.7 (SD 8.4) and mean PD duration was 8.8 years (SD 3.6). There was a statistically significant reduction in UPDRS III from a mean of 50.7 (SD 13.1) pre-operatively to 37.8 (SD 14.8) post-operatively ($p<0.001$). There was no significant difference between pre-operative and post-operative QUIP-RS, PDQ39 and ICD prevalence. A pre-operative regression model that included sex, UPDRS III and QUIP-RS predicted 32.9% of the variance in PDQ39 ($p=0.004$), where sex ($p=0.002$) and UPDRS III ($p=0.035$) were significant predictors. A post-operative regression model including sex, UPDRS III and QUIP-RS explained 44.9% of the variance in PDQ39 ($p<0.001$), where UPDRS III ($p=0.005$) and QUIP-RS ($p<0.001$) were significant predictors. There was no significant reduction in LED after surgery and patient level change in QUIP-RS did not correlate with change in LED.

Discussion: These results highlight the contribution of ICBs as predictors of QoL in post-operative PD-DBS patients. This may reflect the variable effect of DBS on the non-motor symptoms of PD at the individual patient level, with some improving and others worsening, even in the context of stable LED. A limitation of this study is the small sample size which restricted the number of predictor variables that could be included due to the risk of overfitting.

Conclusions: After adjustment for UPDRS III, the relative post-operative contribution of ICBs to QoL increases in PD patients undergoing DBS.

Supplemental Data:

References: None

Acknowledgements: John Eraifej is supported as an MRC Clinical Research Training Fellow.

Learning Objectives: 1) ICBs are significant predictors of QoL in the PD-DBS population. 2) Post-operatively, ICBs explain a greater proportion of the of variation in QoL than pre-operatively. 3) ICBs should be considered when planning therapeutic strategies in PD-DBS patients.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O019

Oral Presentations
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 16:30 - 18:20

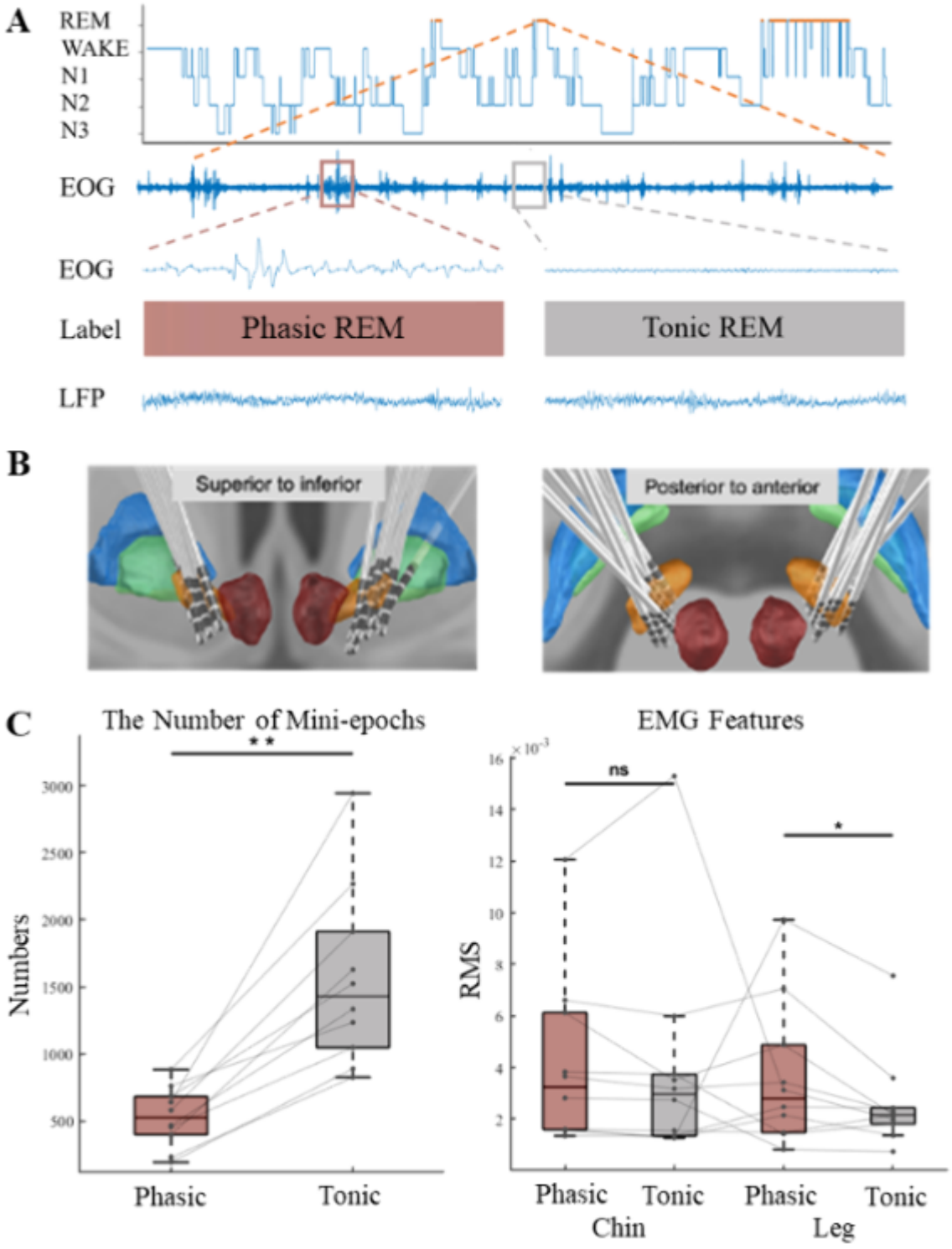
SUBTHALAMIC NEUROPHYSIOLOGICAL FEATURES OF REM SLEEP MICROSTATES IN PATIENTS WITH PARKINSON'S DISEASE

Lingxiao Guan, M.S.[1], Huiling Yu, MD[1], Yue Chen, PhD[1], Chen Gong, PhD[1], Hongwei Hao, PhD[1], Yi Guo, MD[2], Shujun Xu, MD[3], Yuhuan Zhang, B.S.[4], Xuemei Yuan, B.S.[4], Guoping Yin, PhD[4], Jianguo Zhang, MD[5], Huiling Tan, PhD[6], Luming Li, PhD[1,7]
[1]National Engineering Research Center of Neuromodulation, School of Aerospace Engineering, Tsinghua University, Beijing, China, [2]Peking Union Medical College Hospital, Department Of Neurosurgery, Beijing, China, [3]Qilu Hospital of Shandong University (Qingdao), Department Of Neurosurgery, Qingdao, Shandong, China, [4]Tsinghua Changgung Hospital, Department Of Otolaryngology, Beijing, China, [5]Beijing Tiantan Hospital, Capital Medical University, Department Of Neurosurgery, Beijing, China, [6]Nuffield Department of Clinical Neurosciences, University of Oxford, Medical Research Council Brain Network Dynamics Unit, Oxford, United Kingdom, [7]IDG/McGovern Institute for Brain Research at Tsinghua University, Beijing, China

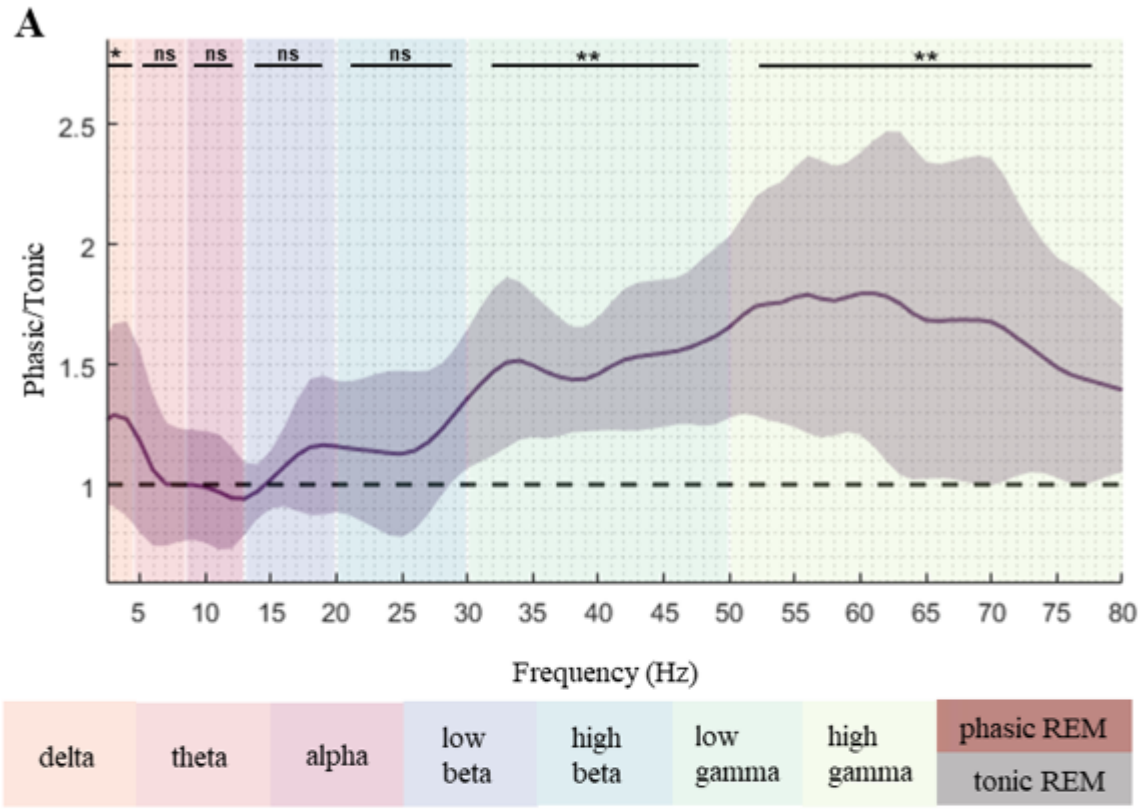
Introduction: Associations between rapid eye movement sleep behavior disorder (RBD) and Parkinson's disease (PD) have been widely explored, highlighting the importance for further study on REM sleep. Most studies have regarded REM sleep as an integral process. However, emerging evidence have revealed that REM sleep is not a homogeneous part, which can be further divided into distinct microstates known as phasic and tonic REM with differences in environmental alertness and information processing. The neurophysiological features of REM microstates in patients with Parkinson’s disease (PD) remain unclear. As subthalamic nucleus (STN) is one of the main targets of DBS in PD, local field potentials from it are used as closed-loop modulation reference. Hence, the primary objectives of this study are to investigate the neurophysiological features of STN during different microstates of REM sleep and its correlation with RBD, one of the major sleep disorders in PD.

Materials / Methods: Ten PD patients with STN-DBS bilateral implants were included in this study, of which four were diagnosed of RBD. Sleep data was collected one month after the surgery, prior to the initial DBS programming. Simultaneous recordings of STN-LFP and Polysomnography (PSG) were obtained. Timestamps were adopted to ensure synchronization, and movement artifacts to validation and correction. REM microstates were determined by the EOG channel (lasting over 2s and amplitudes over 80μV as Phasic REM), and accuracy was visually inspected after thresholding

methods.

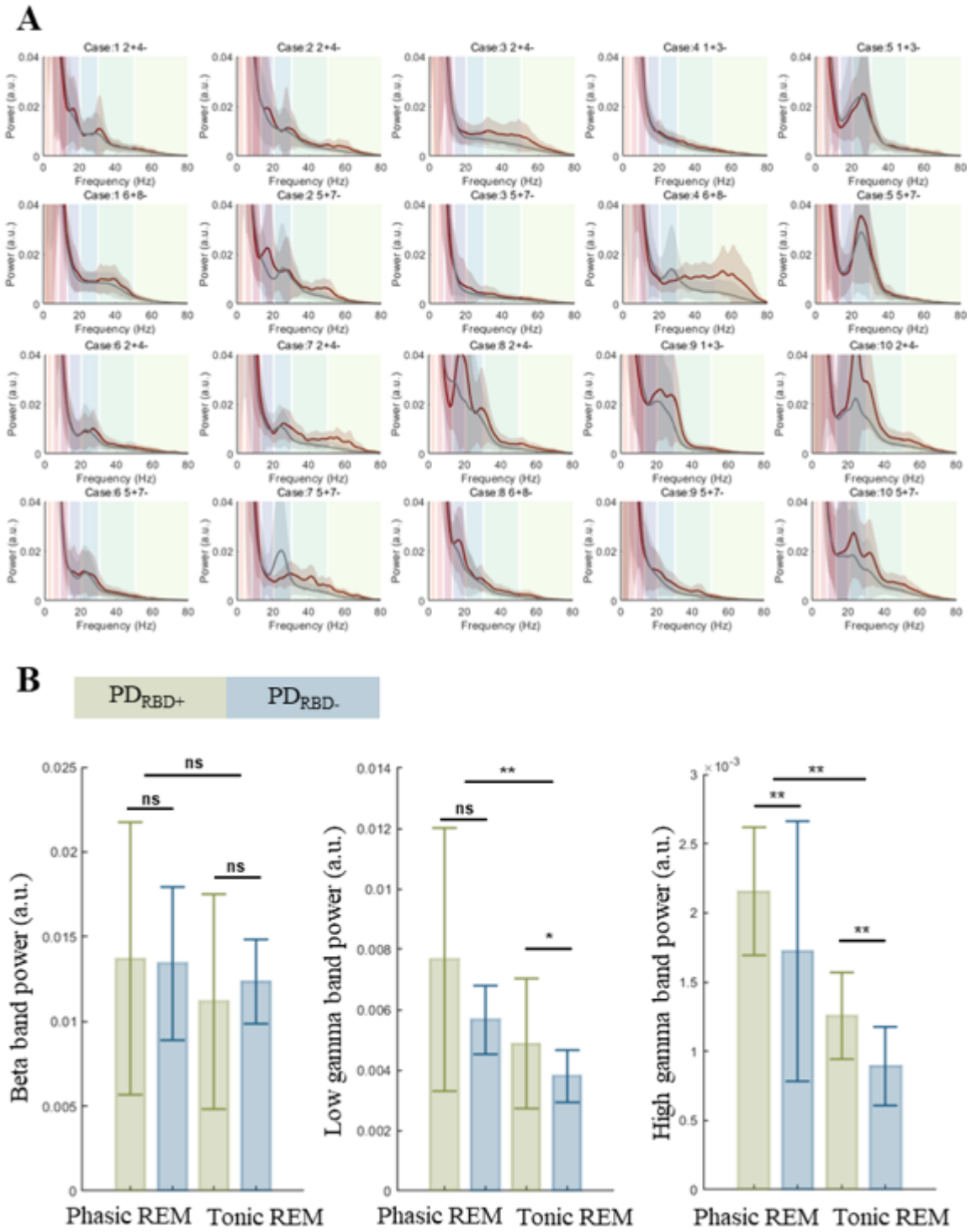


Results: Both electromyographic (EMG) of chins and lower limbs were higher in phasic REM than tonic REM(p_{leg}=0.037). Comparing with tonic REM, phasic REM demonstrated elevated power in delta (2-4Hz p=0.0027), low gamma (30-50 Hz, p=0.002) and high gamma (50-80Hz, p=0.002) oscillations.



Comparing with patients without RBD(PD_{RBD-}), patients with RBD(PD_{RBD+}) shown stronger gamma oscillations throughout REM sleep(PD_{RBD+} vs. PD_{RBD-}: low gamma oscillations, $p_{phasic\ REM}$= 0.056, $p_{tonic\ REM}$ = 0.010; high gamma band oscillations, $p_{phasic\ REM}$ = 0.004, $p_{tonic\ REM}$ =

0.009).



Discussion: Gamma power in STN-LFP variations difference between REM microstates may relate to the movements of muscle activities and cognitive process. Furthermore, gamma activity fluctuations throughout REM sleep exhibited a correlation with the RBD. Our findings indicate that gamma oscillations could serve as an important biomarker during REM sleep.
The gamma frequency band of STN-LFP shows similarities to previous EEG studies which may suggest cortical-subcortical synchronized brain electrical activity. However, due to limitations in synchronization accuracy, further connectivity analysis was not conducted.

Conclusions: Our study extends the understanding of STN activity patterns across microstates and connection with RBD, which may further inspire DBS closed-loop strategies.

Supplemental Data:

References: [1] Simor, Péter, et al. "The microstructure of REM sleep: Why phasic and tonic?." *Sleep medicine reviews* 52 (2020): 101305. [2] Chen, Yue, et al. "Automatic sleep stage classification based on subthalamic local field potentials." *IEEE Transactions on Neural Systems and Rehabilitation Engineering* 27.2 (2019): 118-128. [3] Ch, Schenck. "Chronic behavioral disorders of human REM sleep: a new category of parasomnia." *Sleep* 9 (1986): 293-308. [4] Simor, Péter, et al. "EEG spectral power in phasic and tonic REM sleep: different patterns in young adults and children." *Journal of sleep research* 25.3 (2016): 269-277. [5] Verma, Ajay K., et al. "Basal ganglia engagement during REM sleep movements in Parkinson's disease." *npj Parkinson's Disease* 8.1 (2022): 116.

Acknowledgements:

Learning Objectives: 1：Synchronization of implanted devices and external devices, followed by validation and correction using pseudotraces with aligned timestamps. -Achieving explicit data synchronization validation and further controlling synchronization errors. 2、Adopting an approach utilizing automatic thresholding and visual inspection for sub-staging classification. -Improving analysis efficiency while ensuring objectivity and consistency. 3、Using a mixed-effects model to analyze unpaired and stratified data. -More effectively explored the inter-patient differences in sub-staging characteristics.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O020

Oral Presentations
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 16:30 - 18:20

LONG-TERM EFFECT OF DEEP BRAIN STIMULATION ON SPATIAL-SPECTRAL CHANGES OF STN-LFP IN PARKINSONIAN PATIENTS

Yu Fan, BEng[1], Huiling Yu, MD[1], Yue Chen, PhD[1], Chen Gong, PhD[1], Ye Tian, MSc[1], Jianguo Zhang, MD[2], Yi Guo, MD[3], Shujun Xu, MD[4], Changqing Jiang, PhD[1], Hongwei Hao, PhD[5], Luming Li, PhD[6,7]
[1]National Engineering Research Center of Neuromodulation, School of Aerospace Engineering, Tsinghua University, Beijing, China, [2]Beijing Tiantan Hospital, Capital Medical University, Department Of Neurosurgery, Beijing, China, [3]Peking Union Medical College Hospital, Department Of Neurosurgery, Beijing, China, [4]Qilu Hospital of Shandong University (Qingdao), Department Of Neurosurgery, Qingdao, Shandong, China, [5]National Engineering Research Center of Neuromodulation, School of Aerospace Engineering, Beijing, China, [6]National Engineering Research Center of Neuromodulation, Tsinghua University, Beijing, China, [7]IDG/McGovern Institute for Brain Research at Tsinghua University, Beijing, China

Introduction: Previous studies have shown long-term neurophysiological changes of subthalamic nucleus (STN) in patients with Parkinson's disease (PD) with deep brain stimulation (DBS). However, the Spatial-Spectral features of STN oscillations have not been fully explored. Here we conducted a long-term follow-up study to illustrate the impact of DBS on the Spatial-Spectral changes of STN oscillations.

Materials / Methods: Fourteen PD patients implanted with bilateral STN-DBS were visited at 1,3,6 and 12 months post-surgery (NCT02937727). Local field potentials (LFP) were recorded using DBS with real-time wireless recording capacity (G106RS, Beijing PINS Medical Co®, China) in both On-DBS and Off-DBS states. Patients were in Off-Medication state. Locations of the electrodes were identified based on presurgical structural MRI and postsurgical CT and reconstructed with Lead-DBS tool. We projected the contacts towards the right STN via non-linear registration according to MNI locations. Spatial-Spectral changes of STN-LFP were illustrated using VD-Hemisphere-Ratio for Off-DBS analysis and VD-Group-Ratio for On-DBS analysis as
following:

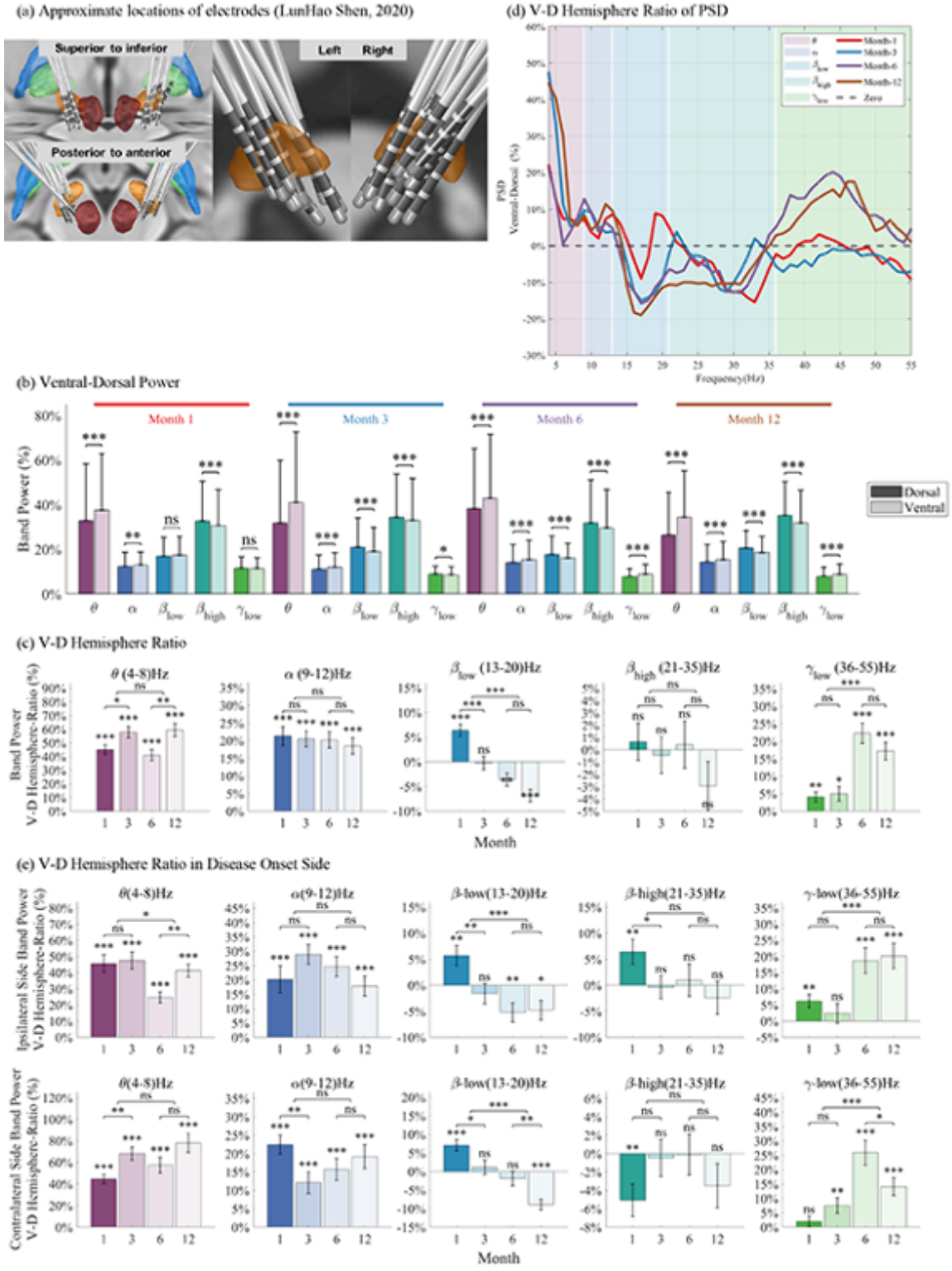
$$VD_{Hemisphere} = \frac{1}{N_i}\sum_i \frac{PowVentral_i - PowDorsal_i}{PowDorsal_i},$$

$$VD_{Group} = \frac{\frac{1}{N_i}\sum_i PowVentral_i - \frac{1}{N_i}\sum_i PowDorsal_i}{\frac{1}{N_i}\sum_i PowDorsal_i}.$$

The relative ventral-dorsal division in the VD-Hemisphere-Ratio was determined based on the average contact locations of each electrode lead, while in the VD-Group-Ratio, it is determined by averaging across all subjects.

Results: LFP signals in Off-DBS and Off-medication states were firstly analyzed. During all visits, theta and alpha oscillations demonstrated higher power in dorsal sides while high-beta oscillations displayed higher in ventral sides (Fig-c). We next separated the hemisphere into contralateral sides (the limb side of disease onset) and ipsilateral sides. VD-Hemisphere-Ratios in the theta and alpha bands remained consistently positive. In the low-beta band, VD-Hemisphere-Ratio decreased over time on both sides (p<0.001), transitioning from higher ventral power at 1-month post-surgery towards

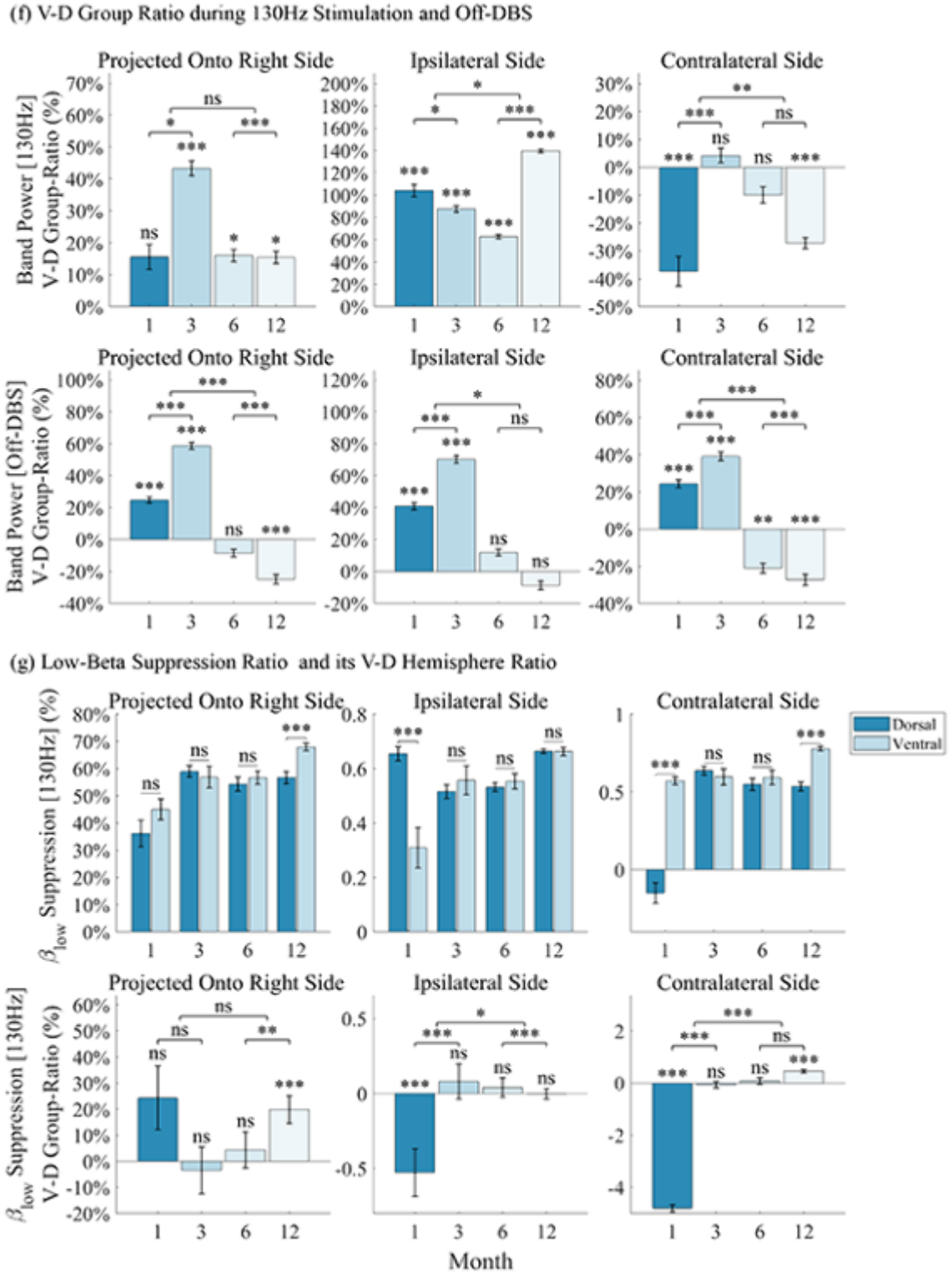
an increasing dorsal power (Fig-



d).

We analyzed the VD-Group-Ratio in low-beta oscillation and its suppression-ratio with therapeutic 130Hz stimulation. During long-term follow-up visits, low-beta oscillations consistently exhibited a ventral-dorsal relationship: higher ventral energy on the ipsilateral sides (p<0.001) while higher dorsal energy on the contralateral side (p<0.001). Simultaneously, we observed an increase in the VD-Group-Ratio of low-beta suppression

(p<0.001).



Discussion: Long-term DBS induces distinct spatiotemporal dynamics characteristics between Off-DBS and On-DBS conditions, implying that it helps balance neural circuit function by modulating local nucleus energy transmission. Variations in spatial-spectral dynamics underscore the importance of spatial location in optimizing DBS modes and the need for site-specific closed-loop strategies.

Conclusions: Long-term spatial-spectral changes in STN-LFP contribute to a comprehensive understanding of the spatiotemporal effects of DBS on regional neural networks, which offer valuable insights into the optimization of multidimensional stimulation strategies.

Supplemental Data:

References: [1] Shen, Lunhao et al. “Subthalamic Nucleus Deep Brain Stimulation Modulates 2 Distinct Neurocircuits.” *Annals of neurology* vol. 88,6 (2020): 1178-1193. doi:10.1002/ana.25906 [2] Averna, Alberto et al. “Spectral Topography of the Subthalamic Nucleus to Inform Next-Generation Deep Brain Stimulation.” *Movement disorders : official journal of the Movement Disorder Society* vol. 38,5 (2023): 818-830. doi:10.1002/mds.29381

Acknowledgements:

Learning Objectives: [1]Objective: To deepen understanding of the latest advancements and trends in the field.
Desired Result: Gain insights into cutting-edge research and innovative approaches. [2]Objective: To foster collaboration and networking opportunities with experts and peers in the field.
Desired Result: Establish connections and engage in meaningful discussions with like-minded professionals. [3]Objective: To foster collaboration and networking opportunities with experts and peers in the field. Desired Result: Gain inspiration and motivation for future research projects and collaborations.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O021

Oral Presentations
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 16:30 - 18:20

PROSPECTIVE, MULTICENTER, INTERNATIONAL REGISTRY OF DEEP BRAIN STIMULATION FOR DYSTONIA: SUB-ANALYSIS OF CERVICAL DYSTONIA PATIENTS

Alberto Albanese, MD[1], Alfons Schnitzler, MD[2], Andrea Kuehn, MD[3], David Arkadir, MD[4], David Ledingham, MD[5], David Pedrosa, MD[6], Edward Newman, MD[7], Griet Loret, MD[8], Ignacio Regidor, MD[9], Jens Volkmann, MD[10], Marcin Rudas, MD[11], Maria Fiorella Contarino, MD[12], Mariachiara Sensi, MD[13], Michael Barbe, MD[14], Monika Pötter-Nerger, MD[15], Norbert Kovacs, MD[16], Ralph Lehrke, MD[17], Ryoong Huh, MD[18], Steffen Paschen, MD[19], Tomasz Mandat, MD[20], Tommaso Tufo, MD[21], Veerle Visser-Vandewalle, MD[22], Volker Coenen, MD[23], Yen Tai, MD[24], Lilly Chen, MD[25], Edward Goldberg, MD[25], Joachim Krauss, MD[26]
[1]Catholic University of the Sacred Heart, Neurology, Milan, Italy, [2]Heinrich Heine University, Neurology, Düsseldorf, Germany, [3]Charité Universitätsmedizin Berlin, Neurology, Berlin, Germany, [4]Hadassah Medical Center, Neurology, Jerusalem, Israel, [5]Newcastle University, Campus for Ageing and Vitality, Neurology, Newcastle, United Kingdom, [6]University Hospital Giessen and Marburg, Neurology, Giessen, Germany, [7]Ross Hall Hospital, Neurology, Glasgow, United Kingdom, [8]AZ Sint Lucas, Neurology, Brugge, Belgium, [9]Hospital Universitario Ramón y Cajal, Neurophysiology, Madrid, Spain, [10]University Hospital Würzburg, Neurology, Würzburg, Germany, [11]Jan Biziel University Hospital No 2, Collegium Medicum, Nicolaus Copernicus University, Neurosurgery And Neurology, Bydgoszcz, Poland, [12]Leiden University Medical Centre, Neurology, Leiden, Netherlands, [13]Azienda Ospedaliero-Universitaria S, Anna,, Neurology, Ferrara, Italy, [14]University Hospital Cologne, Neurology, Cologne, Germany, [15]Universitätsklinikum Hamburg-Eppendorf (UKE), Neurology, Hamburg, Germany, [16]University of Pécs, Neurology, Pécs, Hungary, [17]Klinik Hamm-Heessen, Neurosurgery, Hamm, Germany, [18]Catholic University of Korea, Neurosurgery, Seoul, Korea, Republic of, [19]University Hospital Schleswig-Holstein, Neurology, Kiel, Germany, [20]Warsaw Medical Center, Neurosurgery, Warsaw, Poland, [21]Fakeeh University Hospital, Neurosurgery, Dubai, United Arab Emirates, [22]University Hospital Cologne, Neurosurgery, Cologne, Germany, [23]University of Freiburg, Neurosurgery, Freiburg, Germany, [24]Charing Cross Hospital, Neurology, London, United Kingdom, [25]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America, [26]Hannover Medical School, Neurology, Hannover, Germany

Introduction: Management of dystonia using Deep Brain Stimulation (DBS) is a well-established therapeutic approach. However, optimal DBS target sites (within pallidothalamic loop) in patients with cervical (focal) versus generalized dystonia are thought to diverge and be specific for particular connections.[1] DBS devices equipped with capabilities such as directionality and Multiple Independent Current Control (MICC) offer potential for improved neurostimulative precision. Here, we report a sub-analysis of patients with cervical dystonia only or dystonia with cervical involvement from an on-going, multicenter registry.

Materials / Methods: This is a sub-analysis of patients with focal (cervical) dystonia only or cervical dystonia in context of segmental or generalized dystonia derived from a prospective, multicenter, international dystonia registry (NCT02686125). Participants receive an MICC-based, directional DBS system (Boston Scientific). Patients are followed up to 3-years (post-implant). Study assessments collect the following: TWSTRS, quality-of-life, overall satisfaction, and adverse events.

Results: A total of 50-patients (mean age 56.1-years, 62% females) with focal (cervical) dystonia only, and 95-patients (mean 43.6-years, 58% females) with cervical dystonia in context of segmental or generalized dystonia have been evaluated to date. In the cervical only cohort, a 20-point improvement in overall TWSTRS score (baseline: 42.4) was noted at 6-months (n=35) and sustained up to 1-year (23.1-point improvement, n=30). In those with cervical dystonia in context of segmental or generalized dystonia, an 8.3-point and 7.8-point improvement in overall TWSTRS scores (baseline: 35.1) was noted at 6- (n=62) and 12-months (n=48), respectively. The percentage of those who reported significant improvement as compared with Baseline (Global Impression of Change) at 12-

months follow-up was the following: 91% of patients with cervical only and 82% of patients with cervical and other involved regions.

Discussion: This registry represents the first comprehensive, large-scale collection of real-world outcomes associated with dystonia patients implanted with a directional, MICC-based DBS system.

Conclusions: Preliminary results demonstrate significant improvement in patients with cervical dystonia (alone or in context of segmental or generalized dystonia) following DBS using a system capable of directionality and MICC.

Supplemental Data:

References: 1. Horn A, Reich MM, Ewert S, Li N, Al-Fatly B, Lange F, Roothans J, Oxenford S, Horn I, Paschen S, Runge J, Wodarg F, Witt K, Nickl RC, Wittstock M, Schneider GH, Mahlknecht P, Poewe W, Eisner W, Helmers AK, Matthies C, Krauss JK, Deuschl G, Volkmann J, Kühn AA. Optimal deep brain stimulation sites and networks for cervical vs. generalized dystonia. Proc Natl Acad Sci U S A. 2022 Apr 5;119(14):e2114985119.

Learning Objectives: To assess the following clinical measures: 1) status of cervical dystonia (TWSTRS) 2) assess quality of life 3) assess treatment satisfaction

Financial Disclosures: Prof Albanese has a consulting agreement with Boston Scientific. a) Boston Scientfic b) consultant c) 5-20k

Disclosure: This study is sponsored by Boston Scientific.

O022

Oral Presentations
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 16:30 - 18:20

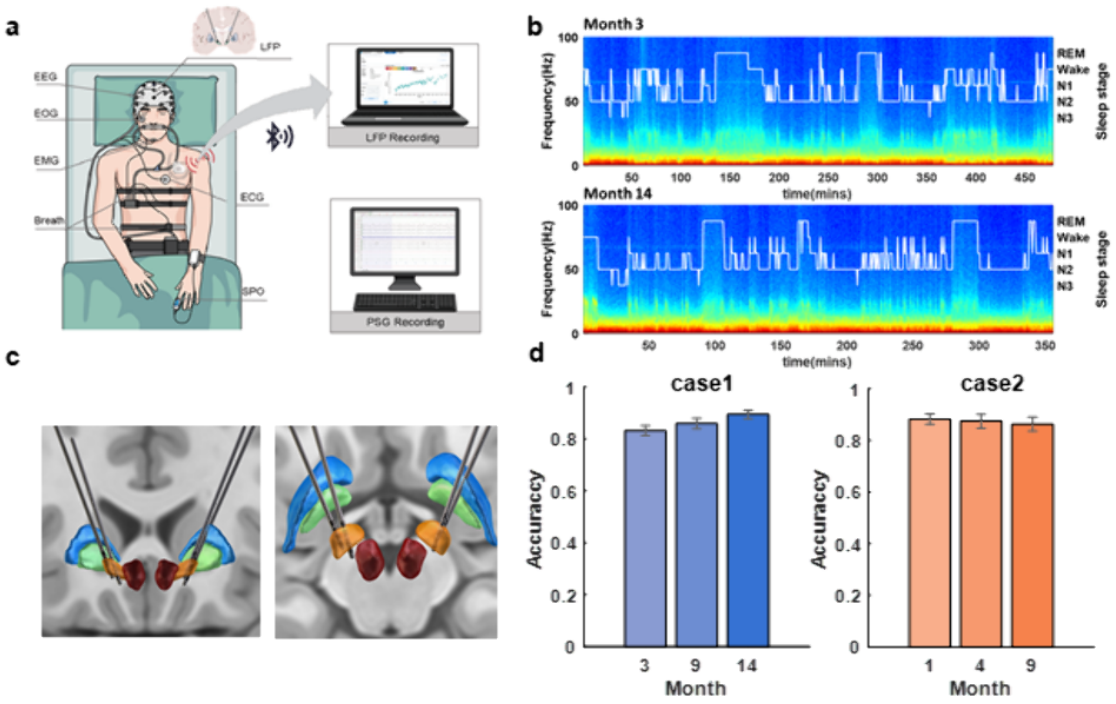
SLEEP STAGE CLASSIFICATION AND APERIODIC ACTIVITY OF STN-LFP AFTER LONG-TERM NEUROSTIMULATION IN PARKINSON'S DISEASE

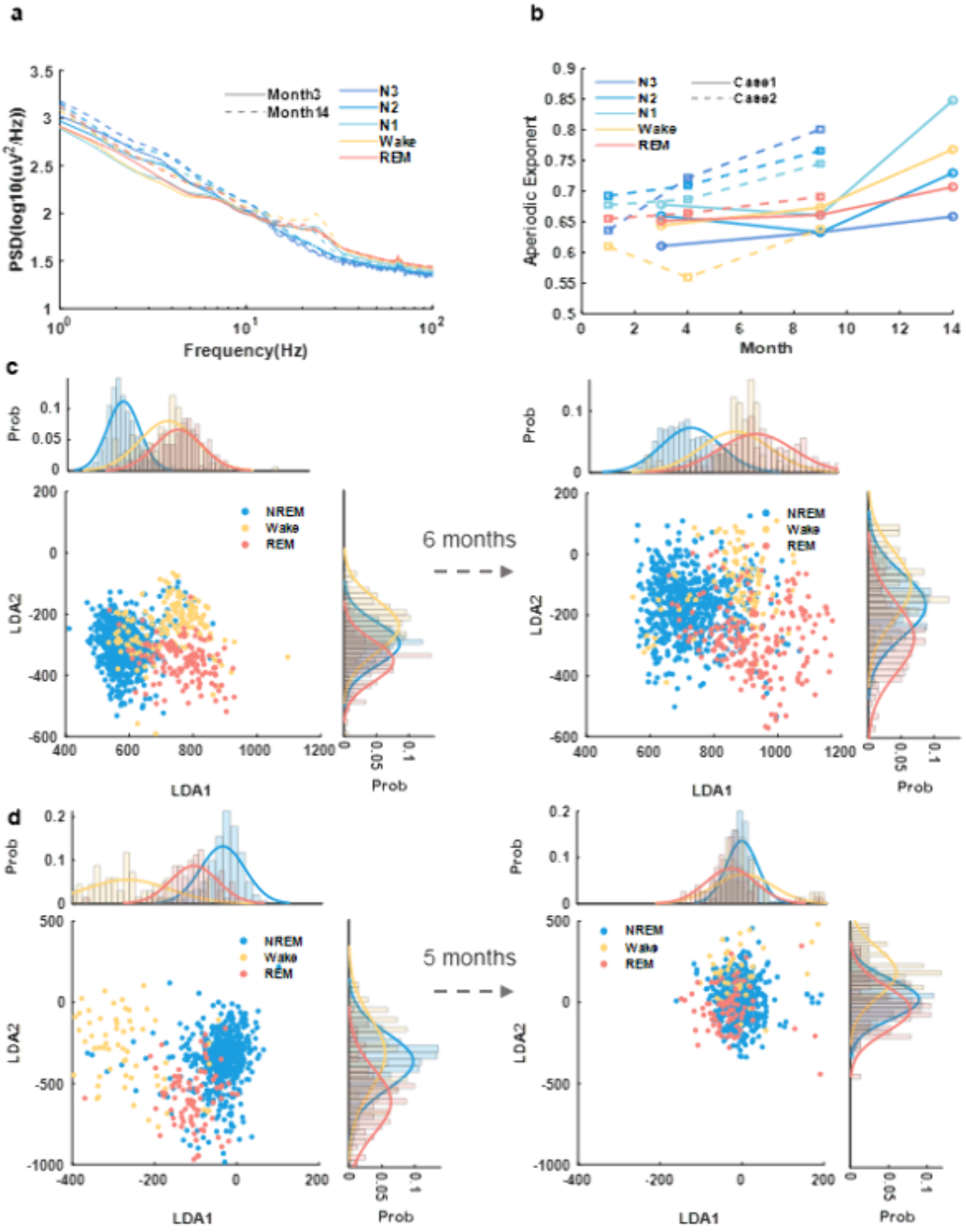
Guokun Zhang, MSBmE, Huiling Yu, MD, Lingxiao Guan, M.S., Yu Fan, BEng, Yuxuan Wu, MSBmE, Hongwei Hao, PhD, Luming Li, PhD
National Engineering Research Center of Neuromodulation, Tsinghua University, Beijing, China

Introduction: Local field potentials (LFPs) of basal ganglia during sleep are associated with sleep dysfunction in Parkinson's disease[1,2] and serve as an indicator for closed-loop DBS based on sleep stage classification[3,4]. However, the feasibility of using subthalamic nuclei (STN) LFPs for sleep stage classification after long-term neuromodulation and their long-term patterns of change remain unknown.

Materials / Methods: We recorded STN-LFPs in two Parkinson's patients with sensing-enabled DBS (G106RS, Beijing PINS Medical Co, China) and polysomnogram during a nocturnal sleep at different follow-up points (Figure1a). Moving window STFT with 2-second Hanning window and 50% overlap was used to estimate power spectra. Random 10-cross-validation was repeated 50 times for sleep stage classification (NREM, Wake and REM) within each follow-up point, utilizing Support Vector Machine (SVM) and the average power of 5 frequency bands (delta, theta, alpha, beta, low gamma). We utilized the FOOOF algorithm[5] to extract aperiodic activity and compared the patterns of exponent changes across the different follow-up points.

Results: Sleep-stage dependent characteristics of STN LFP during DBS ON persisted even after long-term neuromodulation (Figure1b). Furthermore, the accuracy of sleep stage classification within each follow-up point, assessed through cross-validation in the same night, remained consistent over the course of DBS treatment (Figure1d). However, spectra variations were observed across different follow-up points (Figure2a for case1). Exponent of aperiodic activity increased with the duration of DBS treatment (Figure2b). Furthermore, alternation of spectra after long-term neuromodulation resulted in the bias in outputs of sleep classification model. The dimensionality reduction results using the same linear discriminant analysis model, which derived from data collected at the first follow-up point, exhibited shifts after approximately a half year, leading to the misclassifications by the model (Figure2c, d for case1 and case2
respectively).


a
LFP
EEG
EOG
EMG
ECG
Breath
SPO
LFP Recording
PSG Recording
b
Month 3
Month 14
Frequency(Hz)
time(mins)
REM
Wake
N1
N2
N3
Sleep stage
c
d
case1
case2
Accuracy
Month
3
9
14
1
4
9



Discussion: Sleep stage classification based on STN-LFPs facilitates more flexible closed-loop DBS during sleep. Recent research highlights spectral changes, including aperiodic activity[6], in STN-LFPs during wakefulness after long-term DBS treatment. Our findings in sleep STN-LFPs aligned with this observation and indicated the challenge posed by spectral alterations for the long-term effectiveness of parameters of sleep stage model. Consequently, long-term recording is necessary for validating closed-loop algorithms during sleep.

Conclusions: STN-LFPs in DBS ON state could still serve as indicators for decoding sleep stage after long-term neuromodulation. However, the increasement of e aperiodic exponent and other alterations in the spectra after long-term modulation could decrease the accuracy of initial sleep stage classification model.

Supplemental Data:

References: 1. Mizrahi-Kliger AD, Kaplan A, Israel Z, Deffains M, Bergman H. Basal ganglia beta oscillations during sleep underlie Parkinsonian insomnia. *Proc Natl Acad Sci U S A*. 2020;117(29):17359-17368. doi:10.1073/pnas.2001560117 2. Zahed H, Zuzuarregui JRP, Gilron R, Denison T, Starr PA, Little S. The Neurophysiology of Sleep in Parkinson's Disease. *Mov Disord*. 2021;36(7):1526-1542. doi:10.1002/mds.28562 3. Chen Y, Gong C, Hao H, et al. Automatic Sleep Stage Classification Based on Subthalamic Local Field Potentials. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*. 2019;27(2):118-128. doi:10.1109/TNSRE.2018.2890272 4. Gilron R, Little S, Wilt R, Perrone R, Anso J, Starr PA. Sleep-Aware Adaptive Deep Brain Stimulation Control: Chronic Use at Home With Dual Independent Linear Discriminate Detectors. *Front Neurosci*. 2021;15:732499. doi:10.3389/fnins.2021.732499 5. Donoghue T, Haller M, Peterson EJ, et al. Parameterizing neural power spectra into periodic and aperiodic components. *Nat Neurosci*. 2020;23(12):1655-1665. doi:10.1038/s41593-020-00744-x 6. Darmani G, Drummond NM, Ramezanpour H, et al. Long-Term Recording of Subthalamic Aperiodic Activities and Beta Bursts in Parkinson's Disease. *Movement Disorders*. n/a(n/a). doi:10.1002/mds.29276

Acknowledgements:

Learning Objectives: 1. Educational Objective: Foster an understanding of the evolving dynamics in neurostimulation and sleep research. **Desired Result:** Encourage attendees to appreciate the broader implications of research in neurostimulation and sleep dynamics by showcasing how these fields intersect and evolve over time. **2. Educational Objective:** Promote critical thinking about the applications of LFP data in closed-loop neuromodulation. **Desired Result:** Inspire critical thinking among participants on how LFP data can be used for dynamic neuromodulation and the potential hurdles and opportunities it presents. **3. Educational Objective:** Encourage a long-term perspective in algorithm validation. **Desired Result:** Motivate researchers to think beyond immediate results by highlighting the importance of long-term data collection for refining and validating algorithms in various scientific domains.

Financial Disclosures: No significant relationships

Disclosure: Luming Li and Hongwei Hao serve on the scientific advisory board for Beijing Pins Medical Co., Ltd and are listed as inventors in issued patents and patent applications on the deep brain stimulator used in this work.

O023

Oral Presentations
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 16:30 - 18:20

STIMULATION OF MONOPOLAR SENSING-DEFINED OPTIMAL CONTACTS FOR PARKINSON'S DISEASE DBS PROGRAMMING CORRELATES WITH IMPROVED KINEMATICS AND REDUCED LOCAL FIELD POTENTIAL AMPLITUDE IN THE BETA FREQUENCY

John Thompson, PhD[1], Erin Radcliffe, BSc (Hons)[2], Abbey Holt-Becker, PhD[3], Michelle Case, PhD[3], Caleb Zarns, BS[3], Robert Raike, PhD[3], Steven Ojemann, MD[2], Daniel Kramer, MD[2], Drew Kern, MD[4]
[1]University of Colorado Anschutz Medical Campus, Psychiatry, Aurora, United States of America, [2]University of Colorado Anschutz Medical Campus, Neurosurgery, Aurora, United States of America, [3]Medtronic, Minneapolis, United States of America, [4]University of Colorado Anschutz Campus, Neurology, Aurora, United States of America

Introduction: Introduction: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective surgical treatment for advanced Parkinson's disease (PD) characterized by motor complications including motor fluctuations and dyskinesias. Use of sensing-guided stimulation programming remains under investigation. Features derived from the beta frequency range (13-30 Hz) in STN local field potentials (LFP) are electrophysiological signatures of PD that correlate with impaired movement regulation. These temporal and spectral features of oscillatory beta may be useful signals of interest for DBS programming and adaptive DBS (aDBS) control algorithm development.

Materials / Methods: Methods/Materials: Methods/Materials: To examine whether monopolar sensing-defined contacts exhibited improved outcomes, we compared MDS-UPDRS assessments between two conditions: 1) contacts defined by monopolar sensing of beta power (temporary investigational software unlock on the Medtronic Percept™ PC; Minneapolis MN, USA) and 2) traditional monopolar review (amplitude adjusted while pulse width (60 ms) and frequency (130 Hz) held constant to evaluate for adverse effects and clinical benefit). We collected kinematic timeseries data (extrapolated from video recordings using deep learning-based neural network classification) synchronized with LFP from 1 PD patient (N=2 hemispheres). For each stimulation condition, patients performed motor tasks used in the Movement Disorder Society Unified Parkinson's Disease Rating Scale Part III: Motor Examination (MDS-UPDRS III): Finger Tapping, Hand Movements, Pronation-Supination Movement of Hands, and Tremor items. Computer vision hardware, semi-automated markerless motion tracking methods, and trained residual deep learning-based neural networks were utilized to measure and classify neuromotor behavior based on 2D coordinate timeseries data. Video data was composed of anatomically labeled points to generate X and Y positional data that were used to compute timeseries representations of displacement, velocity, and acceleration to characterize motor performance.

Results: Results: As a proof of concept, in N = 1 STN-DBS subject, we observed that for 6 movements in each condition, the monopolar sensing-defined contact condition induced increased motor mobility (3%) across MDS-UPDRS movements and decreased the LFP beta power magnitude (35%), compared to traditional monopolar review.

Discussion: Discussion: Preliminary results (in n = 1 subject) suggest that utilizing monopolar sensing to select optimal contacts for therapeutic stimulation may perform as well as traditional monopolar review and is potentially associated with improved movement metrics and decreased beta power magnitude in STN.

Conclusions: Conclusions: Findings demonstrate the efficacy and efficiency of computational PD evaluation tools used in clinical applications and expand upon the utility of electrophysiology-guided and kinematics-informed strategies for optimizing DBS contact localization and therapeutic targeting.

Supplemental Data:

References: Yin, Z., Zhu, G., Zhao, B., Bai, Y., Jiang, Y., Neumann, W.-J., Kühn, A. A., & Zhang, J. (2021). Local field potentials in Parkinson's disease: A frequency-based review. *Neurobiology of Disease*, *155*, 105372. https://doi.org/10.1016/j.nbd.2021.105372 Lewis, S., Radcliffe, E., Ojemann, S., Kramer, D. R., Hirt, L., Case, M., Holt-Becker, A. B., Raike, R., Kern, D. S., & Thompson, J. A. (2023). Pilot Study to Investigate the Use of In-Clinic Sensing to Identify Optimal Stimulation Parameters for Deep Brain Stimulation Therapy in Parkinson's Disease. *Neuromodulation: Technology at the Neural Interface*. https://doi.org/https://doi.org/10.1016/j.neurom.2023.01.006 Radcliffe, E. M., Baumgartner, A. J., Kern, D. S., Borno, M. A., Ojemann, S., Kramer, D. R., & Thompson, J. A. (2023). Oscillatory beta dynamics inform biomarker-driven treatment optimization for Parkinson's disease. *Journal of Neurophysiology*, *129*(6), 1492-1504. https://doi.org/10.1152/jn.00055.2023 Torrecillos, F., Tinkhauser, G., Fischer, P., Green, A. L., Aziz, T. Z., Foltynie, T., Limousin, P., Zrinzo, L., Ashkan, K., Brown, P., & Tan, H. (2018). Modulation of Beta Bursts in the Subthalamic Nucleus Predicts Motor Performance. The Journal of Neuroscience, 38(41), 8905-8917. https://doi.org/10.1523/jneurosci.1314-18.2018 Tien, R. N., Tekriwal, A., Calame, D. J., Platt, J. P., Baker, S., Seeberger, L. C., Kern, D. S., Person, A. L., Ojemann, S. G., Thompson, J. A., & Kramer, D. R. (2022). Deep learning based markerless motion tracking as a clinical tool for movement disorders: Utility, feasibility and early experience [Perspective]. Frontiers in Signal Processing, 2. https://doi.org/10.3389/frsip.2022.884384

Acknowledgements: We are ever grateful for the participation of the subjects in this study.

Learning Objectives: 1. Objective: Gain an overview of Parkinson's disease (PD), the application of subthalamic nucleus (STN) deep brain stimulation (DBS) , and the significance of local field potential (LFP) features within the beta frequency range (13-30 Hz) in relation to PD symptom severity. **Desired Result**: Attendees will gain an understanding of general PD characteristics, the therapeutic purpose of DBS, and how oscillatory beta features correlate with PD motor symptoms. **2. Objective**: Learn about computational tools and methods used to quantify neuromotor behavior and neuromodulation responses in PD.
- Desired Result: Attendees will appreciate the combination of computer vision and streaming LFP for assessing PD motor behavior and symptom response to stimulation. **3. Objective**: Understand the increasing complexity of DBS therapy programming and the value of applying computational tools. **Desired Result**: Attendees will comprehend how objective assessments via computer vision and brain signal processing can potentially guide enhancements in DBS therapy approaches for improved patient outcomes.

Financial Disclosures: JAT: research support and speaking honoraria from Medtronic, research support from Boston Scientific ER: No significant relationships DRK: No significant relationships AHB: Employee of Medtronic MC: Employee of Medtronic CZ: Employee of Medtronic RSR: Employee of Medtronic SO: Fellowship support from Medtronic DSK: research support from Medtronic, research support from Boston Scientific, research support from Abbott

Disclosure: JAT: research support and speaker honoraria from Medtronic

O024

Oral Presentations
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 16:30 - 18:20

ELECTRICAL STIMULATION OF THE SUBTHALAMIC NUCLEUS VERSUS FOREL'S FIELD IN PATIENTS WITH PARKINSON'S DISEASE. EFFECTS ON MOTOR SYMPTOMS AND QUALITY OF LIFE

Juliana Passinho, MD[1], Maria Rocha, MD[1], Paulo Filho, MD[1], Diogo Soriano, MD[2], Fábio Godinho, PhD[3]
[1]Santa Marcelina hospital, Division Of Neurosurgery, SAO PAULO, Brazil, [2]Federal University of ABC, Engineering Department, SAO PAULO, Brazil, [3]University of São Paulo, Division Of Neurosurgery, SAO PAULO, Brazil

Introduction: Gait and balance disorders are challenging issues in Parkinson's disease. Deep brain stimulation (DBS) centered at the Fields of Forel has been proposed as an alternative to subthalamic nucleus to treat motor symptoms, including gait disorders. No long-term follow-up study has compared the two targets.[1,2,3,4]

Materials / Methods: Twenty-two patients were evaluated before and five years after DBS (10 Forel and 12 STN). Motor symptoms were assessed using Unified Parkinson's Disease Rating Scale (UPDRS III), quality of life with PDQ-39 scale, and axial symptoms with the Freezing of Gait questionnaire (FOG-Q). Cognitive function was measured using the Mattis Scale. Levodopa-equivalent dosage was measured.

Results: Forel DBS group was older (P= < 0.0001) and showed longer time of disease (P= < 0.0001) than STN patients. Compared to preoperative period, Forel DBS resulted in a reduction of 32.16 % in UPDRS III scores (P= < 0.0002), a decrease of 35,3 % in FOG scores (P =0.0083), and a 25,94 % improvement in PDQ-39 scores (P=0.002). There was a 7.5 % decline in cognition (P= 0.0069). Daily levodopa dosage was reduced by 19% (P= 0.001). STN DBS resulted in a 39,45% reduction in UPDRS III scores (P=< 0.0001), a decrease in PDQ-39 scores by 33,16% (P=<0.0001), and a 23,67 % reduction in FOG scores (P= 0.0007). There was a decline of 1.6 % in cognition (P= 0.0032), and a reduction in daily levodopa dosage by 15.06% (P =0.02).

Discussion: Fields of Forel allow the passage of most pallidothalamic fibers within a 4mm diameter area. Operating in this location is less invasive than making multiple internal pallidal penetrations, which would be necessary to achieve equivalent thalamic desinhibition [5,6]. Improvements in axial symptoms support the FF as a potential target to treat these symptoms. Anatomical studies have shown that pallidotegmental fibers course through the FF[7,8] and may drive the pedunculopontine tegmental nucleus (PPN) to a dysfunctional state, participating to axial symptoms in PD.

Conclusions: Both Forel and STN DBS provided motor and quality of life improvement over a 5-year period. Forel demonstrated a remarkable reduction in FOG compared to STN. This suggests that Forel could be a promising therapeutic option for severe PD patients with significant axial symptoms resistant to levodopa. Forel group showed a higher decline in cognition compared to the STN group. This could be attributed to the older age and longer duration of disease in the Forel group.

Supplemental Data: None

References: 1 -Raccagni C, Nonnekes J, Bloem BR, et al. Gait and postural disorders in parkinsonism: a clinical approach. J Neurol. 2020;267(11):3169-3176.
2- Godinho F, Magnin M, Filho PT, et al. Stereotactic lesion in the Forel's field H: a 2-years prospective open-label study on motor and nonmotor symptoms, neuropsychological functions, and quality of life in Parkinson disease. Neurosurgery. 2019;85(4): E650-E659.
3 - Chung BS, Park JS. Whole course of pallidothalamic tracts identified on the sectioned images and surface models. Clin Anat. 2020;33(1):66-76.

4- Parent M, Parent A. The pallidofugal motor fiber system in primates. Parkinsonism Relat Disord. 2004;10(4):203-211.
5 -August Forel. Untersuchungen über die Haubenregion und ihre oberen Verknüpfungen im Gehirne des Menschen und einiger Säugethiere, mit Beiträgen zu den Methoden der Gehirnuntersuchung. Archiv für Psychiatrie und Nervenkrankheiten volume7, pages 393–495(1877).
6 -christoph aufenberg. A revival of Spiegel's campotomy: long term results of the stereotactic pallidothalamic tractotomy against the parkinsonian thalamocortical dysrhythmia Thalamus & Related Systems, 2005, 3(2), 121–132. #2007 Cambridge University Press doi:10.1017/S147292880700012X Printed in the United Kingdom
7 -Magnin M, Jeanmonod D, Morel A, Siegemund M. Surgical control of the human thalamocortical dysrhythmia. II: Pallidothalamic tractotomy in Parkinson's disease. Thalamus Related Sys. 2001;1(1):81-89.
8 -Sakai ST, Inase M, Tanji J. Comparison of cerebellothalamic and pallidothalamic projections in the monkey (Macaca fuscata): a double anterograde labeling study. J Comp Neurol.

Acknowledgements: None

Learning Objectives: 1- Understand the difference in the long-term effects of deep brain stimulation (DBS) targeting the Fields of Forel and DBS in the Subthalamic Nucleus (STN) in patients with Parkinson's disease. 2- Evaluate whether DBS in the Fields of Forel is a promising therapeutic option for severe Parkinson's disease patients with axial symptoms resistant to levodopa treatment. 3- Identify the factors contributing to differences in outcomes, such as age, disease duration, and cognitive decline, and comprehend how these factors can impact the selection of the DBS target for patients with Parkinson's disease.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O025

Oral Presentations
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 16:30 - 18:20

COMPARISON OF DENTATO-RUBRO-THALAMIC TRACTOGRAPHY METHODS BASED ON THE ANATOMY OF THE RUBRAL WING

Assaf Berger, MD[1], Jongchul Chung, MD[1], Zane Schnurman, MD[1], Valentin Stepanov, MD[2], Ling Pan, MD[1], Timothy M. Shepherd, MD[2], Alon Mogilner, MD, PhD[3]
[1]NYU Langone Medical Center, Department Of Neurological Surgery, New York, United States of America, [2]NYU Langone Medical Center, Department Of Radiology, New York, United States of America, [3]New York University Grossman School of Medicine, New York, United States of America

Introduction: Precise localization of the dentato-rubro-thalamic (DRT) tract can facilitate anatomical targeting in MRI-guided high-intensity focused ultrasound (HIFU) thalamotomy and thalamic deep brain stimulation (DBS) for tremor. The anatomical segment of DRT fibers adjacent to the Ventral Intermediate Nucleus of the Thalamus (VIM), referred to as the rubral wing (RW), may be directly visualized on the fast gray matter acquisition T1 inversion recovery (FGATIR). We compared reproducibility, lesion overlap and clinical outcomes when reconstructing the DRT tract using a novel anatomically-defined RW region of interest (ROI), DRT-RW, to an existing tractography method based on the posterior subthalamic area ROI (DRT-PSA).

Materials / Methods: We reviewed data of 23 patients with either essential tremor (n=18) or tremor-predominant Parkinson's disease (n=5) that underwent HIFU thalamotomy, targeting the VIM. DRT-tractography, ipsilateral to the lesion, was created based on either DRT-PSA or DRT-RW. Volume sections of each tract were created and Dice similarity coefficients (DSC) were used to measure spatial overlap between the 2 tractographies. Post-HIFU lesion size and location (on post-operative T2 MRI) was correlated with tremor outcomes and side-effects for both DRT-tractography methods and the RW itself.

Results: DRT-PSA passed through the RW and DRT-RW intersected with the ROIs of the DRT-PSA in all 23 cases. A higher percentage of the RW was ablated in patients that achieved tremor control (19±6%) versus those without tremor relief (7±6%, p=0.017). In patients with tremor control 6-months post-op (n=12), those with side-effects (n=6) had larger percentages of their tracts ablated in comparison to those without side-effects in both DRT-PSA (44.82±12.10% vs 24.25±11.29%, p=0.025) and DRT-RW (35.42±13.22% vs 21.74±8.64%, p=0.03).

Discussion: We looked at the feasibility of reconstructing the DRT based on MRI-visible anatomical landmarks, including rubro-thalamic connections known as the "rubral-wing" and the SCP, defined as the DRT-RW. In all patients, both methods created DRT tracts that cross mutual ROIs and did not overlap with motor or sensory tracts in the vicinity of the HIFU-lesion. Patients with tremor control had a higher degree of ablation of the RW itself. Both DRT-PSA, DRT-RW and the RW itself were significantly more affected by the lesion in subjects with treatment-related adverse-effects, particularly ataxia.

Conclusions: Tractography of the dentato-rubro-thalamic tract could be reconstructed by direct anatomical visualization of the RW. Further development of anatomically-based methods is expected to enable quicker, more reproducible and less operator-dependent treatment planning.

Supplemental Data:

References: Bot M, Pauwels R, van den Munckhof P, et al. The Fast Gray Matter Acquisition T1 Inversion Recovery Sequence in Deep Brain Stimulation: Introducing the Rubral Wing for Dentato-Rubro-Thalamic Tract Depiction and Tremor Control. *Neuromodulation*. Published online January 15, 2022:S1094-7159(21)06948-8. doi:10.1016/j.neurom.2021.11.015

Acknowledgements:

Learning Objectives: 1. We looked at the feasibility of reconstructing the DRT based on MRI-visible anatomical landmarks, including rubro-thalamic connections known as the “rubral-wing” and the SCP, defined as the DRT-RW. 2. Assessing the reproduciblity of the tractography 3. Assessing the complexity and duration to perform each of the tractography methods.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O026

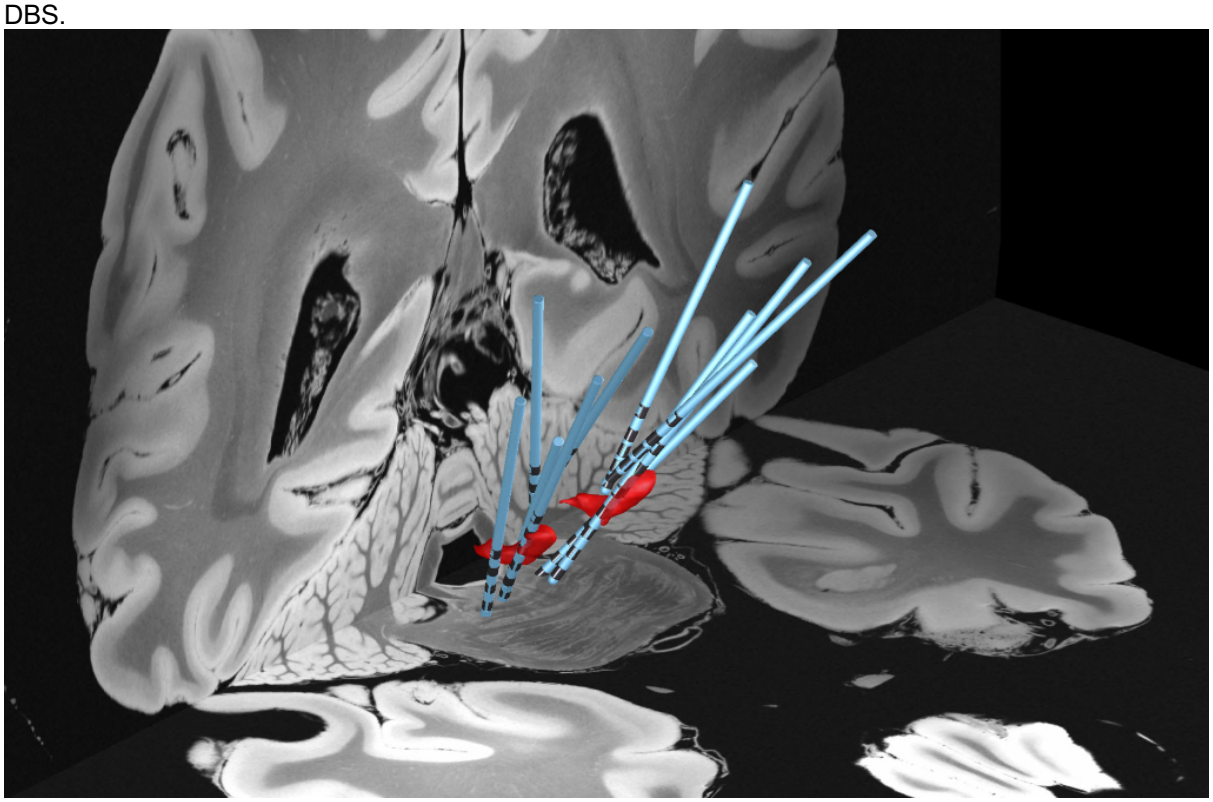
Oral Presentations
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 16:30 - 18:20

FIRST-IN-MAN TRIAL OF PEDUNCULOPONTINE REGION DEEP BRAIN STIMULATION FOR AUTONOMIC AND GAIT DYSFUNCTION IN MULTIPLE SYSTEM ATROPHY

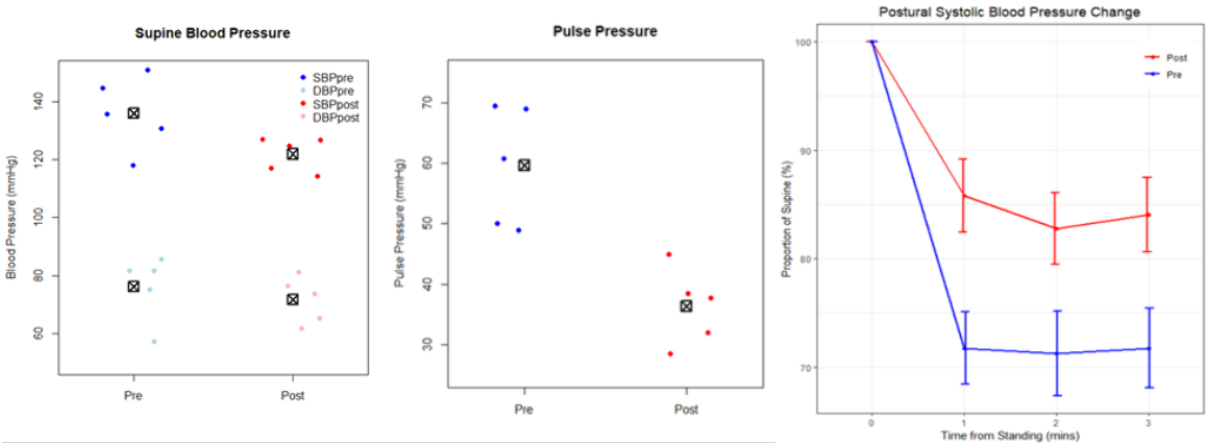
Sean Martin, FRCS(SN)[1], Amir Divanbeighi Zand, BA BM BCh[1], Alceste Deli, MD, MSc, DPhil[1], Nagaraja Sarangmat, MD[2], Marko Bogdanovic, PhD[3], Michele Hu, PhD[3], Tipu Aziz, FMedSci[1], Tim Denison, PhD[3], James Fitzgerald, MB ChB, PhD[1], Alexander Green, PhD FRCS(SN)[1]
[1]University of Oxford, Nuffield Department Of Surgical Sciences, Oxford, United Kingdom, [2]Oxford University Hospitals, Neurology, Oxford, United Kingdom, [3]University of Oxford, Nuffield Deparment Of Clinical Neurosciences, Oxford, United Kingdom

Introduction: Multiple system atrophy is a rare progressive neurodegenerative disease, with an average survival of 6 to 10 years [1-3]. It is characterised by severe autonomic failure and parkinsonism. The PPN is a region critically involved in the control of locomotion, and modulation of autonomic outflow [4].

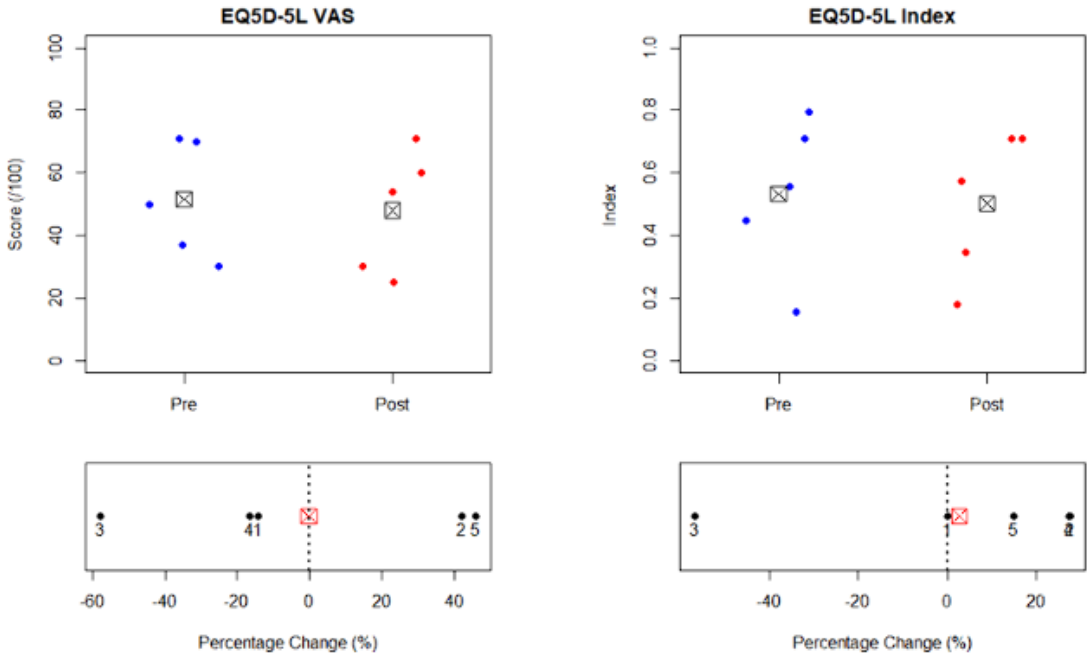
Materials / Methods: Five patients with MSA underwent gait, autonomic, disease activity, and quality of life assessments before and after bilateral PPN
DBS.

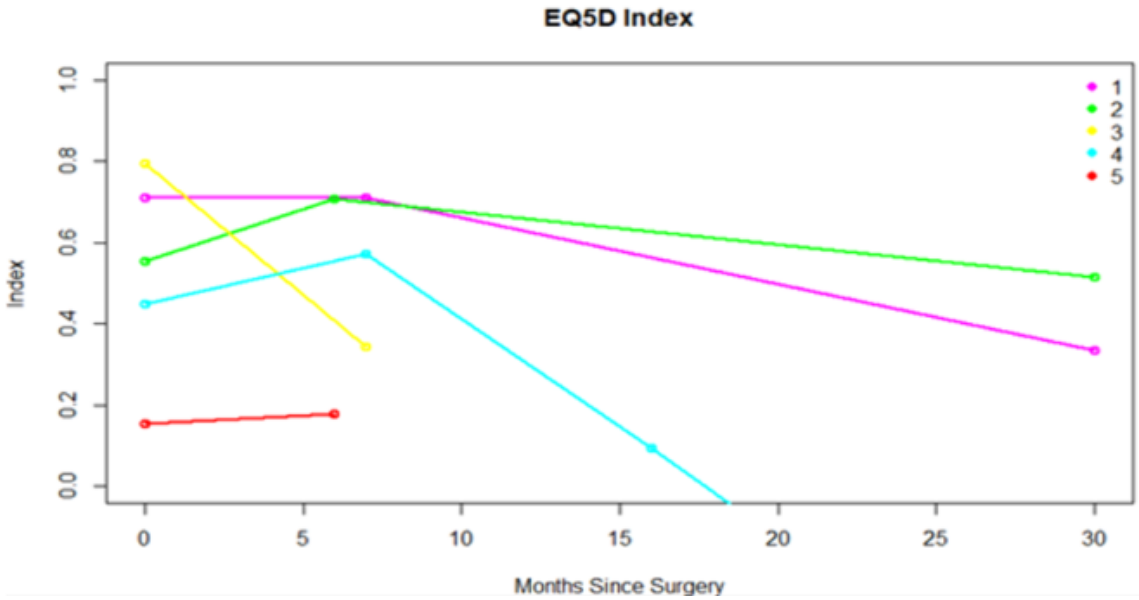


Results: Blood pressure: Mean supine systolic blood pressure improved (135.9±12.7mmHg vs. 121.9±5.9mmHg, p=0.02). In those with orthostatic hypotension (4/5), all had improved postural drop (mean improvement in drop of 45.4% compared to baseline , p=0.03). Pulse pressure reduced significantly (59.6mmHg vs. 36.4mmHg,
p=0.005).



Gait: Gait velocity and balance (GAITRite®) were improved. Median FOGQ reduced from 17 to 11, (p=0.02) and remained better than baseline at one year (p=0.04). **Bladder function:** Participant recorded input and output volumes (72 hour) showed fewer night-time urinary events, and larger volumes passed with each event. Functional bladder capacity (total capacity - residual volume) increased. **Quality of life:** The EQ5D-5L is a generic measure of health-related quality of life – a higher score is better. The mean visual analogue scale score before surgery was 51.6, and after surgery was 48 (p=0.76). The mean preoperative EQ5D-5L utility was 0.533 and was 0.502 post-operatively (p=0.79) - though early improvements were seen in most patients (bottom panel).





MSA disease activity: Unified MSA Rating Scale history score worsened after surgery (20.0 to 20.8 p=0.48). Motor score improved though not significantly, (21.2 to 17.6, p=0.13). **Autonomic symptoms:** COMPASS-31 (autonomic symptom severity) reduced from 35.4 to 25.0 (p=0.31).Orthostatic intolerance subscore improved from 19.6 to 11.6 (p=0.18) and bladder subscore from 5.2 to 3.4 (p=0.18).

Discussion: Blood pressure, orthostatic hypotension, walking balance and speed, urinary bladder capacity and emptying can all be modulated with stimulation of the PPN in MSA. Given that MSA is relentless and rapid, it is remarkable that post-operative results are stable or better in most measured domains. However, we were unable to show that these interventions made an appreciable impact on quality of life.

Conclusions: PPN DBS objectively improves some physiological parameters in MSA but does not improve quality of life.

Supplemental Data:

References: 1. Ben-Shlomo, Y., et al. (1997). Survival of patients with pathologically proven multiple system atrophy: a meta-analysis. *Neurology*, *48*(2), 384-393. https://doi.org/10.1212/wnl.48.2.384 2. Low, P. A., et al. (2015). Natural history of multiple system atrophy in the USA: a prospective cohort study. *Lancet Neurol*, *14*(7), 710-719. https://doi.org/10.1016/S1474-4422(15)00058-7 3. Wenning, G. K., et al., European Multiple System Atrophy Study, G. (2013). The natural history of multiple system atrophy: a prospective European cohort study. *Lancet Neurol*, *12*(3), 264-274. https://doi.org/10.1016/S1474-4422(12)70327-7 4. Hyam, J.A., et al., *The pedunculopontine region and breathing in Parkinson's disease.* Ann Clin Transl Neurol, 2019. **6**(5): p. 837-847.

Acknowledgements:

Learning Objectives: 1. PPN region DBS is safe in MSA 2. PPN region DBS improves autonomic physiology in MSA 3. PPN region DBS does not improve quality of life in MSA

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O027

Oral Presentations
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 16:30 - 18:20

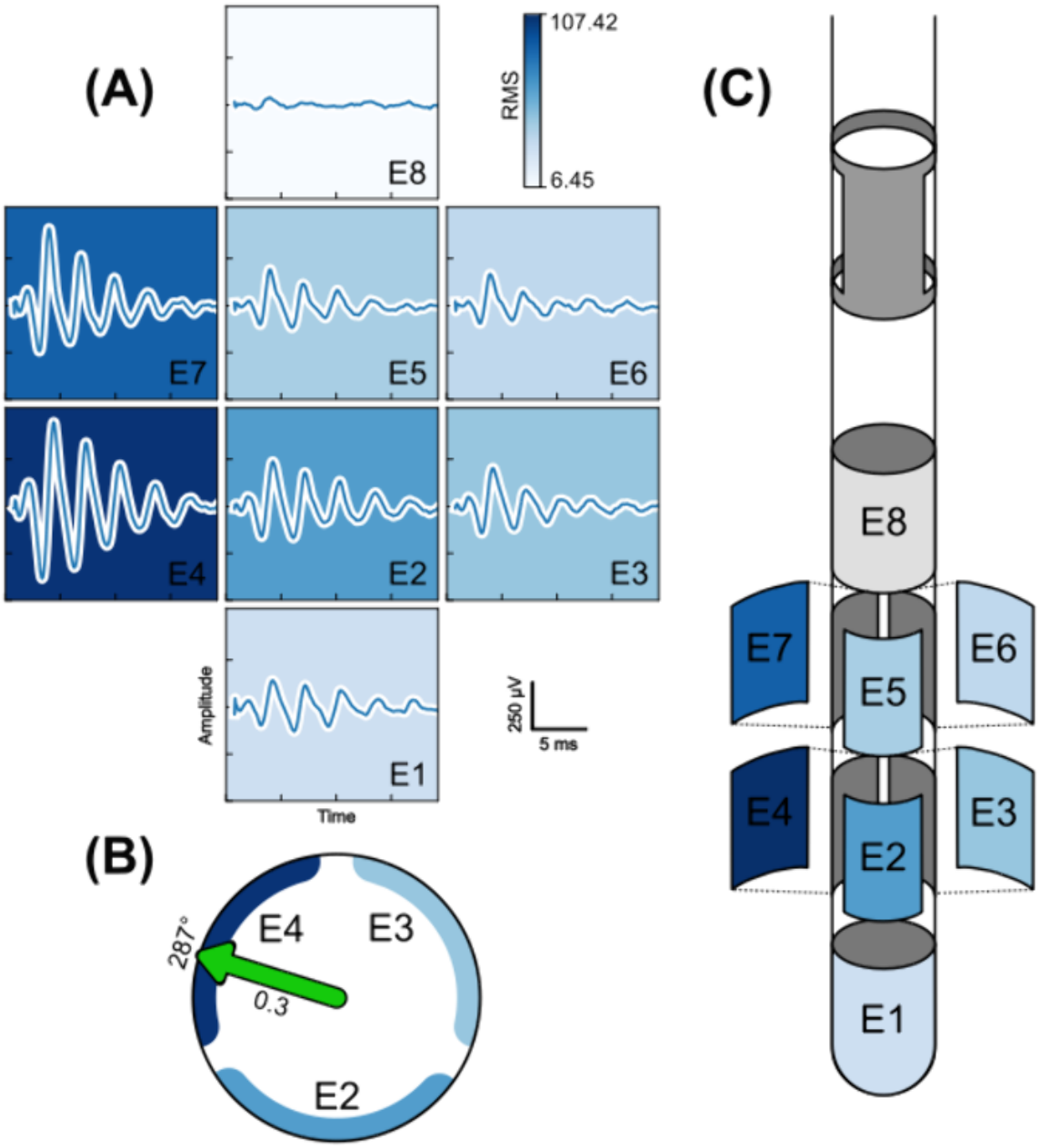
EVOKED RESONANT NEURAL ACTIVITY CAN CONFIRM LEAD PLACEMENT IN SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION

Thomas Tonroe, BEng(Hons)[1,2], Wee-Lih Lee, PhD[1,3], Matthew Petoe, PhD[1,3], Ashton Moorhead, BSc (Hons)[1], Kiaran Lawson, PhD[1], Kristian Bulluss, PhD[1,4,5,6,7], Wesley Thevathasan, PhD[1,7,8,9], Hugh McDermott, PhD[3,7], Thushara Perera, PhD[1,3,7]
[1]Bionics Institute, Melbourne, Australia, [2]RMIT University, School Of Engineering, Melbourne, Australia, [3]University of Melbourne, Medical Bionics Department, Melbourne, Australia, [4]Austin Hospital, Department Of Neurosurgery, Melbourne, Australia, [5]Cabrini Hospital, Department Of Neurosurgery, Melbourne, Australia, [6]St Vincent's Hospital Melbourne, Department Of Neurosurgery, Melbourne, Australia, [7]Deep Brain Stimulation Technologies, Melbourne, Australia, [8]Austin Hospital, Department Of Neurology, Melbourne, Australia, [9]The Royal Melbourne Hospital, Department Of Neurology, Melbourne, Australia

Introduction: Deep brain stimulation (DBS) is an effective therapy for people with movement disorders. Evoked resonant neural activity (ERNA, Fig. 1a) is a decaying waveform evoked by DBS pulses applied near the dorsal region of the subthalamic nucleus (STN) [1]. The ERNA amplitude and its distribution across electrodes vary with distance from the dorsal STN, characteristics which could be harnessed to aid DBS lead implantation [2]. Here, we report the performance of an ERNA-based binary classifier trained to confirm acceptable positioning of DBS leads.

Materials / Methods: Following informed consent, 65 people with Parkinson's disease were recruited into the study. Each participant had directional DBS electrodes (Vercise™ Cartesia™ DB-2202, Boston Scientific, USA, Fig. 1c) bilaterally implanted, targeting each dorsal STN. Lead placement was guided by microelectrode recordings, test stimulation, and intraoperative neuroimaging. When the clinicians judged the lead placement to be unsatisfactory, it was shifted to a new trajectory. ERNA and neuroimaging were collected for 141 trajectories. Features extracted from ERNA included maximum amplitude across the eight electrodes and the centre-of-mass magnitude and direction (Fig. 1a, b). To train the classifier, lead positions were evaluated using postoperative neuroimaging by an expert neurologist. If most of the lead diameter lay outside the STN boundary or the lead was >1.5mm from the dorsal STN midpoint, the position was judged to be unacceptable; otherwise, the position was acceptable. A supervised K-nearest Neighbours binary classifier was trained using these judgements. A nested 5-fold cross-validation was repeated ten times to evaluate the classifier's performance in predicting the acceptability of lead

positions.



Results: Using ERNA, the classifier predicted an acceptable or unacceptable trajectory with 81.2% balanced accuracy (positive predictive value: 83.9%; negative predictive value: 81.6%).

Discussion: ERNA could be used in conjunction with other tools to position leads in the dorsal STN thereby improving implantation accuracy. This has immediate benefit to patient outcomes and could reduce the incidence of revision surgery.

Conclusions: This evidence supports potential use of ERNA in surgical decision-making.

Supplemental Data:

References: [1] N. C. Sinclair *et al.*, "Subthalamic nucleus deep brain stimulation evokes resonant neural activity," *Annals of Neurology,* vol. 83, no. 5, pp. 1027-1031, 2018, doi: 10.1002/ana.25234. [2] W. Thevathasan, N. C. Sinclair, K. J. Bulluss, and H. J. McDermott, "Tailoring Subthalamic Nucleus

Deep Brain Stimulation for Parkinson's Disease Using Evoked Resonant Neural Activity," *Frontiers in Human Neuroscience,* vol. 14, 2020, doi: 10.3389/fnhum.2020.00071.

Acknowledgements: The authors acknowledge Amanda Goy, Deanne Dawe, Jennifer Nagao, Joy Tan, Paul Minty, and San San Xu for their contributions to the studies that are the basis of this analysis. The support of Deep Brain Stimulation Technologies for this project is gratefully acknowledged.

Learning Objectives: 1. Describe three features of the ERNA signal that hold useful information about acceptable DBS lead placement within the dorsal STN. 2. Recognize the performance of ERNA in predicting the acceptability of a leads position during initial implantation for STN-DBS. 3. Understand the potential of ERNA in assisting surgical decision-making for improving implantation accuracy.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O028

Oral Presentations
NEUROMODULATION FOR NEUROPSYCHIATRIC DISORDERS
13-05-2024 16:30 - 18:20

NEUROMODULATORY DISRUPTION OF PATHOLOGICAL CIRCADIAN NEURAL RHYTHMS RESTORES APPROACH-AVOIDANCE BALANCE IN OCD

Nicole Provenza, PhD[1], Sandesh Reddy, BSc (Hons)[1], Sameer Rajesh, BSc (Hons)[1], Anthony Allam, BSc (Hons)[1], Nabeel Diab, BSc (Hons)[1], Gabriel Reyes, BSc (Hons)[1], Kalman Katlowitz, MD[1], Huy Dang, BSc (Hons)[1], Ricardo Najera, MD[1], Nisha Giridharan, MD[1], Garrett Banks, MD[1], Ben Shofty, MD[2], Benjamin Hayden, PhD[1], Jeffrey Herron, PhD[3], Eric Storch, PhD[4], Ankit Patel, PhD[5], Wayne Goodman, MD[4], Sameer Sheth, MD[1]
[1]Baylor College of Medicine, Neurosurgery, Houston, United States of America, [2]University of Utah, Neurosurgery, Salt Lake City, United States of America, [3]University of Washington, Seattle, United States of America, [4]Baylor College of Medicine, Menninger Department Of Psychiatry And Behavioral Sciences, Houston, United States of America, [5]Baylor College of Medicine, Neuroscience, Houston, United States of America

Introduction: Formulating the diagnosis of psychiatric disorders within a cognitive neuroscience framework may increase mechanistic understanding and help interpret neural biomarkers of response. One such framework, response selection and inhibitory control, describes a continuum of behavior from unbridled “approach” conduct marked by impulsivity to “avoidant” phenotypes characterized by fear and anxiety (Fig. 1). Obsessive-compulsive disorder (OCD) lies squarely in the latter extreme (Fig. 1A). The efficacy of therapies such as exposure and response prevention is thought to derive from their ability to promote the approach and tolerance of otherwise triggering stimuli. Initiation of DBS therapy often produces acute increases in talkativeness and extroversion reminiscent of healthy approach behaviors (Fig. 1B), and over-stimulation can induce disinhibited behavior indicating overabundance of the approach phenotype (Fig. 1C). Here, our goal was to understand the neurophysiological basis of the shift from avoidant to approachful behaviors that leads to clinical response after DBS for OCD.

Materials / Methods: In five individuals with treatment-resistant OCD receiving DBS targeted to the ventral striatum (VS), we recorded local field potential (LFP) power in the alpha-theta (9 Hz) band in continuous 10-minute intervals for several months. These long-term recordings were initiated during surgery and endured throughout periods of persistent OCD symptoms, disinhibition, and clinical response.

Results: Our results reveal neurophysiological correlates of the approach-avoidance framework that enable prediction of clinical state from neural data. The central neural feature, circadian fluctuations of low-frequency (9 Hz) power, is highly prominent prior to VS DBS initiation, a state that is marked by the highly avoidant behavior characteristic of severe OCD. The degree of pro-approach behavior acutely elicited by VS DBS closely mirrors the extent of disruption of this circadian pattern (Fig. 2E,F). In the chronic state, the statistical measure of sample entropy, which encompasses both diminution in circadian strength and increased dispersion of LFP power across the day, reliably predicts long-term clinical status (Fig. 3A,B; $p<10^{-5}$).

Discussion: The availability of chronic, continuous neural data provides new perspectives for neurobehavioral analyses. Traditionally, neural biomarkers of psychiatric states have relied on brief snapshots of neural data. Our findings indicate that neural biomarkers of slowly evolving clinical states may not be episodic variations from baseline but rather features of variation in the baseline itself, as reflected by circadian neural patterns.

Conclusions: These results reveal a reliable neurophysiological biomarker corresponding to location along an approach-avoidance axis and a predictor of eventual response to treatment for disorders of inhibitory control.

Supplemental

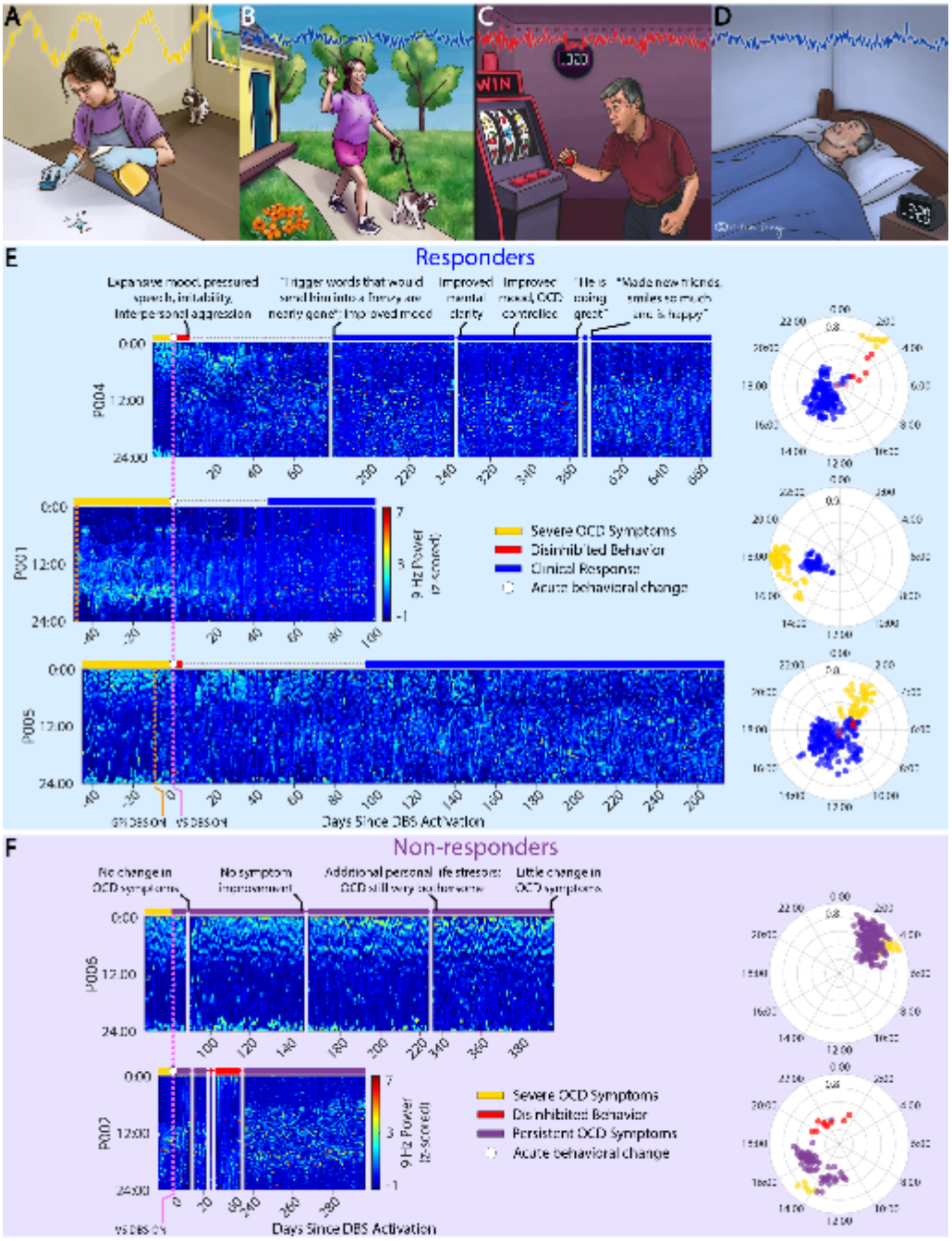


Figure 1: Temporal dynamics of VS neural activity mirrors behavioral phenotype and clinical status. (A-D), Illustration depicting prototypical clinical/behavioral states associated with OCD and its treatment with DBS. (A), Avoidant rituals of the severely symptomatic state. (B,D) Balanced behaviors of stable clinical response. (C), Excessively approachful disinhibited behaviors. In P004, this behavior consisted of expansive mood, pressured speech, and irritability causing interpersonal strife. In P005, the disinhibition manifested as an overabundance of energy, decreased need for sleep, and overactive and inappropriate interpersonal contact. (E) (left), Heatmaps of left hemisphere VS 9 Hz power vs. time of day (y-axis) and days since VS DBS activation (x-axis) in the three clinical responders. Colored bars over heatmaps indicate behavioral/clinical state. (right), Polar plots with cosinor fit amplitude vs. acrophase (i.e., time of day corresponding to peak amplitude of cosinor fit) over time. The amplitude of the circadian pattern clearly distinguishes between severe symptomatic state (yellow; strong circadian pattern), overly disinhibited state (red; abolished circadian pattern), and clinically stable response (blue; reduced circadian pattern). (F), Same as in (E) but for non-responders. There is less separation between the symptomatic state (yellow) and the state of long-term symptom persistence (purple).

Data:

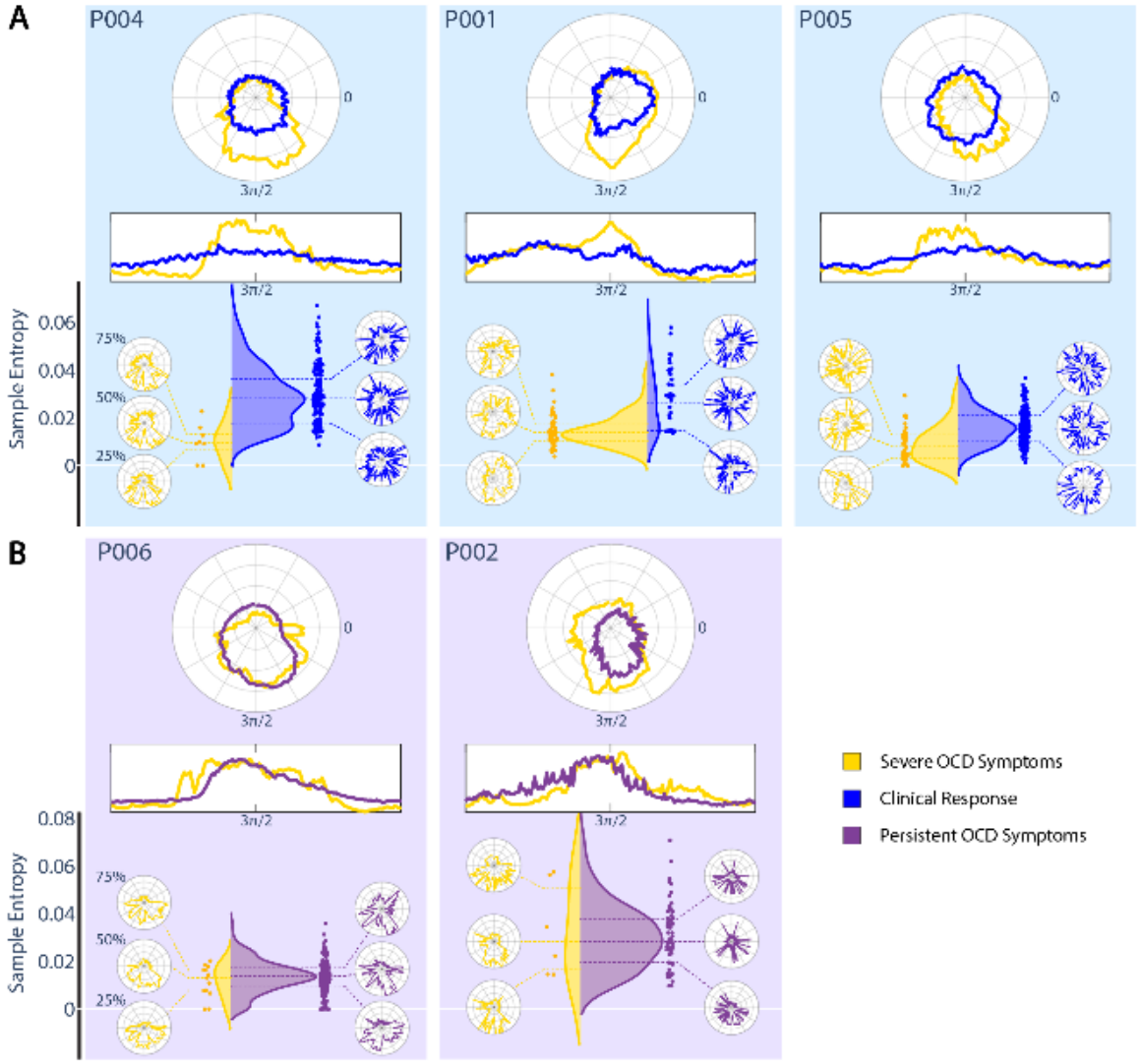


Figure 2: Sample entropy of daily neural activity distributions distinguishes clinical state. (A) Top: Circular plots depict mean 9 Hz power "templates" (rotated to align the peak daily amplitude to 3π/2 to allow averaging across days) across the pre-DBS severe OCD symptom (yellow) and the clinical response (blue) states for the three treatment responders. Middle: Linearized and demeaned templates show two full cycles to facilitate comparison of the clinical state profiles. The decreased eccentricity (reduced circadian tendency) of the clinical response state is evident as a lower amplitude profile in both circular and linearized depictions. Bottom: Half-violin plots indicate distribution of sample entropy for days within each clinical state, with single day circular representations of 9 Hz power shown at the 25th, 50th, and 75th percentiles of each distribution. (B) Identical plots as in (A) for non-responders. Templates in non-responders show reduced or absent differences between yellow and purple trace. Sample entropy distributions similarly show greater similarity in non-responders (B) than responders (A) between pre-DBS and post-DBS states.

References: None

Acknowledgements:

Learning Objectives: 1. Understand how to use commercially available DBS devices to record neural activity 2. Understand how to identify neural biomarkers related to circadian rhythm changes after DBS 3. Understand neurophysiology underlying OCD-related behaviors

Financial Disclosures: Sameer A. Sheth: consultant for Boston Scientific, Zimmer Biomet, Koh Young, Sensoria Therapeutics, Varian Medical, Neuropace; co-founder of Motif Neurotech. Wayne K. Goodman: receives royalties from Nview, LLC and OCDscales, LLC. Eric A. Storch: reports receiving research funding to his institution from the Ream Foundation, International OCD Foundation, and NIH. He is a consultant for Brainsway and Biohaven Pharmaceuticals. He owns stock less than $5000 in NView and Limbix. He receives book royalties from Elsevier, Wiley, Oxford, American

Psychological Association, Guildford, Springer, Routledge, and Jessica Kingsley. Ankit B. Patel: advisor to Endoluxe, CSDISCO, SCAN Health Plan; co-founder and CEO of Audit AI.

Disclosure: No significant relationships.

O029

Oral Presentations
NEUROMODULATION FOR NEUROPSYCHIATRIC DISORDERS
13-05-2024 16:30 - 18:20

EVALUATION OF THE EFFECTIVENESS AND SAFETY OF RTMS AND TDCS WITH INIRS IN THE TREATMENT OF PATIENTS WITH COGNITIVE IMPAIRMENTS.

Joanna Woźniak, MD, Jakub Kaźmierski, MD, PhD
Medical University of Lodz, Department Of Old Age Psychiatry And Psychotic Disorders, Lodz, Poland

Introduction: Alzheimer' s disease (AD) belongs to progressive neurodegenerative disorders and is the most common cause of dementia in the elderly population. Currently about 47.5 million people worldwide suffer from AD, only in Poland there are 300 000 patients. Medications used in AD were introduced in the 1990s, however, despite their use, patients experience progression of the disease leading to a complete lack of autonomy and death. Therefore, a continuous need to investigate novel therapeutic options exists. In the last few years, studies on the effectiveness of non- pharmacological forms (rTMS, tDCS, iNIRS) in the treatment of AD were conducted. rTMS (repetitive transcranial magnetic stimulation), tDCS (repetitive transcranial current stimulation) and iNIRS (intranasal near infrared stimulation) are low risk and non- invasive methods which penetrates through skull bones into the cerebral cortex and stimulates neurons with their synapses.

Materials / Methods: The group of 25 patients with a diagnosis of AD (median age 75 years, 17 women- 68% and 8 men- 32%) were evaluated using ADAS-Cog, MMSE scales before and after the rTMS or tDCS with iNIRS treatment. Conditions of the procedure for rTMS: frequency 5Hz, sequences 10sec. 1800 impulses per session. Conditions of the procedure of tDCS with iNIRS: direct current, 2mA, IR diode 850 nm wavelength. The group of 8 women and 7 men underwent 20 sessions in the period of 4 weeks of rTMS. 9 women and only 1 man underwent procedure of tDCS with iNIRS including 40 sessions in the period of 10 weeks. Patients were recruited into study on different time points.
Exclusion criteria: Epilepsy or a history of epileptic seizures, pacemaker, metal implants of CNS.

Results: Following the rTMS procedure, two clinical scores changed over time, showing a statistically significant improvement (MMSE score: 14 vs 18 points, before and after therapy, respectively, p =0,009; ADAS-Cog: 48 vs 45 points; p=0,045).
For tDCS with iNIRS procedure there are statistical significance for MMSE score: 22,8 vs 26,4 points, before and after therapy, respectively, p=0,024; ADAS-Cog 31 vs 24,6 point, p=0,048.

Discussion: According to present findings, rTMS and tDCS with iNIRS therapy has a positive impact on cognitive functions of patients with AD, however, more significant effects are noticed in MMSE scores.

Conclusions: Current findings indicate that non- pharmacological methods have potential to be effective and even breakthrough therapy for AD patients. Of note, further studies with more considerable number of participants and the use of sham (placebo) procedure are needed.

Supplemental Data:

References: 1. Frontiers in Aging Neuroscience., 09 October 2014; A double-blind randomized clinical trial on the efficacy of cortical direct current stimulation for the treatment of Alzheimer's disease; Eman M. Khedr et al. 2. International Journal of Geriatric Psychiatry 2019 Sep;34(9):1336-1345, "Noninvasive brain stimulation for behavioural and psychological symptoms of dementia: A systematic review and meta-analysis"; Sara M Vacas et al. 3. Kim, Wang-In, et al. "Cognitive Function Improvement in Mouse Model of Alzheimer's Disease Following Transcranial Direct Current Stimulation." Brain Sciences (2076-3425), vol. 10, no. 8, Aug. 2020, p. 547 4. Khedr EM, Salama RH, Abdel Hameed M, Abo Elfetoh N, Seif P. Therapeutic Role of Transcranial Direct Current Stimulation

in Alzheimer Disease Patients: Double-Blind, Placebo-Controlled Clinical Trial. Neurorehabilitation and Neural Repair. 2019;33(5):384-394. doi:10.1177/1545968319840285 5. Chang CH, Lane HY, Lin CH. Brain Stimulation in Alzheimer's Disease. Front Psychiatry. 2018;9:201. Published 2018 May 22. doi:10.3389/fpsyt.2018.00201 6. Magalhães TNC, Gerbelli CLB, Pimentel-Silva LR, de Campos BM, de Rezende TJR, Rizzi L, Joaquim HPG, Talib LL, Forlenza OV, Cendes F, Balthazar MLF. Differences in structural and functional default mode network connectivity in amyloid positive mild cognitive impairment: a longitudinal study. Neuroradiology. 2022 Jan;64(1):141-150. doi: 10.1007/s00234-021-02760-5. Epub 2021 Jul 19. PMID: 34278511. 7. WHO The Global Observatory WHO/MSD/MER/18.1 8. Chao LL. Effects of Home Photobiomodulation Treatments on Cognitive and Behavioral Function, Cerebral Perfusion, and Resting-State Functional Connectivity in Patients with Dementia: A Pilot Trial. Photobiomodul Photomed Laser Surg. 2019 Mar;37(3):133-141. doi: 10.1089/photob.2018.4555. Epub 2019 Feb 13. PMID: 31050950. 9. Liu, T.; Spector, A.; Mograbi, D.C.; Cheung, G.; Wong, G.H.Y. Changes in Default Mode Network Connectivity in Resting-State fMRI in People with Mild Dementia Receiving Cognitive Stimulation Therapy. Brain Sci. 2021, 11, 1137. https://doi.org/10.3390/brainsci11091137 10. Saltmarche AE, Naeser MA, Ho KF, Hamblin MR, Lim L. Significant Improvement in Cognition in Mild to Moderately Severe Dementia Cases Treated with Transcranial Plus Intranasal Photobiomodulation: Case Series Report. Photomed Laser Surg. 2017 Aug;35(8):432-441. doi: 10.1089/pho.2016.4227. Epub 2017 Feb 10. PMID: 28186867; PMCID: PMC5568598. 11. Chan AS, Lee TL, Yeung MK, Hamblin MR. Photobiomodulation improves the frontal cognitive function of older adults. Int J Geriatr Psychiatry. 2019 Feb;34(2):369-377. doi: 10.1002/gps.5039. Epub 2018 Dec 10. PMID: 30474306; PMCID: PMC6333495.

Acknowledgements: The support of Medical University of Lodz for this project is gratefully acknowledged.

Learning Objectives: 1. Implement innovative evidence- based interventions as adapted for an acceptance- based model. 2. Strengthen clinical skills - predict proper group of patients who has need 3. Correctly interpret and predict the likely outcomes

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O030

Oral Presentations
NEUROMODULATION FOR NEUROPSYCHIATRIC DISORDERS
13-05-2024 16:30 - 18:20

TRANSCUTANEOUS AURICULAR NEUROSTIMULATION (TAN) IS A PROMISING TREATMENT FOR DEPRESSION ON THE INPATIENT PSYCHIATRIC UNIT: THE IWAVE PILOT TRIAL

Christopher Austelle, MD[1,2], Mutaz Sarhan, MSc[2], Brenna Baker-Vogel, B.S.[2], Xiaolong Peng, PhD[2], Andrew Manett, MD[2], E Short, MD[2], Bashar Badran, PhD[2]
[1]Stanford University, Psychiatry And Behavioral Sciences, Stanford, United States of America, [2]Medical University of South Carolina, Psychiatry And Behavioral Sciences, Charleston, United States of America

Introduction: Brain stimulation has a growing number of indications for psychiatric disorders. Historically, electroconvulsive therapy (ECT) has been the only form of neuromodulation used as treatment for patients admitted to the psychiatric ward. Portable and noninvasive forms of brain stimulation, like transcutaneous auricular neurostimulation (tAN), are ideal treatment candidates to investigate in this novel setting. This study evaluates the safety and feasibility of tAN as an adjunct to standard of care on the inpatient psychiatric unit.

Materials / Methods: We recruited 5 patients (N=2 females; age: mean ± SD = 22.6±5.3) from the general adult inpatient psychiatric unit with a primary diagnosis of depression for this open-label safety and feasibility trial. Patients were randomized to receive either A) 3 sessions of tAN on 3 consecutive days (9 sessions total) (N=2) or B) 9 sessions of tAN on 1 day (N=3). We assessed depression and anxiety daily using the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI), respectively.

Results: All planned tAN stimulation sessions were completed, demonstrating feasibility of inpatient tAN. However, one participant was unable to complete their final 3 stimulation sessions due to receiving an anti-psychotic medication between days 2 and 3. Additionally, there were no adverse events during the stimulation sessions. BDI scores significantly decreased after completion of all stimulation sessions ($p=0.042$; pre-stimulation: mean ± SD = 28.4±15.5; post-stimulation: mean ± SD = 5±3.5). BAI scores also significantly decreased after completion of all stimulation sessions ($p=0.034$; pre-stimulation: mean ± SD = 25±10.7; post-stimulation: mean ± SD = 5.5±4.3).

Discussion: tAN profoundly decreased depression and anxiety scores in a group of 5 patients admitted to the inpatient psychiatric unit. These results indicate that further investigation is needed, and that tAN may be an excellent adjunct to inpatient psychiatric treatment. This study was limited by design (open-label) and small sample size (pilot trial).

Conclusions: Our findings demonstrate tAN is both safe and feasible in patients admitted to the inpatient psychiatric unit. tAN may be a successful adjunct to treatment of inpatient depression and anxiety. We plan to expand this study to determine wide-scale efficacy of tAN for treatment of depression in the inpatient setting.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1. Understand available brain stimulation treatments for psychiatric disorders and the settings where they are used. 2. Describe a novel treatment paradigm using transcutaneous auricular neurostimulation (tAN) in the inpatient psychiatric setting. 3. Demonstrate safety and feasibility of this new approach, and review promising early results demonstrating the treatment's impact on depression and anxiety.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O031

Oral Presentations
NEUROMODULATION FOR NEUROPSYCHIATRIC DISORDERS
13-05-2024 16:30 - 18:20

DEEP BRAIN STIMULATION OF THE GLOBUS PALLIDUS INTERNA WITH ANTERIOR LIMBS OF THE INTERNAL CAPSULE LESIONECTOMY FOR COMORBID TOURETTE'S SYNDROME AND OBSESSIVE-COMPULSIVE DISORDER

Shu Wang, MD, Fangang Meng, MD, PhD, Jianguo Zhang, MD
Beijing Tiantan Hospital, Capital Medical University, Department Of Neurosurgery, Beijing, China

Introduction: Deep brain stimulation (DBS) of the globus pallidus interna (GPi) has been shown to improve motor symptoms of Tourette's syndrome (TS). However, the treatment options and efficacies for patients with TS comorbid obsessive-compulsive disorder (OCD) remain to be further explored. This study was conducted to compare the efficacy, safety, and influencing factors of GPi-DBS combined with anterior limbs of the internal capsule (ALIC) lesionectomy versus GPi-DBS only in the treatment of TS with OCD.

Materials / Methods: A consecutive cohort of patients with TS and OCD who underwent GPi-DBS combined with ALIC lesionectomy (combined group) GPi-DBS only (DBS only group) between 2017 and 2022 were included. The YGTSS, Y-BOCS, GTS-QOL, HAMD, HAMA, MoCA, and MMSE were used to evaluate and compare the outcomes at 3, 6, 12 months, and the last follow-up after surgery. Linear regression analysis was used to identify prognostic indicators.

Results: A total of 12 patients were included and 6 patients in each group, and there were no significant differences in baseline characteristics between the two groups (all $P > 0.05$). Postoperative scores on the YGTSS, Y-BOCS, GTS-QOL, HAMD, HAMA were significantly improved at all time points (all $P < 0.05$), and there was a trend of further improvement with increasing follow-up duration in both of groups. Postoperative MoCA and MMSE scores did not significantly differ from preoperative scores (all $P > 0.05$). The combined group showed significantly greater improvement on the Y-BOCS score at 12 months postoperatively compared with the DBS only group ($P = 0.005$). Linear regression analysis showed that lower age at surgery was a positive influencing factor for the improvement rate of YGTSS scores in the DBS only group ($\beta = 0.859$), while lower age at symptom onset was a positive influencing factor for the improvement rate of Y-BOCS scores in the combined group ($\beta = 0.835$).

Discussion: Both GPi-DBS combined with ALIC lesionectomy and GPi-DBS only can achieve safe and effective improvement of tic symptoms and obsessive-compulsive symptoms in patients with TS and OCD, with significant improvement in anxiety and depression and a significant improvement in quality of life, but without affecting cognitive function. GPi-DBS combined with ALIC lesionectomy may have potential for better efficacy in treating obsessive-compulsive symptoms.

Conclusions: Comprehensive preoperative evaluation should be conducted to select an appropriate treatment strategy based on individual characteristics to achieve comprehensive diagnosis and treatment of both tic and comorbid psychiatric symptoms, thereby improving quality of life in patients with TS.

Supplemental Data:

References: None.

Acknowledgements: None.

Learning Objectives: 1. To compare the clinical efficacy, safety, and influencing factors of GPi-DBS combined with anterior limbs of the internal capsule (ALIC) lesionectomy versus GPi-DBS only in the treatment of TS with OCD. 2. To provide perspectives for potential treatments of TS and combined

psychiatric symptoms. 3. To discuss combined neuromodulation treatments for movement/psychiatric disorders.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O032

Oral Presentations
NEUROMODULATION FOR NEUROPSYCHIATRIC DISORDERS
13-05-2024 16:30 - 18:20

HOW DEPRESSIVE SYMPTOMS MAY AFFECT SUPRASPINAL FUNCTIONAL CONNECTIVITY IN VETERANS WITH GULF WAR ILLNESS-RELATED CHRONIC PAIN

Albert Leung, MD[1], Lauren Collin, MSc[2], Anni Zeynalvand, B.S.[2], Elise Kim, N/A[2], Stephen Kim, MD[2]
[1]University of California, San Diego, School of Medicine, Anthesiology, La Jolla, United States of America, [2]VA San Diego Healthcare System, Center For Pain And Headache Research, San Diego, United States of America

Introduction: Both chronic pain and depressive symptoms are highly prevalent in Veterans with Gulf War illness(GWI)[1,2]. However, how the severity of depressive symptoms may correlate with pain symptomology and supraspinal pain modulatory connectivity or vice versa in patients with GWVI-related headache, and body muscle and joint pain (GWI-HAP) is unknown. This study assessed how the severity of depressive symptoms may correlate with pain symptomology and supraspinal pain modulatory functional connectivity(FC) in the Veterans with GWI-HAP.

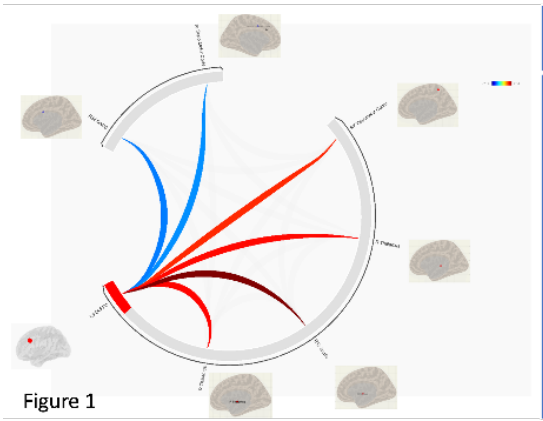
Materials / Methods: Resting state functional magnetic resonance imaging (rs-fMRI) scans were performed in Veterans with GWI-HAP and moderate to severe depressive symptoms reflected by Hamilton Rating Scale for Depression score(HRSD) >/=14(GWI>/=14 Group), and no to mild depressive symptoms reflected by HRSD<14(GWI<14 Group). In addition, pain, headache, quality of life and functional assessments were performed.

Results: rs-fMRI region of interest(ROI)-to-ROI functional connectivity(FC) analyses indicated the GWI>/=14 Group(N=33) showed significantly enhanced FC with the adjacent frontal cortex(Brodmann Area[BA] 44; $P < 0.001$; $t = 4.64$) and the contralateral Insula(BA 13; $P < 0.001$; $t = 7.14$), and two regions of contralateral thalamus($P < 0.01$, $P < 0.001$; $t = 5.32$, $t = 5.25$ respectively); and decreased FC with the ipsilateral premotor cortex(BA 6; $P < 0.01$; $t = -3.34$) and contralateral anterior cingulate cortex(BA 32; $P < 0.001$; $t = -3.64$) than their counterparts with no or mild depressive symptoms(GWI<14, N=33) (see Figure 1). These findings are correlated with more pain symptomology, and functional and quality of life impairments found in the GWI>/=14 group.

Discussion: The result of the current study suggests patients with higher degree of mood impairment exhibit a significantly lesser degree of pain modulatory FC from the prefrontal cortex to both premotor cortex and anterior cingulate cortex. In addition, GWV with more severe degree of depressive symptoms also demonstrated a higher level of headache and body pain than those with no or mild degree of symptoms. Furthermore, this difference in mood impairment also corresponds to higher degrees of sleep disturbance, quality of life interference and functional impairment. Thus, knowing the function of prefrontal cortex plays an important role of regulating both mood and pain, this change of FC in networks relevant to both pain and mood networks does appear to have a negative impact on both co-morbid conditions.

Conclusions: Potential therapeutic interventions such as transcranial magnetic stimulation (TMS) applicable for addressing both pain and depression should take these intrinsic brain modulatory FC differences into consideration.

Supplemental Data:



Hemisphere	Region of Interest	T-value	Cluster size (In voxel)	Brodmann Area	Peak Coordinate (x, y, z)	P-value
Left	Response & neuromodulatory					
	Frontal Cortex	4.64	162	44	(-46, 18, 12)	***
	Motor Cortex	-3.34	62	6	(-10, 4, 44)	**
Right	Affective and emotional					
	Insula	7.14	205	13	(42, -6, 2)	***
	Cingulate Cortex	-3.64	72	32	(10, 8, 32)	***
	Sensory/discriminatory					
	Thalamus	5.32	181		(0, -8, 2)	***
	Thalamus	5.25	199		(12, -22, 4)	***
	Visuomotor Cortex	4.82	144	7	(4, -48, 60)	***
	**P < 0.01, ***P < 0.001					

Figure1: Group Resting State Functional Magnetic Resonance Imaging (rs-fMRI) Region of Interest (ROI)-to-ROI functional connectivity analyses with left dorsolateral prefrontal cortex as the seeded ROI and GWI³14 > GWI<14 contrast.

References: 1. Rayhan, R. U., Ravindran, M. K. & Baraniuk, J. N. Migraine in gulf war illness and chronic fatigue syndrome: prevalence, potential mechanisms, and evaluation. Front Physiol 4, 181, doi:10.3389/fphys.2013.00181 (2013). 2. Lei K, Kunnel A, Metzger-Smith V, Golshan S, Javors J, Wei J, Lee R, Vaninetti M, Rutledge T, Leung A. 2020. Diminished corticomotor excitability in Gulf War Illness related chronic pain symptoms; evidence from TMS study. Sci Rep 10:18520.

Acknowledgements: The authors thank the Department of Defense Office of the Congressionally Directed Medical Research Programs (CDMRP) and Veteran Affairs Clinical Science Research and Development (VA CSRD) Program for their funding supports.

Learning Objectives: 1) Understand how pain and depressive symptoms may affect Gulf War Veterans; 2) Understand how the severities of depressive symptoms may mechanistically affect supraspinal pain modulatory functional connectivity; 3) Understand how the severities of depressive symptoms may affect pain, quality of life and functional impairments in Gulf War Veterans.

Financial Disclosures: The authors have no financial conflict of interest to disclose

Disclosure: No significant relationships.

O033

Oral Presentations
NEUROMODULATION FOR NEUROPSYCHIATRIC DISORDERS
13-05-2024 16:30 - 18:20

DIFFERENTIAL STIMULATION OF THE NAC-ALIC IN OCD：CLINICAL OUTCOMES AND INTRACRANIAL ELECTROPHYSIOLOGY

Wei Wang, MD, Yuan Gao, MD, Botao Xiong, MD
West China Hospital, Sichuan University, Chengdu, China

Introduction: The implantable pulse generator (IPG) used in previous obsessive-compulsive disorder-deep brain stimulation (OCD-DBS) studies is the same IPG used for movement disorders, which does not allow independent programming among different contacts. The OCD-DBS targets, namely the nucleus accumbens (NAc) and anterior limb of the internal capsule (ALIC), involve different neural tissue and therefore have different tolerances and efficacies for stimulation. Consequently, conventional DBS does not allow for the independent programming of stimulation parameters for NAc and ALIC, which may impact the therapeutic efficacy of DBS for treating OCD.

Materials / Methods: In this study, 12 OCD patients from a multi-center randomized controlled trial (ClinicalTrials.gov: NCT04967560) were implanted with a novel electrode design and IPG for differential stimulation parameters for NAc and ALIC. The primary effectiveness measure was the change in scores on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) from baseline to 3-month and 6-month follow-up. Fourteen patients from both our previous trial (ClinicalTrials.gov: NCT02398318) and the current trial with local field potential (LFP)-sensing IPG had NAc-ALIC oscillatory recordings. The least absolute shrinkage and selection operator (LASSO) regression was then used to identify neural oscillatory activity associated with the response to DBS.

Results: At the 3-month follow-up, a significant difference in Y-BOCS reduction rates was observed between the active and control treatment groups (61.5% vs. 2.9%; p = 0.034). Following the initiation of DBS for the control group, there was no significant difference in Y-BOCS reduction rates between the active and control treatment groups (64.0% vs. 45.8%; p = 0.4) at the 6-month follow-up. Out of the 12 patients, 10 were categorized as responders. The LASSO model selected high-gamma band activity in the left NAc and ventral ALIC as having the best predictions. There was a moderate and significant correlation (r = 0.569; p = 0.034) between the predicted reduction rate of Y-BOCS scores by DBS and the actual measured reduction rate, indicating a high predictive performance of the model.

Discussion: The full response rate of 83.3% of severely affected patients is the highest rate in studies with a sample size of more than 10 subjects. This underscores the capability and efficacy of differential stimulation of NAc-ALIC.

Conclusions: Individualized differential stimulation of NAc and ALIC shows promise in improving the effectiveness of DBS and enhancing outcomes for patients with refractory OCD. The analysis of LFPs recorded in targeted regions provides valuable insights into the neurophysiological mechanisms underlying the effects of DBS on OCD.

Supplemental Data:

References: None

Acknowledgements: None

Learning Objectives: 1. DBS stimulation of NAc-ALIC for OCD is effective. 2.Designing new IPG and more individualized stimulation modes can further improve the effect of DBS 3. The analysis of LFPs

recorded in targeted regions provides valuable insights into the neurophysiological mechanisms underlying the effects of DBS on OCD.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O034

Oral Presentations
NEUROMODULATION FOR NEUROPSYCHIATRIC DISORDERS
13-05-2024 16:30 - 18:20

REAL-WORLD EFFICACY FOR TREATING ANXIETY SYMPTOMS—A COMPARISON BETWEEN DIFFERENT STIMULATION METHODS OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION

Galen Chin Lun Hung, MD, Hsiang-Ting Yu, MSc, Cheng Ruey Jou, MD
Blossom Clinic of Psychosomatic Medicine, Taipei, Taiwan

Introduction: Repetitive transcranial magnetic stimulation (rTMS) is a well-established non-invasive brain stimulation technique for treating major depressive disorder (MDD). It has demonstrated comparable efficacy in alleviating depressive symptoms across different stimulation methods. However, anxiety symptoms can also be significant and debilitating for MDD patients. Currently, there is limited evidence regarding the anxiolytic efficacy of rTMS and the comparison of therapeutic responses between different stimulation methods.

Materials / Methods: We enrolled 104 patients undergoing rTMS treatment at a TMS clinic in Taipei, Taiwan. These participants were diagnosed with MDD according to DSM-V criteria, and the degree of treatment resistance was assessed using the Maudsley Staging Method (MSM). Three different stimulation methods were applied, with the target intensity of 120% motor threshold: 10 Hz, 3,000 pulses over the left dorsolateral prefrontal cortex (DLPFC); 1 Hz, 1,200 pulses over the right DLPFC; and 18 Hz Deep TMS, involving 1,980 pulses. Anxiety symptoms were evaluated using the Hamilton Rating Scale for Anxiety at baseline and after the 10th session. A therapeutic response was defined as a reduction of more than 50% in anxiety symptoms.

Results: Out of the 104 patients, 58 (55.8%) were female, with a mean age of 37.9 (SD=15). Most patients had moderate to severe treatment-resistant depression, as determined by the MSM. Among them, 55 (52.9%) received 10 Hz stimulation over the left DLPFC, achieving a 36% response rate for anxiety symptoms. Thirty (28.8%) patients received 1 Hz stimulation over the right DLPFC, with a response rate of 50%. Nineteen (18.3%) patients underwent deep TMS, resulting in a 42% response rate. Chi-square analysis showed no significant differences in response rates among the three stimulation methods.

Discussion: The anxiolytic effect was substantial across all three types of stimulation methods. Notably, significant improvement was observed after only 10 sessions, suggesting a rapid response to rTMS in reducing anxiety symptoms. Unfortunately, we couldn't assess the anxiolytic effects after 20 or more sessions because, in real-world practice, stimulation methods were often adjusted after the initial 10 sessions.

Conclusions: rTMS may offer benefits for alleviating anxiety symptoms in patients with MDD, with a potentially faster response compared to the treatment of depressive symptoms. High-frequency stimulation over the left DLPFC, low-frequency stimulation over the right DLPFC, and deep TMS appear to have comparable anxiolytic effects.

Supplemental Data:

References: None

Acknowledgements: The support of Taiwan Clinical TMS Society is gratefully acknowledged.

Learning Objectives: 1. Anxiety symptoms are prevalant and debilitating among patients with major depressive disorder 2. repetitive transcranial magnetic stimulation (rTMS) can achieve a rapid anxiety-reducing effect 3. High-frequency stimulation over the left DLPFC, low-frequency stimulation over the right DLPFC, and deep TMS appear to have comparable anxiolytic effects

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O035

Oral Presentations
NEUROMODULATION FOR NEUROPSYCHIATRIC DISORDERS
13-05-2024 16:30 - 18:20

EFFECTS OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION ON THE DEMORALIZATION SYNDROME IN PATIENTS AFFECTED BY TREATMENT-RESISTANT DEPRESSION

Tommaso Toffanin, PhD, Dario Ambrosio, MD, Francesca Romagnolo, MD, Marcello Gavesi, MD, Alfonso Tarricone, MD, Nicola Bendin, MD, Stefano Bitturini, MD, Marco Ricchiari, MD, Marco Emanuele, MD, Enrico Vescovo, MD, Elisa Dolifini, DPsych, Giovanni Nazzaro, DPsych, Giacomo Koch, MD, Luciano Fadiga, MD, Luigi Grassi, MD
University of Ferrara, Of Neuroscience And Rehabilitation, Ferrara, Italy

Introduction: Demoralization is a multidimensional phenomenon characterized by a combination of distress and subjective incompetence (1). Demoralization may be particularly relevant in patients affected by organic and psychiatric diseases, since it produces dysfunctional behaviours, psychological
suffering, and lowers the quality of life (2). Demoralization has shown a partial clinical and neurobiological overlap with depression, thus suggesting that these disorders might belong to the same spectrum (3-4). Ripetitive transcranial magnetic stimulation (rTMS) has been proven as an effective treatment in affective and depressive disorders, as demonstrated by the most recent literature(5). Accordingly, we theorize that it could prove effective for the treatment of both treatment-resistant depression (TRD) and demoralization syndrome. The principal aim of our study was to evaluate the effects of rTMS treatment on the dimension of the demoralization syndrome in patients affected by TDR. Our second aim was to analyse the correlation between depression and demoralization – before and after treatment –, to further increase the knowledge of the psychopathological basis of the demoralization-depression spectrum.

Materials / Methods: This is a prospective study, which included outpatients with an age > 18 years and a diagnosis of treatment resistant major depressive disorder. The patients received 20 sessions of rTMS with the intermittent Theta Burst Stimulation (iTBS) protocol on the left dorsolateral prefrontal cortex (DLPFC). The daily sessions consisted of 3 consecutive sessions of 600 pulses. Each session consisted of triplets of pulses at a frequency of 50 Hz, repeated every 200ms (5 Hz frequency). Beck Depression Inventory (BDI) and Demoralization Scale (DS-1) were administered before treatment (T0) and after treatment (T1).

Results: At the end of the treatment sessions, we found a statistically significant reduction of the BDI ($p=0.005$) and the DS-1 scores ($p=0.008$). Regarding the four dimensions of DS-1, we observed both a significant reduction of “dysphoria” ($p<;0.05$) and a significant trend of “disheartenment” ($p=0.059$). Furthermore, we found a direct correlation of BDI with DS-1 at T0 and T1 times ($p<;0.05$).

Discussion: The study confirms the efficacy of rTMS-iTBS in the treatment of TRD. Results from our data suggest that rTMS-iTBS positively influences some dimensions of demoralization, supporting the hypothesis that there are some shared dimensional and neurobiological factors between these two syndromes.

Conclusions: Our data evidenced that iTMS might be a tool for the treatment of demoralization syndrome, since it acts on depressive symptoms, thus facilitating a subsequent psychotherapeutic approach.

Supplemental Data: None.

References: 1) Nanni, M. G., et al . Embitterment in psychological trauma: Demoralization and embitterment. Psychol Trauma 10, 14–21 (2018). 2) De Figueiredo, J. M; Gostoli, S. Culture and demoralization in psychotherapy. Adv Psychosom Med 33,75–87 (2013). 3) Belvederi Murri, M. et al.

The relationship between demoralization and depressive symptoms among patients from the general hospital: network and exploratory graph analysis: Demoralization and depression symptom network. J Affect Disord 276, 137–146 (2020). 4) Leach, J. 'Give-up-itis' revisited: Neuropathology of extremis. Med Hypotheses 120, 14–21 (2018). 5) Toffanin T., et al Cognitive functioning as predictor and marker of response to repetitive transcranial magnetic stimulation in depressive disorders: A systematic review. Gen Hosp Psychiatry. 2022;79:19-32.

Acknowledgements: None

Learning Objectives: 1) To explore the effects of rTMS on treatment-resistant depression 2) To explore the efefcts of rTMS on demoralization syndrome 3) To increase the knowledge of the psychopathological basis of the demoralization-depression spectrum.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O036

Oral Presentations
NEUROMODULATION FOR NEUROPSYCHIATRIC DISORDERS
13-05-2024 16:30 - 18:20

EVALUATING THE EFFICACY OF HIGH-FREQUENCY RTMS ON EXECUTIVE FUNCTIONS: A COMPARATIVE STUDY IN OCD, ADULT ADHD AND SUBSTANCE USE DISORDERS

K Srinivas, MD[1,2,3], Kolluri Maithri, MD[3], Chilukuri Raviteja, MD[1], P Spandana, MBBS[4], Bandita Sharma, BA Psychology[4]
[1]KARLA NEUROMODULATION, Psychiatry, hyderabad, India, [2]KAMINENI INSTITUTE OF MEDICAL SCIENCES, Psychiatry, HYDERABAD, India, [3]KARLA NEUROMODULATION, Psychiatry, HYDERABAD, India, [4]KARLA NEUROMODULATION, Psychiatry, Hyderabad, India

Introduction: Evidence reveals significant impairments in executive in various psychiatric disorders which impacts functional outcome of patients1 2 3. Executive functions encompass a multifaceted set of cognitive processes, including working memory, cognitive flexibility, inhibitory control, and decision-making, all of which are crucial for effective self-regulation and goal-directed behavior. Dysfunction in these cognitive domains is prevalent in individuals suffering from OCD, Adult ADHD, and SUD, resulting in substantial impairments in their daily lives and potential exacerbation of their primary symptoms

Materials / Methods: This comparative study explores efficacy of high frequency repetitive Trans cranial magnetic stimulation in improving executive function, as assessed by Behavior rating inventory of executive functions scale- adult version scale [BRIEF –A]8 across individuals diagnosed with obsessive compulsive disorder [OCD], adult attention –deficit hyperactivity disorder and substance use disorder. Total sample size was 90, divided into 3 groups of 30 each.

Results: Initial results revealed there is significant improvement in response inhibition (20%), initiation (17.1), organization (11.4), mild improvement in emotional control (4%) and behavioral regulation (6%), no improvement in working memory and metacognition. Ongoing study statistics are yet to be calibrated.

Discussion: rTMS can modulate neuronal excitability, activity, and plasticity in a non-invasive manner. It has been found to be a potentially remediating procedure to improve executive function in recent studies4 5 6 7Subjects in the OCD group and adult ADHD group were on ongoing maintenance medication while those in the poly-substance group were not on any psychotropic medication. BRIEF –A scores were recorded before starting rTMS sessions. Participants then underwent 16 sessions, 4-week course with 20Hz HF rTMS on left DLPFC. BRIEF –A scores were recorded again after completion. Results were then compared with analysis of variance and linear regression.

Conclusions: rtms had showing improve executive functions difficulties in ocd, adult ADHD,polysubstance individuals only in few domains

Supplemental Data:

References: 1] Manarte, L. et al. (2021) ‘Executive functions and insight in OCD: A comparative study’, BMC Psychiatry, 21(1). doi:10.1186/s12888-021-03227-w. 2] Roselló, B. et al. (2020) ‘Empirical examination of executive functioning, ADHD associated behaviors, and functional impairments in adults with persistent ADHD, remittent ADHD, and without ADHD’, BMC Psychiatry, 20(1). doi:10.1186/s12888-020-02542-y. 3] Crivelli, D. et al. (2022) ‘Screening executive functions in substance-use disorder: First evidence from testing of the battery for executive functions in addiction (BFE-A)’, International Journal of Mental Health and Addiction [Preprint]. doi:10.1007/s11469-022-00928-5. 4] Ilieva, I.P. et al. (2018) ‘Age-related repetitive transcranial magnetic stimulation effects on executive function in depression: A systematic review’, The American Journal of Geriatric Psychiatry, 26(3), pp. 334–346. doi:10.1016/j.jagp.2017.09.002. 5]] Nagy, N.A.S., Amin, G.R., Khalil, S.A. et al.

The therapeutic role of repetitive transcranial magnetic stimulation in children with attention deficit/hyperactivity disorder in Egypt a randomized sham controlled clinical trial. Middle East Curr Psychiatry 29, 55 (2022). https://doi.org/10.1186/s43045-022-00210-3 6] Tong, J.; Zhang, J.; Jin, Y.; Liu, W.; Wang, H.; Huang, Y.; Shi, D.; Zhu, M.; Zhu, N.; Zhang, T.; et al. Impact of Repetitive Transcranial Magnetic Stimulation (rTMS) on Theory of Mind and Executive Function in Major Depressive Disorder and Its Correlation with Brain-Derived Neurotrophic Factor (BDNF): A Randomized, Double-Blind, Sham-Controlled Trial. Brain Sci. 2021, 11, 765. https://doi.org/10.3390/brainsci11060 7] The role of prefrontal cortex in working-memory capacity, executive attention, and general fluid intelligence: an individual-differences perspective. Psychon Bull Rev. 2002; 9: 637-671 8] Roth, R.M., Isquith, P.K. and Gioia, G.A. (2005) 'Behavior rating inventory of executive function®--adult version', PsycTESTS Dataset [Preprint]. doi:10.1037/t86244-000.

Acknowledgements: no specific acknowledgments

Learning Objectives: 1]EVALUATION AND COMPARISION OF RTMS EFFICACY IN IMPROVING EXECUTIVE DYSFUNCTION IN VARIOUS PSYCHIATRIC ILLNESS [OCD, ADHD,SUBSTANCE ABUSE] 2]CLINICAL APPLICABILITY OF BRIEF A RATING SCALE AS GLOBAL EXECUTIVE COMPOSITIVE INCLUDING BEHAVIOURAL REGULATION INDEX [BRI], METACOGNITION INDEX

Financial Disclosures: no significant relationships

Disclosure: No significant relationships.

O037

Oral Presentations
NEUROMODULATION FOR NEUROPSYCHIATRIC DISORDERS
13-05-2024 16:30 - 18:20

PILOT STUDY ON THE USE OF EXPIRATORY-GATED TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION COMBINED WITH SLOW BREATHING AMONG INDIVIDUALS WITH WAR-RELATED PTSD SYMPTOMS

Mikołaj Szulczewski, PhD[1], Ilse Van Diest, PhD[2], Andrzej Rynkiewicz, PhD[3], Taras Usichenko, MD, PhD[4,5], Yori Gidron, DPsych, PhD[6]
[1]The Institute of Psychology of the Polish Academy of Sciences, Warsaw, Poland, [2]KU Leuven, Faculty Of Psychology And Educational Sciences, Leuven, Belgium, [3]University of Warsaw, Department Of Psychology, Warsaw, Poland, [4]University of Greifswald, Department Of Anesthesiology And Intensive Care Medicine, Greifswald, Germany, [5]McMaster University, Faculty Of Health Sciences, Hamilton, Canada, [6]University of Haifa, Faculty Of Psychology And Educational Sciences, Haifa, Israel

Introduction: War-related mass trauma causes a surge in demand for mental health services. We propose that a hybrid behavioral and neurostimulation intervention that targets vagus nerve activity may have good scalability for these circumstances. This intervention combines expiratory-gated transcutaneous vagus nerve stimulation (taVNS) with slow breathing (six breaths per minute). Based on the successful results of previous studies on the clinical application of each of the methods separately, trauma-related emotional disorders and sympathovagal imbalance are promising targets for this intervention (Szulczewski, 2022).

Materials / Methods: The study was a prospective pragmatic pre-post pilot study with two baseline measurements (one month and one day before the intervention), four-weeks intervention (2 x 20 minutes daily, 6 breaths/min paced by taVNS: 100 Hz on/off 6s/4s). Included were 20 women who have symptoms of PTSD after experience of war in Ukraine and forced migration (The PTSD Checklist for DSM-5 - PCL-5 ≥ 31). The outcome measures were the self-reported PTSD (PCL-5), psychological distress (The Hopkins Symptom Checklist-25), sleep problems (Insomnia Severity Index), well-being (The World Health Organization Five Well-Being Index - WHO-5) and somatic symptoms (Patient Health Questionnaire Physical Symptoms - PHQ-15), as well as treatment acceptability and adverse effects. Furthermore, resting heart rate (HR) and HR variability (HRV), end-tidal CO_2 level ($EtCO_2$) and respiratory rate (RR) were measured during spontaneous and paced breathing (at 0.1 Hz) to test whether the intervention improved vagal heart control and affected resting respiratory rate and arterial CO_2 homeostasis.

Results: The participants reported a high treatment adherence (79% of the prescribed dose) and evaluated the treatment positively. ANOVA for repeated measures (all effects of phase of the study $p < .001$) and post-hoc comparisons of pre- and post-intervention measurements revealed a significant reduction in PTSD symptoms (Cohen's $d = .9$), psychological distress ($d = 1.17$), somatic symptoms (1.17), and improvements in sleep quality ($d = 1.24$). Resting HRV, HR, RR and PetCO2 did not change (all $p > .05$). The symptom improvements were sustained during follow-up assessments two months post-intervention

Discussion: This pilot study indicates high acceptability of taVNS combined with slow breathing and the potential effectiveness of this combination treatment in reducing symptoms of elevated allostatic load, trauma and psychological distress.

Conclusions: The pilot study warrants further investigation in randomised trials.

Supplemental Data:

References: Szulczewski MT. Transcutaneous Auricular Vagus Nerve Stimulation Combined With Slow Breathing: Speculations on Potential Applications and Technical Considerations.

Neuromodulation. 2022 Apr;25(3):380-394. doi: 10.1111/ner.13458. Epub 2021 Jun 23. PMID: 35396070.

Acknowledgements: The work was supported by the National Science Centre in Poland grant number 2021/40/C/HS6/00020

Learning Objectives: 1. Participants will learn about the theoretical and practical aspects of combining taVNS with slow breathing. 2. Participants will learn about the potential therapeutic targets for the hybrid method combining taVNS with slow breathing. 3. Participants will learn about the results of a pilot study in which the taVNS was used with slow breathing among people with symptoms of PTSD following war and forced migration.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O038

Oral Presentations
NEUROMODULATION FOR NEUROPSYCHIATRIC DISORDERS
13-05-2024 16:30 - 18:20

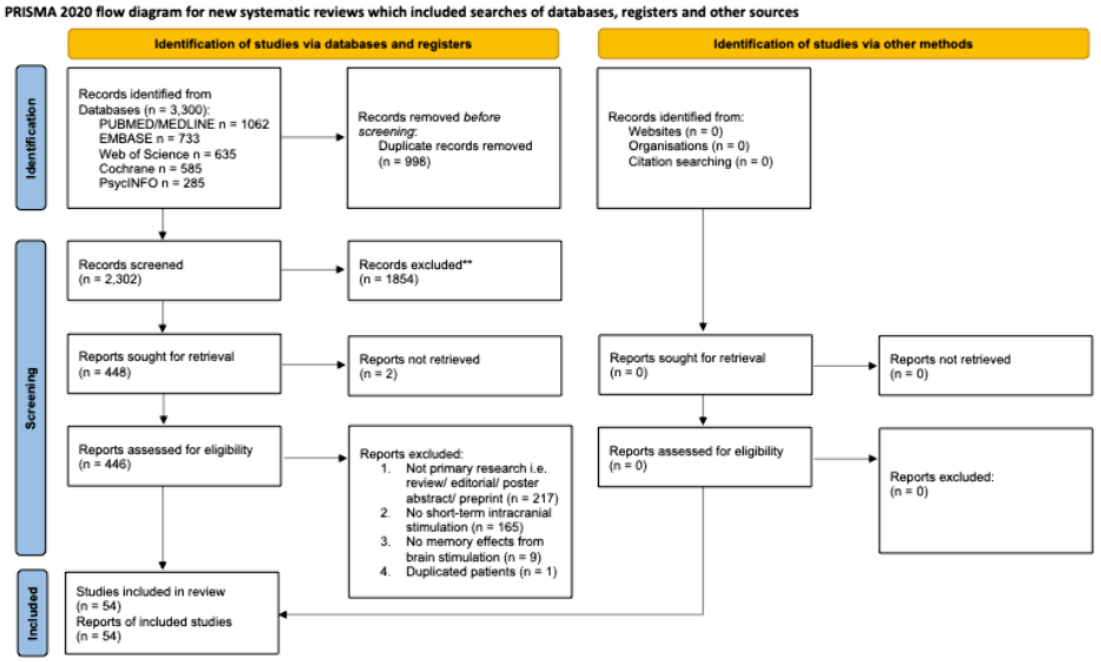
STATE-OF-THE-ART OF MEMORY NEUROPROSTHESIS: A META-ANALYSIS ON THE EFFECTS OF SHORT-TERM INTRACRANIAL STIMULATION ON HUMAN MEMORY

Mervyn Lim, MBBS, MPH, MRCS, Dewei Tan, A Level, Tseng Tsai Yeo, MBBS
National University Hospital, Neurosurgery, Singapore, Singapore

Introduction: With the increased prevalence of dementia worldwide, preventing memory decline and memory restoration using neuroprostheses is increasingly important[1]. Neuromodulation of memory has focused primarily on the medial temporal lobe and its connected areas, but recent publications have also shown memory effects during neocortical stimulation[2]. Moreover, technological advances have enabled the development of closed-loop stimulation protocols for memory neuroprosthesis[3,4]. We conducted a systematic review and individual patient data meta-analysis (IPDMA) summarising the existing international literature on short-term intracranial stimulation to provide a roadmap of the current state-of-the-art in memory neuroprosthesis, as well as to identify intracranial stimulation sites associated with memory effects in humans.

Materials / Methods: We conducted a systematic review of Medline, EMBASE, Web of Science, Cochrane, and PsycINFO databases until 12 September 2023. We included publications reporting the use of short-term intracranial stimulation in patients undergoing a memory task. We excluded articles that did not report primary research, did not utilise short-term intracranial stimulation protocols (on-off methodology), did not report memory effects, or reported secondary analyses from patients of a previous study. The study followed PRISMA guidelines and was registered on PROSPERO (CRD42022324796). 2302 abstracts were reviewed by two independent researchers after duplicates were removed, and a total of 54 articles were included (**Figure 1**). Data was extracted using a standardised form, summarised using descriptive statistics, and IPDMA was conducted to pool individual data across

articles.



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Results: Short-term intracranial stimulation resulting in memory effects were reported in patients with epilepsy (n=38), Parkinson's disease (n=14), and brain tumors (n=2). Memory tasks performed included verbal (n=28), visual (n=18), spatial (n=6), déjà vu (n=3), and working memory tasks (n=15). Data from a total of 458 individual patients across 32 articles performing a memory task while undergoing intracranial stimulation were pooled. Stimulation electrode locations showing memory facilitation or inhibitory effects included the hippocampus, subiculum, entorhinal cortex, parahippocampal gyrus, amygdala, fornix, subthalamic nucleus, anterior thalamus, caudate nucleus, insula, prefrontal, and temporal cortex. Pooled stimulation location sites and effects will be displayed on a standard Montreal Neurological Institute (MNI) brain template.

Discussion: This systematic review summarized the progress and state-of-the-art in memory neuroprosthesis applications over the last two decades, reporting pooled effects of stimulation on memory across all intracranial locations reported in the international literature.

Conclusions: Advances in memory neuroprosthesis have resulted in increased understanding of the neurophysiology of human memory, and will continue to improve memory neuroprosthesis performance in the future.

Supplemental Data:

References: 1 Suthana, N. & Fried, I. Deep brain stimulation for enhancement of learning and memory. *Neuroimage* **85 Pt 3**, 996-1002 (2014). https://doi.org/10.1016/j.neuroimage.2013.07.066 2 Mankin, E. A. & Fried, I. Modulation of Human Memory by Deep Brain Stimulation of the Entorhinal-Hippocampal Circuitry. *Neuron* **106**, 218-235 (2020). https://doi.org/10.1016/j.neuron.2020.02.024 3 Geva-Sagiv, M. *et al.* Augmenting hippocampal-prefrontal neuronal synchrony during sleep enhances memory consolidation in humans. *Nature Neuroscience* **26**, 1100-1110 (2023). https://doi.org/doi:https://dx.doi.org/10.1038/s41593-023-01324-5 4 Hampson, R. E. *et al.* Developing a hippocampal neural prosthetic to facilitate human memory encoding and recall. *JOURNAL OF NEURAL ENGINEERING* **15** (2018). https://doi.org/doi:10.1088/1741-2552/aaaed7

Acknowledgements: Not applicable

Learning Objectives: 1. Short-term intracranial stimulation resulting in memory effects were reported in patients with epilepsy (n=38), Parkinson's disease (n=14), and brain tumors (n=2). 2. Memory tasks performed included verbal (n=28), visual (n=18), spatial (n=6), déjà vu (n=3), and working memory tasks (n=15). 3. Stimulation electrode locations showing memory facilitation or inhibitory effects included the hippocampus, subiculum, entorhinal cortex, parahippocampal gyrus, amygdala, fornix, subthalamic nucleus, anterior thalamus, caudate nucleus, insula, prefrontal, and temporal cortex.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O039

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 01
13-05-2024 16:30 - 18:20

REPORTING GUIDELINES FOR CLINICAL TRIAL PROTOCOLS AND REPORTS OF IMPLANTABLE NEUROSTIMULATION DEVICES: SPIRIT-INEUROSTIM AND CONSORT-INEUROSTIM EXTENSIONS

Sam Eldabe, FRCA[1], Rebecca Bresnahan, PhD[2], Sue Copley, MSc[3], Richard North, PhD[4], Simon Thomson, MBBS[5], Ganesan Baranidharan, FRCA[6], Robert Levy, PhD[7], Rod Taylor, PhD[8], Rui Duarte, PhD[2,9]
[1]James Cook Hospital, Pain Department, Middlesbrough, United Kingdom, [2]University of Liverpool, Institute Of Population Health, LIVERPOOL, United Kingdom, [3]South Tees Hospitals NHS Foundation Trust, Pain Management, Middlesbrough, United Kingdom, [4]Johns Hopkins University, Baltimore, United States of America, [5]Mid & South Essex University Hospitals NHSFT, Pain And Neuromodulation Centre, Basildon, United Kingdom, [6]Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, [7]Anesthesia Pain Care Consultants, Anesthesia Pain Care Consultants, Tamarac, United States of America, [8]University of Glasgow, Population Health Research, Glasgow, United Kingdom, [9]Saluda Medical, Artarmon, Australia

Introduction: SPIRIT and CONSORT statements have improved the reporting quality of trial protocols and randomised controlled trials.[1] Extensions to the SPIRIT and CONSORT statements specific to certain interventions can address additional methodological considerations. The aim of this study was to develop reporting guidelines for protocols and reports of clinical trials of implantable neurostimulation devices.

Materials / Methods: SPIRIT-iNeurostim and CONSORT-iNeurostim extensions were developed through a staged consensus process involving literature review and expert consultation.[2] An initial list of candidate items was generated from previous systematic review findings, published protocols and reports of clinical trials of implantable neurostimulation devices.[3,4] Participants were invited to complete a two-round Delphi survey. In the first round, participants voted on the importance of each item and suggested additional items. In the second round, participants re-scored the items considering feedback and additional items suggested. The Delphi survey results were discussed at a consensus meeting and stakeholders voted on items for inclusion in the extensions. A pilot of the checklists was performed to confirm clarity of the wording of the new items.

Results: The initial list included 42 candidate items relevant to both SPIRIT- and CONSORT-iNeurostim extensions and 7 items relevant to CONSORTiNeurostim only. We received 132 responses to the first round of the Delphi survey and 99 responses to the second round. Participants suggested an additional 34 candidate items during the first round of the survey (14 for SPIRIT-iNeurostim and 20 for CONSORT-iNeurostim). The SPIRIT-iNeurostim extension recommends 5 new checklist items (elaborations) as additions to the current SPIRIT statement for CTs of implantable neurostimulation devices. One item is an intervention checklist that includes 14 candidate items. The CONSORT-iNeurostim extension recommends 7 new checklist items (elaborations) as additions to the current CONSORT statement for clinical trials of implantable neurostimulation devices. One item is an intervention checklist that includes 14 candidate items.

Discussion: Development of the SPIRIT-iNeurostim and CONSORT-iNeurostim extensions followed the EQUATOR framework that involved a staged consensus process involving multiple international stakeholder groups. Future steps include dissemination of findings to increase awareness and implementation of the new iNeurostim checklists.

Conclusions: SPIRIT-iNeurostim and CONSORT-iNeurostim extensions may contribute to increased transparency and to improve the reporting of clinical trial protocols and reports of implantable neurostimulation devices.

Supplemental Data:

References: 1. Ranganathan P. The CONSORT statement and its impact on quality of reporting of trials. Perspect Clin Res 2019;10:145–147. 2. Duarte RV, Bresnahan R, Copley S, et al. Reporting Guidelines for Clinical Trial Protocols and Reports of Implantable Neurostimulation Devices: Protocol for the SPIRIT-iNeurostim and CONSORT-iNeurostim Extensions. Neuromodulation2022;25(7):1045-1049. 3. Duarte RV, McNicol E, Colloca L, Taylor RS, North RB, Eldabe S. Randomized Placebo-/Sham-Controlled Trials of Spinal Cord Stimulation: A Systematic Review and Methodological Appraisal. Neuromodulation 2020;23(1):10-18. 4. McNicol E, Ferguson M, Bungay K, et al. Systematic Review of Research Methods and Reporting Quality of Randomized Clinical Trials of Spinal Cord Stimulation for Pain. J Pain 2021;22(2):127-142.

Acknowledgements: We thank the participants of the Delphi survey, the Consensus meeting and volunteers that piloted the checklists.

Learning Objectives: 1. Reporting guidelines specific to neurostimulation are essential to improve transparency of findings 2. SPIRIT and CONSORT-iNeurostim extensions have the potential to improve the reporting of clinical trial protocols and reports of implantable neurostimulation devices 3. Implementation of the iNeurostim extensions will increase the quality of neurostimulation study protocols and reports

Financial Disclosures: Sam Eldabe (Saluda Medical, consultant, $501 - $5,000 USD) Rebecca Bresnahan (no significant relationships) Sue Copley (no significant relationships) Simon Thomson (Saluda Medical, consultant, $501 - $5,000 USD) Richard North (no significant relationships) Ganesan Baranidharan (no significant relationships) Robert Levy (no significant relationships) Rod Taylor (Saluda Medical, consultant, $501 - $5,000 USD) Rui Duarte (Saluda Medical, company employee)

Disclosure: I am an employee of Saluda Medical. The employer had no role in the research presented within this abstract.

O040

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 01
13-05-2024 16:30 - 18:20

USING A NOVEL HYBRID DECENTRALIZED CLINICAL STUDY TO EVALUATE REAL-WORLD OUTCOMES FOR SPINAL CORD STIMULATION (SCS) THERAPIES

Melissa Murphy, MD[1], Andrew Will, MD[2], Thomas White, MD[3], Velimir Micovic, MD[4], Jugal Dalal, MD[5], Xiaoxi Sun, MA[6], Rupinder Bharmi, MSBmE[6], Grace Santa Cruz Chavez, PhD, MSBmE[6], Louis Archila, BSc[6], Krishnan Chakravarthy, MD, PhD[7]
[1]North Texas Orthopedics & Spine Center, Grapevine, United States of America, [2]Twin Cities Pain Clinic, Minneapolis, United States of America, [3]Procura Pain and Spine PLLC, Shenandoah, United States of America, [4]Pain Management Consultants of Southwest Florida, Fort Myers, United States of America, [5]Novant Health Spine Specialists, Winston-Salem, United States of America, [6]Medtronic Neuromodulation, Minneapolis, United States of America, [7]Coastal Research Institute, Carlsbad, United States of America

Introduction: While Randomized Controlled Trials (RCTs) provide the gold standard for clinical evidence, they also present challenges such as significant costs, drawn-out timelines to report evidence as well as representing highly controlled environments that may not align with real-world clinical practices.[1,2] As the field of SCS continues to evolve rapidly, hybrid Decentralized Clinical Trials (DCTs) represent an opportunity to ensure the SCS evidence base keeps up with the pace of innovation. Hybrid DCTs incorporate traditional and decentralized trial elements, balancing remote outcomes data collection with traditional in-clinic visits and assessments.[3] The use of hybrid DCTs can enable the collection of clinical data at a scale unfeasible in traditional studies, potentially capturing a broad and diverse group of study participants, and allowing timely reporting and publication of clinical outcomes aligned with real-world clinical experience.

Materials / Methods: The SENSE SCS (Study to Evaluate Neuromodulation Subject Experience with Contemporary Spinal Cord Stimulation Modalities for Chronic Pain) clinical study (NCT05775510), is a prospective, multi-center, post-market, non-randomized, observational study with a hybrid decentralized model of execution. Data presented here is an initial characterization of the subjects enrolled in the Pilot phase of this clinical trial.

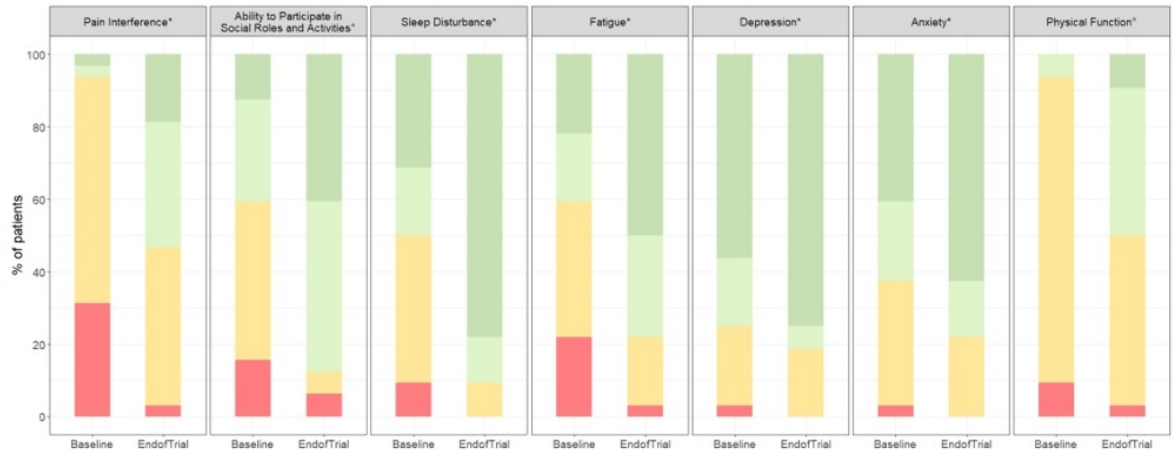
Results: The study was initiated at six US sites and is currently enrolling. Between April 26, 2023 and September 28, 2023, 50 subjects were enrolled. The median subject age was 65 years (min-max 40-84), 44.9% (22/49) female, with a baseline median overall pain score (numeric rating scale) of 7 (min-max 4-10). Most subjects (86.7%) have experienced pain for at least one year, with the most common pain etiologies being spondylosis (38%), failed back syndrome (36%), radicular pain syndrome (36%), and degenerative disc disease (34%). Most subjects were categorized at Baseline as having moderate or severe dysfunction in the PROMIS-29 domains of Pain Interference (93.8%), Ability to Participate in Social Roles and Activities (59.4%), Sleep Disturbance (50.0%), Fatigue (59.4%), and Physical Function (93.8%).

Discussion: Hybrid DCTs represent a novel study approach to advancing the evidence for SCS as the field continues to evolve. Early experience has demonstrated the ability to enroll a significant number of patients in the SENSE SCS study over a relatively short period of time and indicates the potential for rapid data collection across a large patient population as the study continues.

Conclusions: Hybrid DCTs as an adjunct to traditional RCTs can provide a more holistic view of therapy outcomes aligned to clinical experience in both controlled and real-world clinical settings.

Supplemental Data:

Figure 1: PROMIS-29 T-Scores at Baseline and End of SCS Trial



° Defined as: Normal (≥45), Mild (40-45), Moderate (30-40) and Severe (<30)

* Defined as: Normal (<55), Mild (55-60), Moderate (60-70) and Severe (≥ 70)

Table 1: Subject Characteristics

Age (Years), median (min – max) [N=49*]	**65 (40-84)**
Sex Female, n (%) [N=49*]	**22 (44.9%)**
Baseline NRS from PROMIS-29, median (min – max) [N=44*]	**7 (4 – 10)**
Pain Duration, [N=45*]	
< 12 months, n (%)	**6 (13.3%)**
1-3 years, n (%)	**12 (26.7%)**
> 3 years, n (%)	**27 (60%)**
Baseline EQ-5D-5L, mean (± SD) [N=44*]	**0.249 (± 0.328)**
Etiology – n (%) [N=47*]	
SPONDYLOLSIS	**18 (38%)**
FAILED BACK SYNDROME	**17 (36%)**
RADICULAR PAIN SYNDROME	**17 (36%)**
DEGENERATIVE DISC DISEASE	**16 (34%)**
Other	**41 (87%)**
Pain Medication Usage – n (%) [N=45*]**	**38 (84.4%)**

*Of 50 enrolled subjects, baseline pain assessments, medical/surgical history, and demographic information have not been completed for all subjects at time of writing.

**Number of subjects taking at least one pain medication at baseline for pain that the SCS device is intended to treat

References: 1. Blonde L, Khunti K, Harris SB, Meizinger C, Skolnik NS. Interpretation and Impact of Real-World Clinical Data for the Practicing Clinician. Adv Ther. 2018;35(11):1763-1774. doi:10.1007/s12325-018-0805-y 2. Tan YY, Papez V, Chang WH, Mueller SH, Denaxas S, Lai AG. Comparing clinical trial population representativeness to real-world populations: an external validity analysis encompassing 43 895 trials and 5 685 738 individuals across 989 unique drugs and 286 conditions in England. Lancet Healthy Longev. 2022;3(10):e674-e689. doi:10.1016/S2666-7568(22)00186-6 3. Agrawal G, Moss R, Raschke R, et al: No place like home? Stepping up the decentralization of clinical trials. McKinsey Insights, June 10, 2021. https://www.mckinsey.com/industries/life-sciences/our-insights/no-place-like-home-stepping-up-the-decentralization-of-clinical-trials

Acknowledgements: This study was sponsored by Medtronic.

Learning Objectives: 1) Attendees will learn about the structure and value of Hybrid Decentralized Clinical Trials in research 2) Participants will develop an understanding on how Hybrid Decentralized Clinical Trials can be conducted in pain research by using the SENSE SCS clinical trial as a template 3) Participants will understand the utility of real-world evidence in pain medicine, and how it serves as an adjunct to traditional RCT evidence to provide a more representative picture of efficacy in a typical population.

Financial Disclosures: Melissa Murphy: Consultant, Medtronic, Relievant Andrew Will: None Thomas White: Consultant, Speaker, Medtronic Velimir Micovic: Speaker, Medtronic Jugal Dalal: None Krishnan Chakravarthy: Consultant, Vertos Medical, Medtronic, Mainstay Medical; Stock Options, Neuronoff, Higgs Boson Health, Rune Labs; Owner, NXTSTIM INC., Accufix Medical. Xiaoxi Sun, Rupinder Bharmi, Grace Santa Cruz Chavez, and Louis Archila: Employees, Medtronic.

Disclosure: No significant relationships.

O041

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 01
13-05-2024 16:30 - 18:20

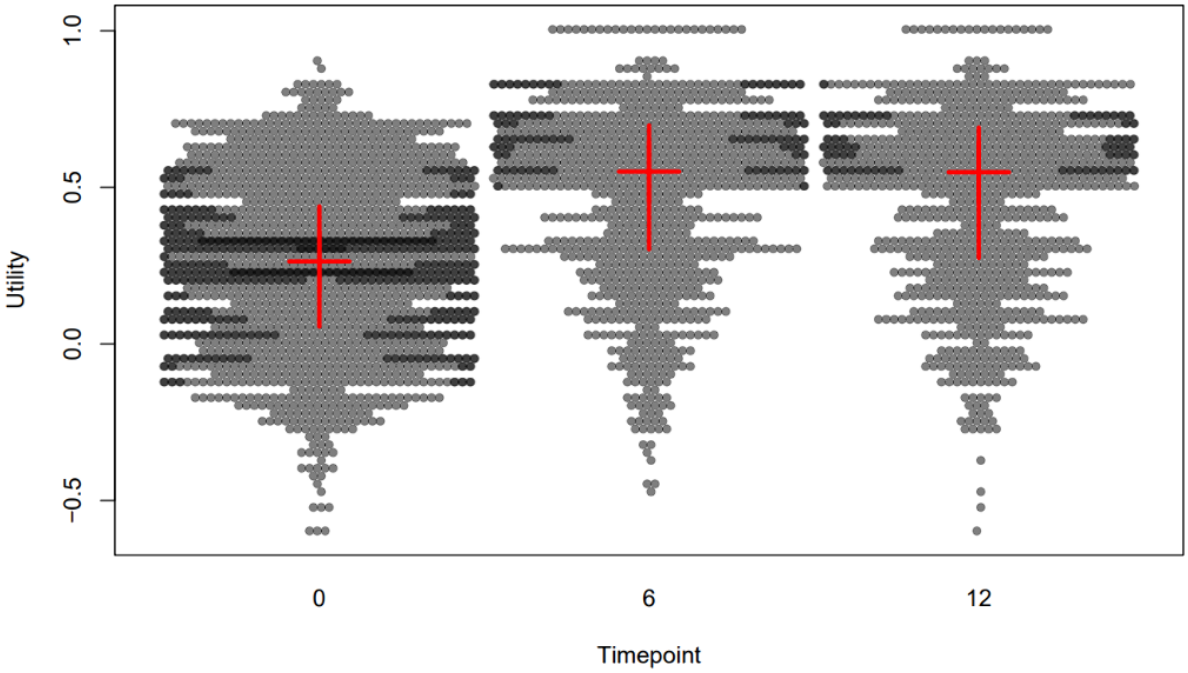
SPINAL CORD STIMULATION IMPROVES QUALITY OF LIFE FOR PATIENTS WITH CHRONIC NEUROPATHIC PAIN - DATA FROM THE BRITISH NATIONAL NEUROMODULATION REGISTRY

Sean Martin, FRCS(SN)[1], Ganesan Baranidharan, FRCA[2], Simon Thomson, MBBS[3], Sam Eldabe, FRCA[4], Roger Strachan, FRCS(SN)[5], Ashish Gulve, MD[4], Stana Bojanic, FRCS(SN)[6], James Fitzgerald, MB ChB, PhD[1]
[1]University of Oxford, Nuffield Department Of Surgical Sciences, Oxford, United Kingdom, [2]Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, [3]Mid & South Essex University Hospitals NHSFT, Pain And Neuromodulation Centre, Basildon, United Kingdom, [4]James Cook University Hospital, Department Of Pain Medicine, MIDDLESBROUGH, United Kingdom, [5]James Cook University Hospital, Department Of Neurosurgery, MIDDLESBROUGH, United Kingdom, [6]Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom

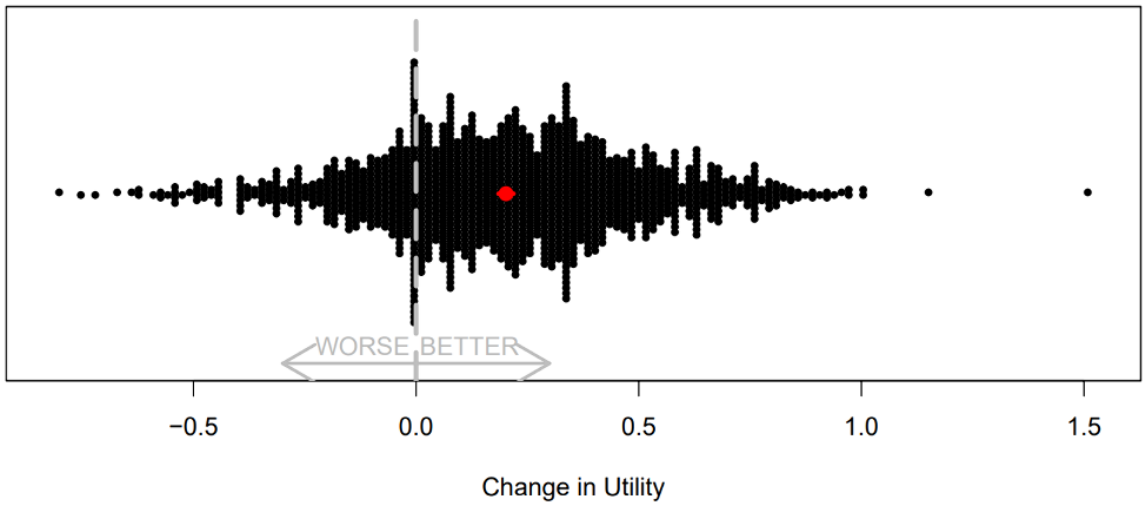
Introduction: Recent papers (including a Cochrane review [1]) have asserted that spinal neuromodulation is not an effective treatment, though these have been robustly criticized [2]. The National Neuromodulation Registry (NNR) is a UK-wide repository of demographic, diagnostic, device identification, and quality-of-life (QoL) outcome data for patients undergoing SCS. It is governed by the Neuromodulation Society of the UK and Ireland (NSUKI), and operated by an independent third party (NEC Software Solutions UK). Large “real-world” datasets showing outcome after SCS for refractory severe neuropathic pain, complementing data from clinical trials, are an important endeavour. QoL outcome data on a standard scale allow comparison with the results of procedures recorded in other similar registries, including the National Joint Registry and British Spine Registry.

Materials / Methods: QoL (EuroQoL 5-dimension 5-level) and demographic data were extracted from the NNR, for patients treated between February 2018 and July 2022 in 27 UK centres. Those without recorded baseline EQ5D data were excluded. Follow-up timepoints were 6 and 12 months. Data were collected confidentially by an independent third party. Data were analyzed using the statistical software platform R. Analyses were parametric or nonparametric depending on data attributes and assessment of normality. Statistical significance was set at $p<0.05$.

Results: Of the 1811 registered patients, 984 (54.3%) were female, 826 (45.6%) were male, and 1 undisclosed. The mean age at surgery was 52.2 years (sd=13.5 years). ***Overall (fig 1).*** Median EQ5D utility index was significantly higher 6 months after surgery than before (0.550 [n=1025] vs. 0.263 [n=1811], $p \ll 0.0001$), and this change was sustained at 12 months after surgery (0.548 [n=970] vs. 0.550 at 6 months [n=1025], p=0.15). This is independent of indication for SCS.



Change in quality of life after SCS (fig 2).



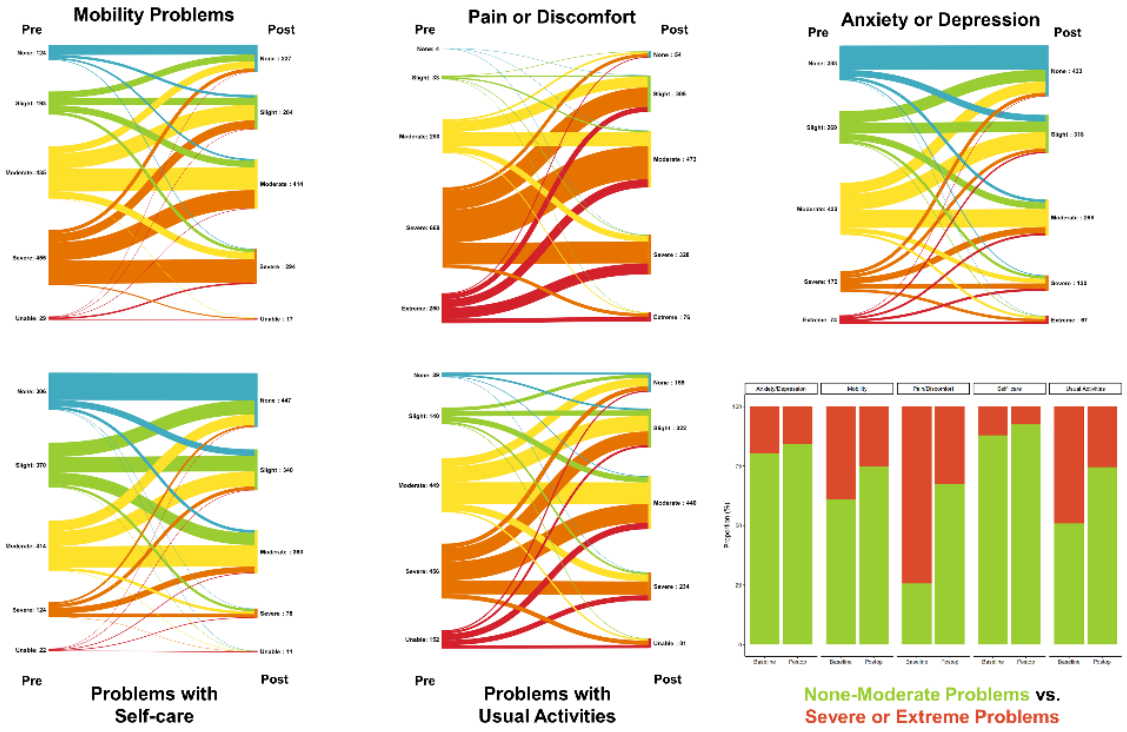
Utility index increased by a mean of 0.202 (95%CI: 0.185-0.219 [n=1236]). 75.2% of patients had an improvement in EQ5D utility.

Discussion: SCS produces a large percentage improvement in mean EQ5D utility, owing to a large effect size and a low baseline utility index (an improvement of 85%). This compares favourably with other well-established surgical interventions for painful conditions with analogous registry data (e.g. spinal surgery 59% improvement [3], total knee replacement 76% improvement [4], total hip replacement 139% improvement [4]).

Conclusions: SCS significantly improved QoL for patients with chronic neuropathic pain in a large prospective multicentre patient cohort. The proportionate improvement exceeds that seen in common surgeries for painful conditions (with the exception of joint replacement).

Supplemental Data: ***EQ5D Components (fig 3), [n=1236].*** For the 1236 patients with paired pre- and post-operative utility scores, the change in each component of the EQ5D-5L was examined. Bottom row, right panel, shows the proportion of patients with a component score of moderate or

better (green) vs. severe or worse (red) before and after surgery. For each of the 5 components there were significantly fewer patients in the severe or worse group after intervention than before (Fisher's exact test, $p \leq 0.01$ for all components). The other five panels are Sankey diagrams depicting the number of patients with each score pre-operatively (left) and the flow to their post-operative scores (right).



References: 1. O'Connell, N.E., et al., *Implanted spinal neuromodulation interventions for chronic pain in adults.* Cochrane Database Syst Rev, 2021. **12**(12): p. CD013756. 2. Russo, M.A., et al., *Problems With O'Connell et al, "Implanted Spinal Neuromodulation Interventions for Chronic Pain in Adults" (Cochrane Review).* Neuromodulation, 2023. **26**(5): p. 897-904. 3. *The British Spine Registry End of Year Annual Report 2021*. 4. NHS Digital. *Finalised Patient Reported Outcome Measures (PROMs) in England for Hip and Knee Replacement Procedures (April 2021 to March 2022).* 2023.

Acknowledgements: Oge Swaby and Richard Armstrong form NEC Software Solutions are acknowledged for their work in the maintenance of the registry.

Learning Objectives: 1. Large datasets from registries of “real world” patients support the clinical effectiveness of spinal cord stimulation as seen from pragmatic randomised trials. 2. The outcomes from spinal cord stimulation for chronic refractory neuropathic pain compare better than spine and even joint replacement surgery in similar “real world” datasets. 3. Multicentre registries are critical for understanding treatment on a population level.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O042

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 01
13-05-2024 16:30 - 18:20

PROSPECTIVE, MULTICENTER OUTCOMES UTILIZING AN SCS-SYSTEM DESIGNED TO ENGAGE SURROUND INHIBITION USING FAST-ACTING SUB-PERCEPTION THERAPY

Magdalena Anitescu, MD[1], Eric Loudermilk, MD[2], Drew Trainor, MD[3], John Noles, MD[4], Jennifer Lee, MD[5], Sayed Wahezi, MD[6], Derron Wilson, MD[7], Lilly Chen, MD[8], Edward Goldberg, MD[8]
[1]University of Chicago Medical Center, Anesthesia And Critical Care, Chicago, United States of America, [2]Piedmont Comprehensive Pain Management Group, Pain Management, Greenville, United States of America, [3]The Denver Spine and Pain Institute, Pain Management, Denver, United States of America, [4]Spine and Pain Specialists, Pain Management, Shreveport, United States of America, [5]Acute and Chronic Pain Therapies, Pain Management, Bellevue, United States of America, [6]Montefiore Multidisciplinary Pain Program, Pain Management, Bronx, United States of America, [7]Goodman Campbell Brain and Spine, Pain Management, Carmel, United States of America, [8]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: Fast-Acting Sub-Perception Therapy (FAST) has been demonstrated to provide robust, profound pain relief at rapid onset (seconds to minutes) in chronic pain patients implanted with Spinal Cord Stimulation (SCS) systems, and these results (including long-term 3-year outcomes) have been corroborated at other centers.[1-3] RRecent published work indicates that Fast-Acting Sub-Perception Therapy -SCS engages the surround inhibition mechanism of action, and activates dorsal column axons and inhibits dorsal horn projection neurons.[4] We studied the effectiveness of Fast-Acting Sub-Perception Therapy -SCS and additional SCS therapy options for chronic pain in a prospective, multicenter, single-arm clinical study and report our preliminary findings.

Materials / Methods: The FAST study is a prospective, multi-center, single-arm study (with adaptive design) of patients implanted with SCS systems (WaveWriter Systems™, Boston Scientific, Valencia, California, United States of America) for chronic pain. The primary endpoint is based on the targeted pain responder rate (2:50% reduction) 3-months post-activation with no increase in average daily opioid medications. Secondary endpoints include (but are not limited to) patient satisfaction (Patient Global Impression of Change, PGIC) and other functional outcomes including disability (Oswestry Disability Index, ODI) and sleep. Key inclusion criteria include diagnosis of predominantly neuropathic pain of trunk and/or limbs for at least 6- months, and no back surgery within 6-months prior to screening.

Results: The study successfully met its primary endpoint ($p<0.0001$) based on a prespecified cohort of 20 subjects. A 6.1-point reduction ($p<0.0001$) in mean low back pain score at 3-months was reported with a 95% responder rate (≥50% improvement in pain relief). A 31-point improvement in disability (ODI) and high patient satisfaction ratings (85% reported much improved or very much improved, PGIC) were found. At the Fast-Acting Sub-Perception Therapy -SCS activation visit, Fast-Acting Sub-Perception Therapy responders achieved maximum paresthesia-free pain relief within a mean of 5.4-minutes. Additional on-going data collection is now underway and updated results will be presented.

Discussion: These obtained results are consistent with a previously published real-world assessment of over 200-patients.[5] With availability of multiple modalities in SCS systems, the capability for rapid onset of analgesia is particularly useful in evaluating what may be best suited for patients.

Conclusions: Preliminary results from this ongoing Fast-Acting Sub-Perception Therapy prospective study suggest that profound, significant pain relief along with improvement in functional outcomes may be achieved in chronic pain patients with Fast-Acting Sub-Perception Therapy -SCS therapy and additional SCS therapy options.

Supplemental Data:

References: 1. Metzger CS, et al. A novel fast-acting sub-perception spinal cord stimulation therapy enables rapid onset of analgesia in patients with chronic pain. Expert Rev Med Devices. 2021 Mar;18(3):299-306.
2. Ferro R, Pei Y, Jain R. Significant Pain Relief Using an SCS System Delivering Novel, Fast Acting Sub-Perception Therapy [Abstract; e-poster]. Annual Meeting of the North American Neuromodulation Society, 2023.
3. Bayerl S, Paz-Solis JF, Matis G, et al. Clinical Outcomes Using A New Fast-Acting Sub Perception Therapy For Chronic Pain: A Multicenter European Observational Real-World Study [Abstract; Poster 113]. Annual Meeting of the North American Neuromodulation Society, 2023.
4. Gilbert JE, Titus N, Zhang T, Esteller R, Grill WM. Surround Inhibition Mediates Pain Relief by Low Amplitude Spinal Cord Stimulation: Modeling and Measurement. eNeuro. 2022 Sep 22:ENEURO.0058-22.2022.
5. Metzger C, Hammond MB, Ferro R, et al. Outcomes ofa Large, Multicenter, RealWorld Study using an SCS System Engaging Surround Inhibition [Abstract; Poster 80]. Annual Meeting of the North American Neuromodulation Society, 2023.

Acknowledgements:

Learning Objectives: 1) To track on-going targeted responder rate in participants in the FAST clinical study. 2) To assess on-going patient satisfaction of participants in the FAST clinical study. 3) To assess on-going functional disabliity of participants in the FAST clinical study.

Financial Disclosures: This clincial study is sponsored by Boston Scientific. Dr Anitescu has a consulting agreement: a) Boston Scientific b) Consultant / Advisory Board c) Level of Compensation - $20,001 - $100,000 USD

Disclosure: This clinical study is sponsored by Boston Scientific. Edward Goldberg is an employee of Boston Scientific.

O043

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 01
13-05-2024 16:30 - 18:20

SPINAL CORD STIMULATION FOR VISCERAL PAIN: A NEW INDICATION FOR PATIENTS WITH THERAPY-RESISTANT PAIN?

Annelotte Van Haaps, MD[1,2], Matthanja Bieze, MD[3], Leonardo Kapural, MD[4], Sean Li, MD[5], Kris Ferguson, MD[6], Ralph De Vries, MSc[7], Michael Schatman, PhD[8,9], Velja Mijatovic, MD, PhD[1,2], Jan Willem Kallewaard, MD[3,10]
[1]Amsterdam UMC, location Vumc, Reproductive Medicine, Amsterdam, Netherlands, [2]Amsterdam University Medical Centres, Amsterdam Reproduction And Development, Amsterdam, Netherlands, [3]Amsterdam UMC, location AMC, Anesthesiology, Amsterdam, Netherlands, [4]Carolina's Pain Institute and Center for Clinical Research, Winston-Salem, United States of America, [5]National Spine and Pain Centers, Shrewsbury, United States of America, [6]Aspirus Langlade Hospital, Pain Clinic, Antigo, United States of America, [7]Vrije Universiteit Amsterdam,, Amsterdam, Netherlands, [8]NYU Grossman School of Medicine, Anesthesiology, Perioperative Care & Pain Medicine, New York, United States of America, [9]NYU Grossman School of Medicine, Population Health, New York, United States of America, [10]rijnstate, Anesthesiology, arnhem, Netherlands

Introduction: Visceral pain, characterized by diffuse and challenging-to-localize pain, occurs frequently and is believed to result from activation of nociceptors of the thoracic, pelvic or abdominal visceral organs. It is difficult to treat, and associated with clinical conditions originating from abdominal organs such as the pancreas, bladder, gallbladder, uterus or intestine (1). When the pain becomes intractable despite optimal medical management, it can negatively affect the patients' Quality of Life (QoL) (2-4). Spinal Cord Stimulation (SCS) has emerged as a potential treatment for intractable visceral pain (5-8). We conducted a narrative review to provide a comprehensive overview of the existing evidence and contribute to the understanding of SCS as a potential therapeutic option for visceral pain across various pain conditions.

Materials / Methods: We conducted a comprehensive literature search in PubMed, Embase and Web of Science which included articles published between October 1st, 1963 up to March 7th, 203. Articles were screened and data was collected independently by three reviewers. The following outcomes were included: effectiveness (pain scores and pain reduction, reduced use of systemic analgesic drugs, patient satisfaction); complications (nerve injury, lead migration and malfunction, infection); functional recovery and QoL.

Results: Seventy articles were included in this review of which most were retrospective cohort studies, case series and case reports. The studies, often with a small number of participants, reported on SCS for chronic pancreatitis, anorectal pain and bowel disorders, gynaecological diagnoses, visceral pelvic pain, urological disorders and finally general visceral pain. They found positive effects on pain and/or symptom relief, opioid consumption, anxiety and depression and QoL. Complications occurred frequently but were often minor and reversible.

Discussion: A positive outcome of a sympathetic nerve block appears to be a potential indicator of SCS effectiveness. Additionally, women receiving SCS for endometriosis had a better outcome compared to other indications. Finally, SCS could also relief functional symptoms such as voiding problems and gastroparesis.

Conclusions: Improved screening and selection criteria need to be established to optimally evaluate eligible patients who might benefit from SCS. Since SCS is expensive, the incorporation of a cost-analysis in future research is recommended. In order to establish a comprehensive treatment plan, rigorous prospective, possibly randomized and controlled studies including selection criteria for SCS that are diagnosis-oriented, with substantial follow-up and adequate sample sizes, are needed.

Supplemental Data:

References: 1. Grundy L, Erickson A, Brierley SM. Visceral Pain. Annu Rev Physiol. 2019;81:261-84. 2. Ong CK, Seymour RA, Lirk P, Merry AF. Combining paracetamol (acetaminophen) with nonsteroidal antiinflammatory drugs: a qualitative systematic review of analgesic efficacy for acute postoperative pain. Anesth Analg. 2010;110(4):1170-9. 3. Davis MP. Drug management of visceral pain: concepts from basic research. Pain Res Treat. 2012;2012:265605. 4. Huygen F, Kallewaard JW, van Tulder M, Van Boxem K, Vissers K, van Kleef M, Van Zundert J. "Evidence-Based Interventional Pain Medicine According to Clinical Diagnoses": Update 2018. Pain Pract. 2019;19(6):664-75. 5. Sdrulla AD, Guan Y, Raja SN. Spinal Cord Stimulation: Clinical Efficacy and Potential Mechanisms. Pain Pract. 2018;18(8):1048-67. 6. Rock AK, Truong H, Park YL, Pilitsis JG. Spinal Cord Stimulation. Neurosurg Clin N Am. 2019;30(2):169-94. 7. Kallewaard JW, D'eer, I., Edelbroek, C., Huygen, F.J.P.M., Kurt, E., Nijhuis, H.J.A., Terwiel, C.T.M., van de Voort, T.W.G., de Vries-Fennis, G.M., Hendriks-Soetens, K.C.M. . Standpunt Neuromodulatie bij Chronische Pijn Nederlandse vereniging voor anesthesiologie: Nederlandse vereniging voor anesthesiologie; 2020 [Available from: https://www.anesthesiologie.nl/documenten/standpunt-neuromodulatie-bij-chronische-pijn. 8. Woodroffe RW, Pearson AC, Pearlman AM, Howard MA, Nauta HJW, Nagel SJ, et al. Spinal Cord Stimulation for Visceral Pain: Present Approaches and Future Strategies. Pain Med. 2020;21(10):2298-309.

Acknowledgements:

Learning Objectives: 1. Aim to extent presentation skills and learn from other presenters. Since this would be the first time presenting at an international conference, this could be reached, also by listening and learning from other presenters. 2. Aim to present the results of our narrative review where all data is collected regarding the appliance of SCS for visceral pain. This is a relatively unique review, since it, to the best of our knowledge, has never been collected. 3. Aim to increase awareness on the effectivity of SCS in reducing visceral pain.

Financial Disclosures: There is no financial support regarding the writing of this narrative review to disclose.

Disclosure: No significant relationships.

O044

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 01
13-05-2024 16:30 - 18:20

EVALUATING SCS AND MEDICAL MANAGEMENT FOR CHRONIC PAIN WITHOUT PRIOR SURGERY: 1-YEAR OUTCOMES (SOLIS RCT)

James North, MD[1], Julio Paez, MD[2], Aaron Calodney, MD[3], Eric Loudermilk, MD[4], Zachary McCormick, MD[5], Drew Trainor, MD[6], John Noles, MD[7], Michael Yang, MD[8], Gregory Phillips, MD[9], Derron Wilson, MD[10], Steven Rosen, MD[11], Maged Guirguis, MD[12], Lilly Chen, MD[13], Edward Goldberg, MD[13]
[1]Carolinas Pain Institute, Pain Management, Winston-Salem, United States of America, [2]South Lake Pain Institute, Pain Management, Clermont, United States of America, [3]Precision Spine Care, Pain Management, Tyler, United States of America, [4]Piedmont Comprehensive Pain Management Group, Pain Management, Greenville, United States of America, [5]University of Utah School of Medicine, Pain Management, Salt Lake City, United States of America, [6]The Denver Spine and Pain Institute, Pain Management, Denver, United States of America, [7]Spine and Pain Specialists, Pain Management, Shreveport, United States of America, [8]Summit Pain Alliance, Pain Management, Santa Rosa, United States of America, [9]Pacific Sports and Spine, Pain Management, Eugene, United States of America, [10]Goodman Campbell Brain and Spine, Pain Management, Carmel, United States of America, [11]Delaware Valley Pain and Spine Institute, Pain Management, Trevose, United States of America, [12]Ochsner Clinic Foundation, Pain Management, New Orleans, United States of America, [13]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: There is growing interest in utilizing Spinal Cord Stimulation (SCS) in chronic pain patients who have not yet undergone previous surgical intervention.1- 5 This is relevant given that contemporary SCS devices offer substantially more safety, novel technology, and/or neurostimulative capabilities than older-generational SCS systems. Correspondingly, interventional treatment approaches capable of multimodal therapeutic strategies are now actively recommended by pain care advocates.6, 7 As such, we sought to carry out a randomized controlled trial (RCT) in patients randomized to receive multimodal SCS compared to those receiving conventional medical management (CMM) alone.

Materials / Methods: SOLIS is a prospective, multicenter RCT that compares SCS (Wavewriter Systems [Boston Scientific]) versus CMM in patients with chronic low back and/or leg pain with no prior spinal surgery (Clinicaltrials.gov: NCT04676022). Enrolled non-surgical back pain (NSBP) patients who meet inclusion criteria are randomized to SCS versus CMM alone. Key inclusion criteria include diagnosis of chronic low back pain, with or without leg pain, for ≥6 months, and documented care of chronic pain for ≥90 days. The primary endpoint is responder rate (≥50% pain relief) with no increase in baseline opioid medications for pain at 3-month follow-up. Other secondary and/or exploratory measures include Quality-of-Life (SF-36; EQ-5D-5L), Disability (Oswestry Disability Index, ODI), and Safety Outcomes.

Results: Of the study participants randomized, 63-subjects were selected to receive SCS+CMM and 65-subjects CMM only (n=128). Primary endpoint analysis demonstrated that multimodal SCS combined with CMM was superior to CMM alone ($p<0.0001$) in treating NSBP patients at 3-months follow-up per obtained responder rates (SCS+CMM: 89.5% [51/57] versus CMM: 8.1% [5/62]). Additionally, those in the SCS+CMM arm were found to have a 28-point ODI score reduction versus a 7-point reduction in those randomized to CMM only. Out to 1-year follow-up, the following was observed: high profound responder rate (≥80% pain relief) of 51.2%; an 84% treatment responder rate (≥50% pain relief); significant improvement in disability (Δ25-point ODI decrease vs Baseline); and mean 58.2% improvement in overall quality-of life (EQ-5D-5L) score. Additionally, CMM randomized subjects who crossed over to SCS+CMM arm achieved a responder rate of 85% (n=39) and a mean reduction in ODI score of 30-points (n=39) at 1-year follow-up.

Discussion: Given the prevalence and economic/societal burden of NSBP, providing SCS within the therapeutic armamentarium for chronic pain represents a key opportunity to address a clinically important need.

Conclusions: Multimodal SCS is effective in treating chronic pain in patients with no prior spinal surgery demonstrating superior outcomes compared with CMM.

Supplemental Data:

References: 1. Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin RH, Gilron I, Haanpfili M, Hansson P, Jensen TS, Kamerman PR, Lund K, Moore A, Raja SN, Rice AS, Rowbotham M, Sena E, Siddall P, Smith BH, Wallace M. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurol. 2015 Feb;14(2):162-73.
2. Al-Kaisy A, Van Buyten JP, Kapural L, Amirdelfan K, Gliner B, Caraway D, Subbaroyan J, Edgar D, Rotte A. 10 kHz spinal cord stimulation for the treatment of non-surgical refractory back pain: subanalysis of pooled data from two prospective studies. Anaesthesia. 2020 Jun;75(6):775-784.
3. Kapural L, Jameson J, Johnson C, Kloster D, Calodney A, Kosek P, Pilitsis J, Bendel M, Petersen E, Wu C, Cherry T, Lad SP, Yu C, Sayed D, Goree J, Lyons MK, Sack A, Bruce D, Rubenstein F, Province-Azalde R, Caraway D, Patel NP. Treatment of nonsurgical refractory back pain with high-frequency spinal cord stimulation at 10 kHz: 12-month results of a pragmatic, multicenter, randomized controlled trial. J Neurosurg Spine. 2022 Feb 11 :1-12.
4. Kapural L, Calodney A. Retrospective Efficacy and Cost-Containment Assessment of 10 kHz Spinal Cord Stimulation (SCS) in Non-Surgical Refractory Back Pain Patients. J Pain Res. 2022 Nov 16;15:3589-3595.
5. Rauck RL, Loudermilk E, Thomson SJ, et al. Long-term safety of spinal cord stimulation systems in a prospective, global registry of patients with chronic pain. Pain Manag. 2023 Feb;13(2):115-127.
6. U.S. Department of Health and Human Services, Alliance to Advance Comprehensive Integrative Pain Management (2019). Pain Management Best Practices Inter-Agency Task Force Report. https://painmanagementalliance.org/resources/hhs-report- 2019/. Accessed October 28th, 2022.
7. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain - United States, 2022. MMWR Recomm Rep. 2022 Nov 4;71 (3):1-95.

Acknowledgements:

Learning Objectives: To assess the following:
1) Responder rate in subjects allocated SCS + CMM arm versus CMM only arm (out to 1-year follow-up)
2) Oswestry Disability Index score in those allocated SCS + CMM arm versus CMM only arm (out to 1-year follow-up)
3) Outcomes in those who crossed over from CMM alone arm to the SCS + CMM arm (out to 1-year follow-up)

Financial Disclosures: Dr. North has a consulting agreement with Boston Scientific. a) Boston Scientific b) Consultant / Advisory Board c) Level of Compensation - $5,001 - $20,000 USD

Disclosure: This study is sponsored by Boston Scientific. Lilly Chen and Edward Goldberg are employees of Boston Scientific,

O045

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 01
13-05-2024 16:30 - 18:20

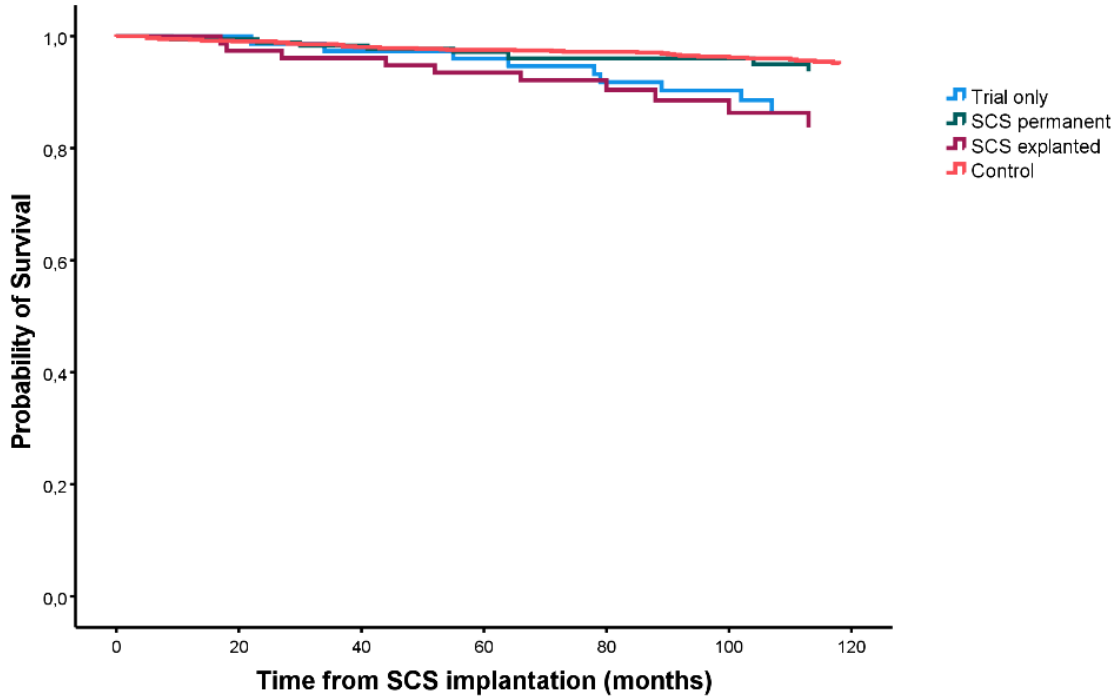
SPINAL CORD STIMULATION WAS ASSOCIATED WITH REDUCED EXCESS MORTALITY IN 331 PATIENTS WITH SEVERE CHRONIC NEUROPATHIC PAIN

Antti Luikku, MD[1], Antti Martikainen, MD[1], Henna-Kaisa Jyrkkänen, MD, PhD[1], Tiina-Mari Ikäheimo, RN[1], Mette Nissen, MD, PhD[1], Mikael Von Und Zu Fraunberg, MD, MSc, PhD[2,3], Jukka Huttunen, MD, PhD[1]
[1]Kuopio University Hospital, Neurocenter - Neurosurgery, Kuopio, Finland, [2]Oulu University Hospital, Neurosurgery At Neurocenter, Oulu, Finland, [3]University of Oulu, Research Unit Of Clinical Medicine, Oulun yliopisto, Finland

Introduction: Spinal cord stimulation (SCS) is an established yet profoundly enigmatic treatment for neuropathic pain. Although effects of SCS on subjective pain scoring and functional ability have been presented, more robust proofs of effect are wanted. In this retrospective, case-controlled study, we present survival and mortality of patients trialed for SCS.

Materials / Methods: 331 consecutive patients (age 65 or younger) referred to Kuopio University Hospital (KUH) for failed back surgery syndrome (FBSS), complex regional pain syndrome (CRPS), or other neuropathic pain were trialed for SCS implantation. Based on a one-week trial, SCS device was implanted for 256 patients, but later explanted from 77 patients. During the follow-up of median 9.1 years, 28 patients and 40 matched controls died. Causes of death were obtained from national registry.

Results: 10-year mortality was increased in trial only group HR = 2.6 (CI 1.3-5.4, p < 0.01), and explanted SCS group HR =3.2 (CI 1.6-6.4, p < 0.001), while there was no increased mortality in permanent SCS group when compared to matched controls (HR = 1.4, CI 0.67-2.8, p = 0.38). Most frequent causes of death by ICD-10 subgroups were malignant neoplasms (26 %), ischemic heart diseases (16 %), and accidental poisoning by and exposure to noxious substances (9 %). There were no significant differences in causes of death between groups.



Discussion: To our knowledge, this is the first study to present increased mortality in trialed SCS population suffering from neuropathic pain, which was reversible by successful SCS therapy. Although not statistically significant, accidental poisoning by and exposure to noxious substances as cause of death was overrepresented in pooled SCS group in comparison to matched controls. Our study population of patients aged 65 and under and SCS implantation by one-week trial is feasible and represents well the general population referred for SCS.

Conclusions: Mortality is increased in patients with neuropathic pain and seems to be normalized with SCS when compared to matched controls. This provides solid evidence for the effects of SCS.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1. Mortality in patients with neuropathic pain - Mortality is increased in patients with severe neuropathic pain, and this is reduced by spinal cord stimulation. 2. Causes of death in patients with neuropathic pain - ICD-10 subgroup "accidental poisoning by and exposure to noxious substances" is overrepresented in patients with severe neuropathic pain. 3. Effects of spinal cord stimulation - Although the specific method of pain alleviation by spinal cord stimulation is still under research, its ability to effect mortality provides solid evidence of its effectiveness.

Financial Disclosures: Antti Luikku - Medtronic - Education/Research - $501 - $5,000 USD Jukka Huttunen - Medtronic - Education/Research - $501 - $5,000 USD and Abbott St Jude Medical - Education/Research - $501 - $5,000 USD Henna-Kaisa Jyrkkänen - Medtronic - Education/Research - $501 - $5,000 USD and Abbott St Jude Medical - Education/Research - $501 - $5,000 USD Tiina-Mari Ikäheimo - Medtronic - Education/Research - $501 - $5,000 USD and Abbott St Jude Medical - Education/Research - $501 - $5,000 USD Mikael von und zu Fraunberg - Medtronic - Education/Research - $501 - $5,000 USD and Abbott St Jude Medical - Education/Research - $501 - $5,000 USD Mette Nissen - Medtronic - Education/Research - $501 - $5,000 USD and Abbott St Jude Medical - Education/Research - $501 - $5,000 USD

Disclosure: No significant relationships.

O046

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 01
13-05-2024 16:30 - 18:20

USING NEUROMODULATION TO HELP PEOPLE WITH CHRONIC PAIN RETURN TO WORK

Silke Kretzschmar, MBBS, Michael Kretzschmar, PhD
Praxis fuer Arbeitsmedizin, Gera, Germany

Introduction: There are only few data available how neuromodulative (spinal cord stimulation, intrathecal drug delivery systems) pain therapy effects the quality of life in patients with chronic pain[1]. So far, the ability to return to work after neuromodulative pain therapy has never been assessed. Surprisingly, the importance of employment to the quality of life is rather underestimated i.e. unemployment seems not only to have an effect on illness, but also seems to be the cause of it[2].

Materials / Methods: From 2011 to 2020, we observed 43 patients treated with electrical (n = 35) or pharmacological (n = 8) neuromodulation for chronic pain who remained or were reintegrated into employment. These patients filled out a questionnaire on work ability (work ability index)[3], pain intensity (VAS) during the last 7 days and self-rated health before and 12 months after the treatment. The patients were asked about their professional situation and their workplace. The data were evaluated by means of a corresponding software[4, 5]. Statistics: Fisher's exact Test, Mann-Whitney-U-Test, Wilcoxon signed-rank Test, significance level $\alpha < 5\%$ ($p < 0,05$).

Results: Significant differences were observed for work ability, VAS and self-rated health (all $p < 0.05$) between the time points before and 1 year after the start of neuromodulative treatment. In addition to improving the ability to work, we also recorded a significant improvement in the quality of life ($p < 0.05$). 5 patients took part in occupational retraining programs. In 11 cases the patients were assigned to a new job within the company.

Discussion: Neuromodulative pain therapy obviously improves the ability to work as well as the quality of life in patients suffering from chronic pain. The integration and also the reintegration into employment is a major part of therapy.

Conclusions: Neuromodulation as such is no contraindication for reintegration into work life. It must be part of an overall treatment plan to manage chronic pain, and must engage health care professionals, patients, and health insurance companies in supporting a return to employment, if possible.

Supplemental Data:

References: 1. Kumar K et al. Neuromodulation. 2014; 17 Suppl 1:22-35. 2. Herbig B et al. Dtsch Arztebl Int 2013; 110: 413–9. 3. Ilmarinen J. Ageing workers in the European Union – Status and promotion of work ability, employability and employment. Helsinki: Finnish Institute of Occupational Health 1999. 4. Ware JE et al. Clin Epidemiol 1998; 51:903–912. 5. Ellert U, Kurth BM. Bundesgesundheitsbl Gesundheitsforsch Gesundheitsschutz) 2004; 47:1027–1032.

Acknowledgements:

Learning Objectives: 1 Neuromodulation itself does not interfere with the ability to work. 2 Preseve earning capacity contributes significantly to an improved quality of life in chronic pain patients. 3 Employment preserves self-esteem in people in general.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O047

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 01
13-05-2024 16:30 - 18:20

ECONOMIC BURDEN AND BUDGETARY IMPACT OF SPINAL CORD STIMULATION IN MANAGING PAINFUL DIABETIC POLYNEUROPATHY: AN ANALYSIS USING GERMAN HEALTH CLAIMS DATA

Thorsten Luecke, MD
Franziskus Hospital Linz-Remagen, Department Of Anaesthesia And Pain Therapy, Linz am Rhein, Germany

Introduction: Painful diabetic polyneuropathy (PDN) has a substantial impact on patients' quality of life and represents a major economic burden on the healthcare system. This study aims to review the economic and resource implications of PDN management and assess the potential fiscal impact of spinal cord stimulation (SCS) interventions. The objective of this study was to examine the cost structure and resource utilisation in patients with PDN from the perspective of German statutory health insurance (SHI) and to construct a budget impact model (BIM) for SCS.

Materials / Methods: A retrospective analysis of health claims of ~4.9 million German SHI enrollees allowed categorisation and stratification of DM patients into PDN subsets using specific pain management criteria. In-depth analyses of annual costs per patient, service area segmentation, and sickness/disability days were performed, followed by a 5-year BIM for SCS, assuming 85% therapeutic success and applying a 2% inflation rate. Further, the comprehensive assessments embraced a meticulous exploration of the cost components, encompassing different service areas, thus providing a granular understanding of the economic footprint of PDN within the German healthcare system.

Results: Of 88,347 DPN patients, 35% were identified as having PDN, with substantially increased annual costs (€22,266 per PDN patient versus €9,727 for non-PDN patients) and a marked increase in disease/disability days and amputations. Despite the immediate financial increase due to SCS device implantation in the first year (additional €18,778 per patient), a cost saving of €4,122 per patient was observed in the third year. Notably, the financial perspective underwent a significant paradigm shift in the trajectory of SCS expenditure and savings, revealing a nuanced financial narrative that demanded judicious fiscal analysis.

Discussion: Despite the initial substantial investment in SCS, particularly in the first year, pronounced economic benefits are evident in subsequent years, highlighting the economic burden of PDN.

Conclusions: The use of SCS, although initially costly, showed as an economical favourable treatment, revealing economic benefits from year three and providing a tangible method to alleviate the various burdens associated with PDN management.

Supplemental Data:

References: Luecke, T., et al. (2022). Kosten und Ressourcenverbrauch. Monitor Versorgungsforschung, 06/22, 61-67. http://doi.org/10.24945/MVF.06.22.1866-0533.2464. Petersen EA, et al. (2021). Effect of high-frequency (10 kHz) spinal cord stimulation. JAMA Neurol, 78(6), 687-698.

Acknowledgements: The authors thank Gerd Gottschalk for valuable discussions and Nevro Germany GmbH for financial support.

Learning Objectives: The study illuminates the economic complexities of PDN management, deepens understanding of the financial landscape, and initiates dialogue on viable intervention strategies in the German context.

Financial Disclosures: Author: Thorsten Luecke, MD Company Name: Nevro Germany GmbH Role: Consultant / Advisory Board and Education / Research Level of Compensation - $501 - $5,000 USD

Disclosure: We did receive financial support for the development of the Budget Impact Model by Nevro Germany GmbH

O048

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 01
13-05-2024 16:30 - 18:20

SPINAL CORD STIMULATION WITH POSTOPERATIVE REMOTE PROGRAMMING MANAGEMENT FOR CHRONIC INTRACTABLE TRUNK OR LIMB PAIN: A MULTICENTER RANDOMIZED WITHDRAWAL TRIAL (CITRIP STUDY)

Yang Lu, MD[1], Siying Guo, MD[2], Peng Mao, MD[3], Bifa Fan, MD[3], James Wang, MD[1], Guihuai Wang, PhD[1], Luming Li, PhD[4]
[1]Department of Neurosurgery, Beijing Tsinghua Changgung Hospital, School of Clinical Medicine, Tsinghua University, Beijing, China, [2]School of Medicine, Tsinghua University, Beijing, China, [3]Department of Pain Medicine, China-Japan Friendship Hospital, Beijing, China, [4]National Engineering Research Center of Neuromodulation, Tsinghua University, Beijing, China

Introduction: Although effective results of many studies support the use of spinal cord stimulation in chronic pain patients, no randomized controlled trial has been undertaken in China to date, a nation characterized by vast territories and unevenly distributed medical resources. This disparity presents a significant challenge for treatments like spinal cord stimulation that necessitate regular post-operative adjustments. CITRIP is a multicenter, enriched-enrollment, placebo-controlled, randomized, withdrawal study designed to evaluate the clinical effectiveness and safety of spinal cord stimulation plus remote programming management in patients with intractable trunk or limb pain.

Materials / Methods: Participants were recruited in 12 centers across China. Those with persistent trunk or limb pain and an average VAS score ≥ 5 underwent spinal cord stimulation testing. Those achieving a VAS score reduction of ≥ 50% proceeded to implanted pulse generator implantation. In the withdrawal period at 3-month, participants randomized to the experimental group (EG) underwent continuous stimulation while ceasing the stimulation in the control group (CG). The primary outcome was the difference of maximal VAS score between EG and CG in the withdrawal period compared with baseline before the withdrawal period. We also assessed VAS score changes at 1, 3, and 6 months; responder rates; achievement of desirable pain state (VAS ≤ 4); sleep disruptions; depression levels (Beck Depression Inventory); quality of life (short-form 36); medication usage, and adverse events. Analysis will be intention-to-treat at 3 and 6 months. Registered at ClinicalTrials.gov, NCT03858790.

Results: Between Dec. 2018, and May. 2020, 109 patients were enrolled and 57 were randomly assigned (29/28 to each treatment group). The primary outcome was achieved with the difference of maximal VAS score between EG and CG in the withdrawal period was 4.11 (CI 3.08–5.14; $p < 0{\cdot}001$). No significant difference was found in VAS scores, responder rate, awake times during sleep, depression evaluation, short-form 36 and drug usage between the two groups at the 6-month follow-up. We observed no differences in safety profiles between the two groups. In the postoperative remote programming, physicians and patients did not encounter any serious adverse events; the most significant complaint was network

instability.

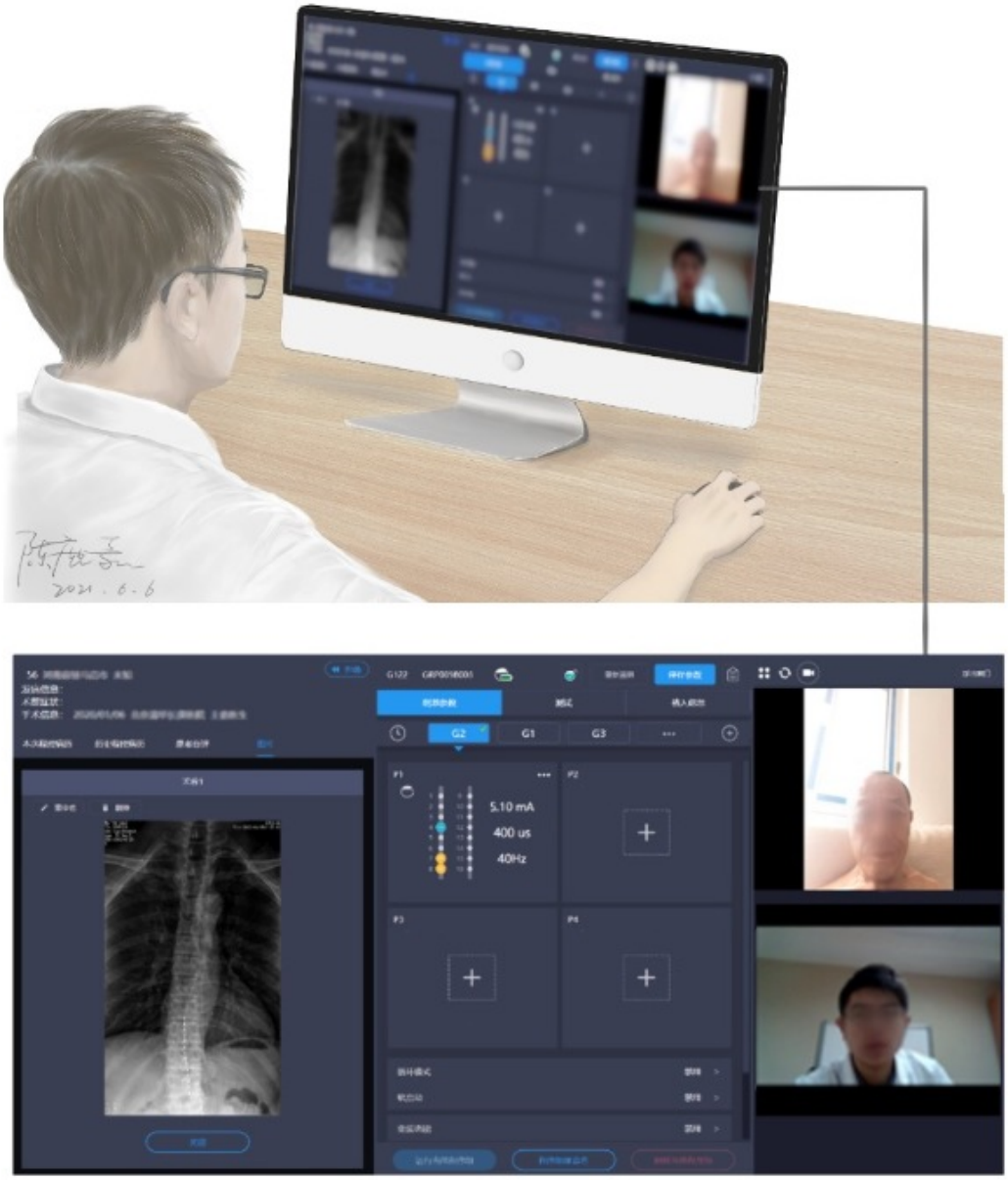


Fig. 1 Demonstration of the remote programming practice

Discussion: Spinal cord stimulation provided significantly pain relief up to 6 months. Remote programming is not only safe, effective, and efficient but is especially beneficial for patients who face challenges in accessing post-operative programming due to economic constraints or unforeseen circumstances like COVID-19.

Conclusions: Spinal cord stimulation with postoperative remote programming management coud provide significant pain relief up to 6 months.

Supplemental Data:

References: 1.Gaskin DJ, Richard P: The economic costs of pain in the United States. J Pain 2012, 13:715-724. 2.Vannemreddy P, Slavin KV: Spinal cord stimulation: Current applications for treatment of chronic pain. Anesth Essays Res 2011, 5:20-27. 3.Chakravarthy K, Richter H, Christo PJ, Williams

K, Guan Y: Spinal Cord Stimulation for Treating Chronic Pain: Reviewing Preclinical and Clinical Data on Paresthesia-Free High-Frequency Therapy. Neuromodulation 2018, 21:10-18. 4.Taylor RS: Spinal cord stimulation in complex regional pain syndrome and refractory neuropathic back and leg pain/failed back surgery syndrome: results of a systematic review and meta-analysis. J Pain Symptom Manage 2006, 31:S13-19. 5.Ubbink DT, Vermeulen H: Spinal cord stimulation for critical leg ischemia: a review of effectiveness and optimal patient selection. J Pain Symptom Manage 2006, 31:S30-35. 6. Chen Y, Hao H, Chen H, Tian Y, Li L: The study on a real-time remote monitoring system for Parkinson's disease patients with deep brain stimulators. Conf Proc IEEE Eng Med Biol Soc 2014, 2014:1358-1361. 7.Chen Y, Hao H, Chen H, Li L: The study on a telemedicine interaction mode for Deep Brain Stimulation postoperative follow-up. Conf Proc IEEE Eng Med Biol Soc 2015, 2015:186-189. 8.Beck AT, Steer RA: Internal consistencies of the original and revised Beck Depression Inventory. J Clin Psychol 1984, 40:1365-1367. 9.Jenkinson C, Coulter A, Wright L: Short form 36 (SF36) health survey questionnaire: normative data for adults of working age. BMJ 1993, 306:1437-1440. 10.Ostelo RW, de Vet HC: Clinically important outcomes in low back pain. Best Pract Res Clin Rheumatol 2005, 19:593-607. 11.Kelly AM: The minimum clinically significant difference in visual analogue scale pain score does not differ with severity of pain. Emerg Med J 2001, 18:205-207. 12. Kelly AM: Does the clinically significant difference in visual analog scale pain scores vary with gender, age, or cause of pain? Acad Emerg Med 1998, 5:1086-1090. 13.Vinik AI, Shapiro DY, Rauschkolb C, Lange B, Karcher K, Pennett D, Etropolski MS: A randomized withdrawal, placebo-controlled study evaluating the efficacy and tolerability of tapentadol extended release in patients with chronic painful diabetic peripheral neuropathy. Diabetes Care 2014, 37:2302-2309. 14.Chakravarthy K, Kent AR, Raza A, Xing F, Kinfe TM: Burst Spinal Cord Stimulation: Review of Preclinical Studies and Comments on Clinical Outcomes. Neuromodulation 2018, 21:431-439. 15.Kapural L, Yu C, Doust MW, Gliner BE, Vallejo R, Sitzman BT, Amirdelfan K, Morgan DM, Brown LL, Yearwood TL, et al: Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: The SENZA-RCT Randomized Controlled Trial. Anesthesiology 2015, 123:851-860. 16.Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, Haythornthwaite JA, Jensen MP, Kerns RD, Ader DN, et al: Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain 2008, 9:105-121. 17.Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, Kerns RD, Stucki G, Allen RR, Bellamy N, et al: Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain 2005, 113:9-19. 18.Kopec JA, Abrahamowicz M, Esdaile JM: Randomized discontinuation trials: utility and efficiency. J Clin Epidemiol 1993, 46:959-971. 19.Famm K, Litt B, Tracey KJ, Boyden ES, Slaoui M: Drug discovery: a jump-start for electroceuticals. Nature 2013, 496:159-161. 20.Reardon S: Electroceuticals spark interest. Nature 2014, 511:18. 21.Wolter T, Winkelmuller M: Continuous versus intermittent spinal cord stimulation: an analysis of factors influencing clinical efficacy. Neuromodulation 2012, 15:13-19; discussion 20. 22.Achey M, Aldred JL, Aljehani N, Bloem BR, Biglan KM, Chan P, Cubo E, Dorsey ER, Goetz CG, Guttman M, et al: The past, present, and future of telemedicine for Parkinson's disease. Mov Disord 2014, 29:871-883. 23.Jitkritsadakul O, Rajalingam R, Toenjes C, Munhoz RP, Fasano A: Tele-health for patients with deep brain stimulation: The experience of the Ontario Telemedicine Network. Mov Disord 2018, 33:491-492. 24.Dorsey ER, Voss TS, Shprecher DR, Deuel LM, Beck CA, Gardiner IF, Coles MA, Burns RS, Marshall FJ, Biglan KM: A U.S. survey of patients with Parkinson's disease: satisfaction with medical care and support groups. Mov Disord 2010, 25:2128-2135. 25.Cheng EM, Swarztrauber K, Siderowf AD, Eisa MS, Lee M, Vassar S, Jacob E, Vickrey BG: Association of specialist involvement and quality of care for Parkinson's disease. Mov Disord 2007, 22:515-522.

Acknowledgements: This work was supported by the Beijing Nova Program (Z211100002121050, 20220484216), Tsinghua Precision Medicine Foundation (LC201906) and The National Key Research and Development Program of China (2016YFC0105502).

Learning Objectives: 1.Objective: Understand the current status and challenges of spinal cord stimulation for chronic pain in China. **Desired Result:** Learners should be able to articulate the unique challenges posed by China's vast territories and uneven distribution of medical resources, especially as they pertain to treatments requiring regular follow-ups like spinal cord stimulation. **2.Objective:** Recognize the significance and design of the CITRIP study in the context of spinal cord stimulation. **Desired Result:** Learners should be familiar with the multicenter, enriched-enrollment, placebo-controlled, randomized withdrawal design of the CITRIP study, and understand its aims and importance in evaluating the clinical effectiveness and safety of spinal cord stimulation

combined with remote programming. **3.Objective:** Comprehend the potential implications of the CITRIP study's results for future spinal cord stimulation practices. **Desired Result:** Upon completion, learners should be able to discuss the potential impacts of the study's findings on the broader adoption and implementation of spinal cord stimulation as a treatment modality in China, and how remote programming might address challenges posed by geographical and medical resource disparities.

Financial Disclosures: Yang Lu, PINS Medical, Education / Research, $1 - $500 USD Peng Mao, PINS Medical, Education / Research, $1 - $500 USD Bifa Fan, PINS Medical, Education / Research, $501 - $5,000 USD James Wang, PINS Medical, Education / Research, $1 - $500 USD Luming Li, PINS Medical, Education / Research, $501 - $5,000 USD

Disclosure: No significant relationships.

O049

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 01
13-05-2024 16:30 - 18:20

LONG-TERM (4-YEAR) OUTCOMES OF SPINAL CORD STIMULATION USING A LONG 4-WEEK TRIAL APPROACH: A 180 PATIENTS EXPERIENCE FROM A SINGLE-CENTRE

José Manuel Trinidad Martin-Arroyo, MD, Gema Gómez-Benítez, MD, Diego Benítez-Pareja, MD, Jose Antonio Lopez Lopez, MD
Puerta del Mar University Hospital, Cádiz, Spain

Introduction: There is lack of consensus about the appropriate length of the trial period for Spinal Cord Stimulation (SCS), although current standard ranges from 3-to-7 days. New trends are advocating for a single-stage procedure in light of a better cost-efficacy and comparable outcomes [1]. However, SCS practitioners must ensure that mid- and long-term outcomes are not jeopardized because of this practice. In this work, we share our long-term results performing a conservative 4-week screening trial for careful selection of patients and progressive opioids withdrawal.

Materials / Methods: This is retrospective review of a single-centre experience in SCS since January 2018. By practice, all patients underwent a conservative trial approach of approximately 4-weeks with progressive opioid withdrawal. Over the trial, patients conducted weekly visits to our pain-unit for physician consultation, wound healing and programming. A ≥50% pain relief is required for permanent implant. SCS manufacturer was diverse: 33.3% Boston Scientific, 26.1% Abbott, 20.0% Medtronic and 20% Nevro.

Results: A 180 implanted patients were revised (47.2% female, 50.2 years). Baseline diagnosis were: post-laminectomy-lumbar-syndrome (135:75%), CRPS (19), neuralgia (7), post-laminectomy-cervical-syndrome (5), peripheral neuropathy (5), and others. Average trial duration was 29.2 days. Trial was positive for 156 patients (86.6%) and hence negative for 23 patients (12.7%). Long-term revision (3.6 years) indicated that: i) outcomes were sustained and satisfactory with a mean of 62.4% pain relief and a 91.3%(105/115) of subjects who discontinued opioids; and ii) only 6 subjects (3.3%) required device explant, and the rate for infections (i.e., need for antibiotics or positive culture) or complications (e.g., pocket pain) were low: 5.5% and 5.7%, respectively.

Discussion: Our experience strongly supports long-term effectiveness of SCS in the treatment of chronic pain and the effectiveness of long trials. We haven't observed higher rates of infections and complications as reported by other authors. Our explant ratio is maintained minimal as compared with other experiences of up-to 30% [2]. Our practice contrasts with the recent Trial-RCT findings, in which trial didn't impact short- or long-term outcomes. However, this trial outcomes were less satisfactory than ours (62% vs. 27% (No-trial) to 34% (trial)). Many factors could be impacting these percentages, but our conservative trial approach might be, to some extent, enabling effective outcomes by proper identification of bad responders and trial-guided selection of device manufacturer.

Conclusions: Long-term SCS satisfactory outcomes are sustained in our centre thanks to a careful selection of patients after an extended trial approach (~4 weeks) with progressive opioids reduction.

Supplemental Data:

References: [1] Eldabe S, Nevitt S, Griffiths S, et al. Does a Screening Trial for Spinal Cord Stimulation in Patients With Chronic Pain of Neuropathic Origin Have Clinical Utility (TRIAL-STIM)? 36-Month Results From a Randomized Controlled Trial. Neurosurgery. 2023 Jan 1;92(1):75-82. [2] Wang VC, Bounkousohn V, Fields K, Bernstein C, Paicius RM, Gilligan C. Explantation rates of high frequency spinal cord stimulation in two outpatient clinics. Neuromodulation 2020; https://doi.org/10.1111/ner.13280.

Acknowledgements:

Learning Objectives: (1) SCS is effective long-term if patients are properly selected (2) Long trials of up to 4 weeks could help in proper selection of patients and device manufacturer (3) Conservative approach to SCS is still valid to maintain long-lasting satisfactory results

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O050

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 02
14-05-2024 16:30 - 18:20

10 KHZ SCS PROVIDES EFFECTIVE LONG-TERM TREATMENT OF PAINFUL DIABETIC NEUROPATHY

Erika Petersen, MD[1], Thomas Stauss, MD[2], James Scowcroft, MD[3], Michael Jaasma, PhD[4], Judith White, MD[5], Shawn Sills, MD[6], Kasra Amirdelfan, MD[7], Maged Guirguis, MD[8], Jijun Xu, MD[9], Cong Yu, MD[10], Ali Nairizi, MD[11], Denis Patterson, DO[12], Vincent Galan, MD[13], Richard Bundschu, MD[14], Neel Mehta, MD[15], Dawood Sayed, MD[16], Nandan Lad, MD, PhD[17], David Dibenedetto, MD[18], Michael Creamer, MD[19], Paul Wu, MD[20], Charles Argoff, MD[21], Christian Nasr, MD[22], Rod Taylor, PhD[23], David Caraway, MD[24], Nagy Mekhail, MD[25]
[1]University of Arkansas for Medical Sciences, Department Of Neurosurgery, Little Rock, United States of America, [2]Advanced Pain Management, Pain Management, Greenfield, United States of America, [3]Pain Management Associates, Pain Management, Lee's Summit, United States of America, [4]Nevro Corp., Clinical Affairs, Redwood City, United States of America, [5]AES Compass Orlando, Medical Affairs, Orlando, United States of America, [6]Touchstone Interventional Pain Center, Pain Management, Medford, United States of America, [7]Boomerang Healthcare, Inc., Pain Management, Walnut Creek, United States of America, [8]Ochsner Clinic Foundation, Pain Management, New Orleans, United States of America, [9]Cleveland Clinic, Pain Management, Cleveland, United States of America, [10]Swedish Pain and Heachache Center, Pain Management, Seattle, United States of America, [11]Reno Tahoe Pain Associates, Pain Management, Reno, United States of America, [12]Nevada Advanced Pain Specialists, Pain, Denver, United States of America, [13]Pain Care, Pain Management, Stockbridge, United States of America, [14]Coastal Orthopedics, Pain Management, Bradenton, United States of America, [15]Weill Cornell Medicine, Pain Management, New York, United States of America, [16]University of Kansas Medical Center, Pain Management, Kansas City, United States of America, [17]Duke University, Pain Management, Durham, United States of America, [18]Boston Pain Care, Pain Management, Boston, United States of America, [19]Central Florida Pain Relief Centers, Pain Management, Orlando, United States of America, [20]Holy Cross Hospital, Pain Management, Fort Lauderdale, United States of America, [21]Albany Medical Center, Department Of Neurology, Albany, United States of America, [22]The University of Arizona College of Medicine - Phoenix, Internal Medicine, Phoenix, United States of America, [23]University of Glasgow, Population Health Research, Glasgow, United Kingdom, [24]Nevro Corp., Medical Affairs, Redwood City, United States of America, [25]Cleveland, Anesthesiology, Cleveland, United States of America

Introduction: Approximately 537 million adults have diabetes worldwide,[1] with ~25% experiencing painful diabetic neuropathy (PDN).[2] Conventional medical management (CMM), which includes pharmacotherapies, is ineffective for many patients,[2] while high-frequency (10 kHz) spinal cord stimulation (SCS) has recently been shown to provide substantial pain relief for PDN.[3] Here we report on 10 kHz SCS treatment of PDN through 24-month (24M) follow-up, which includes findings for improved protective sensation in the feet and substantially improved clinician assessment of overall condition.

Materials / Methods: The Senza-PDN RCT evaluated 10 kHz SCS with these key inclusion criteria: PDN symptoms ≥12M refractory to medications, lower limb pain ≥5cm (0-10cm visual analog scale (VAS)), and hemoglobin A1c ≤10%. Participants (n=216) were randomized 1:1 to 10 kHz SCS plus CMM or CMM alone, with optional crossover at 6M. We evaluated lower limb pain (via 10-cm VAS), loss of protective sensation (LOPS) in the feet (via monofilament sensory function testing and an associated risk of foot ulceration per American Diabetes Association guidelines[4]), and clinician-assessed overall improvement (via clinician global impression of change (CGIC)).

Results: At the 6M study visit, participants randomized to 10 kHz SCS had significantly greater pain relief than participants treated with CMM alone (pain relief of 76% vs. pain increase of 2%; $p<0.001$; Fig. 1). After 6M, 93% of eligible CMM participants crossed over to 10 kHz SCS, while no 10 kHz SCS participants crossed over to CMM. When evaluating all participants who received 10 kHz SCS, the

mean pain relief was 80% at 24M postimplantation (p<0.001). For the LOPS analysis (Fig. 2), at 6M the number of participants with low risk of foot ulceration decreased by 11% for participants randomized to CMM alone but improved by 90% for participants randomized to 10 kHz SCS (p<0.001). At 24M postimplantation, the number of participants with low risk of foot ulceration improved by 103% (p=0.006) for those receiving 10 kHz SCS. For CGIC (Fig. 3), over 90% of participants receiving CMM alone had their condition assessed to be “almost the same” or “no change” at 6M, whereas over 70% of participants who received 10 kHz SCS had their condition assessed to be “better” or “a great deal better” at 6M and 24M postimplantation.

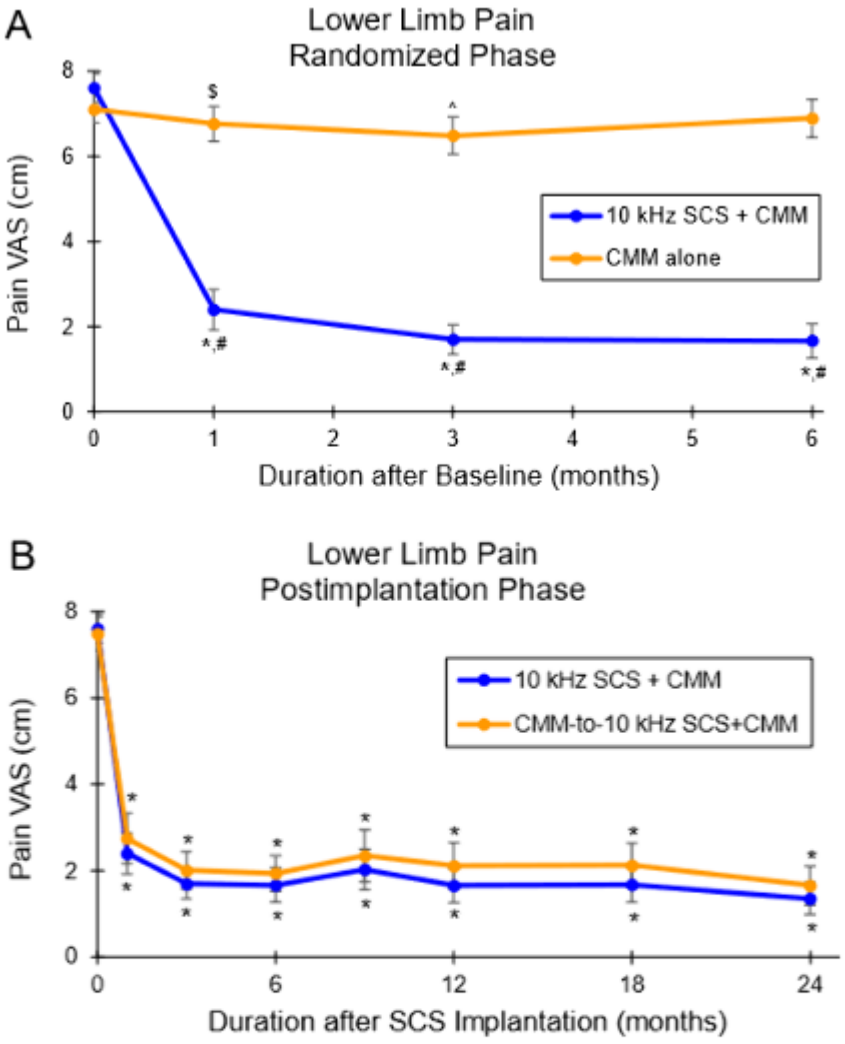


Figure 1. Lower Limb Pain: 10 kHz SCS provides significant, durable reductions in pain through 24 months. (**A**) Lower limb pain intensity (10 cm VAS) during the 6-month Randomized Phase (participants received 10 kHz SCS + CMM or CMM alone). (**B**) Lower limb pain during the 24-month Postimplantation Phase. For CMM arm participants who opted to cross over to 10 kHz SCS, (B) includes only the Postimplantation Phase after crossover. Mean data (±95% confidence intervals) are presented for all available data at each time point, with SCS data only for participants who received a permanent implant. To evaluate time and group effects, missing data was first imputed using multiple imputation. Each imputed dataset was then analyzed with a repeated-measures model, and these results were summarized using the MIANALYZE procedure. The repeated-measures model included time and group as fixed effects, and participant as a random effect. An autoregressive correlation structure of order 1 was specified. *p<0.001 vs. Baseline or Preimplantation time point; #p<0.001 vs. CMM; ^p=0.003 vs. Baseline; $p=0.023 vs. Baseline.

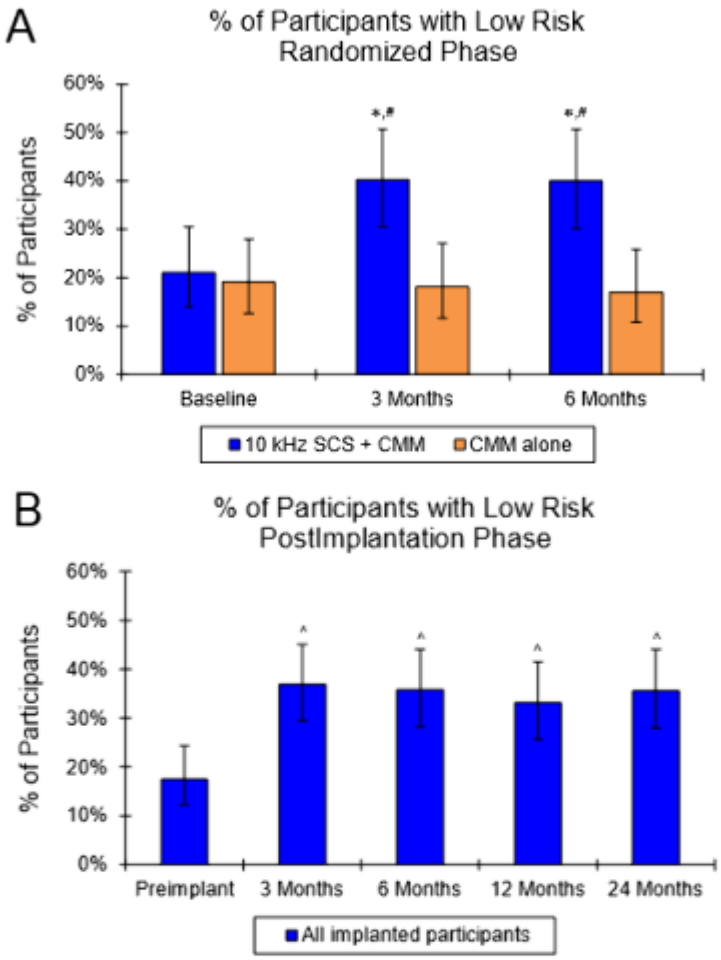


Figure 2. Risk of Foot Ulceration: 10 kHz SCS provides significant, durable improvements in percentage of participants with low risk of foot ulceration. Per ADA recommendations, monofilament sensory testing was conducted, with 4 locations evaluated per foot. A participant is at low risk of foot ulceration if there are zero insensate locations of the 8 tested. (**A**) Proportion of participants at low risk of foot ulceration during the 6-month Randomized Phase (participants received 10 kHz SCS + CMM or CMM alone). (**B**) Proportion of participants at low risk of foot ulceration during the 24-month Postimplantation Phase. For CMM arm participants who opted to cross over to 10 kHz SCS, (B) includes only the Postimplantation Phase after crossover. Mean data ±95% confidence intervals (from all available data and imputed missing data) are presented at each time point, with SCS data only for participants who received a permanent implant. To evaluate time and group effects, missing data was first imputed using multiple imputation. Each imputed dataset was then analyzed with a repeated-measures logistic model, and the log odds ratios were summarized using the MIANALYZE procedure. The repeated-measures model included time and group as fixed effects, and participant as a random effect. An autoregressive correlation structure of order 1 was specified. P-values represent testing for the significance of the estimated odds ratio for each time point. *p≤0.011 vs. Baseline; #p≤0.006 vs. CMM alone; ^p≤0.006 vs. Preimplantation.

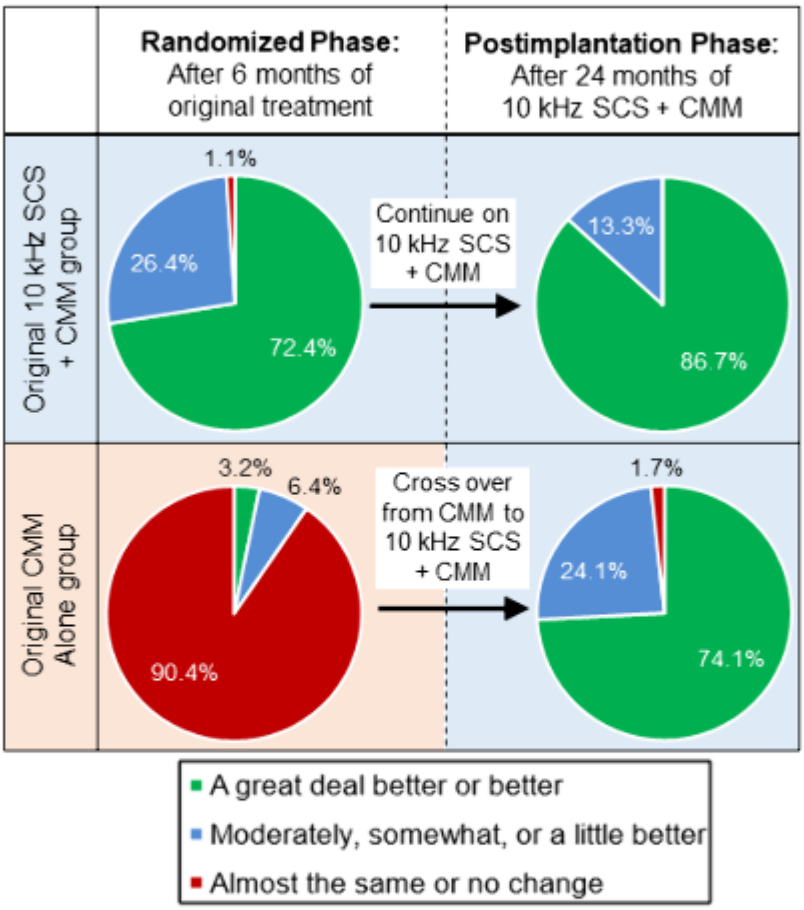


Figure 3. Clinician Global Impression of Change (CGIC): 10 kHz SCS provides substantial improvement in CGIC through 24 months. For the CGIC assessment, the clinician is asked to evaluate the change since baseline in activity limitations, symptoms, emotions, and overall quality of life on a 7-point Likert scale (1=No change, 2=Almost the same, 3=A little better, 4=Somewhat better, 5=Moderately better, 6=Better, and 7=A great deal better). Results shown percentage of participants in each category for all available data.

Discussion: In addition to high pain relief, 10 kHz SCS provided significant, durable reversal of LOPS and substantially improved overall health condition.

Conclusions: In conclusion, 10 kHz SCS offers a comprehensive therapy for the treatment of PDN.

Supplemental Data:

References: [1]IDF Diabetes Atlas 2021: https://diabetesatlas.org. [2]Shillo et al. *Curr Diab Rep* 2017;14(2):162. [3]Petersen et al. *Diabetes Res Clin Pract* 2023;203:110865. [4]Boulton et al. *Diabetes Care* 2008;31:1679-1685.

Acknowledgements: This study was funded by Nevro Corp.

Learning Objectives: 1. Participants will be able to discuss with their PDN patients how SCS can provide significant pain relief, with average pain relief of 80% at 24 months post-implantation. 2. Participants will be able to discuss with their PDN patients how SCS can provide improved sensory function in the feet, which reduces the risk of diabetic foot ulcers. 3. Participants will be able to discuss with their PDN patients how SCS can be an effective treatment option when medications are ineffective or not tolerated.

Financial Disclosures: Erika A. Petersen has received consulting fees from Abbott Laboratories, Biotronik, Boston Scientific, Medtronic Neuromodulation, Nalu Medical, Neuros Medical, Nevro Corp, Presidio Medical, Saluda, and Vertos Medical, research support from Mainstay, Medtronic Neuromodulation, Nalu Medical, Neuros Medical, Nevro Corp, ReNeuron, Saluda, and SPR, and stock options from neuro42 and SynerFuse. Thomas G. Stauss has received research support from Nevro Corp. James A. Scowcroft has received research support from Boston Scientific, Nevro Corp, Saluda Medical, and Vertiflex. Michael J. Jaasma is an employee of Nevro Corp. Judith L. White has received consulting fees from California Institute for Biomedical Research and Eli Lilly and research support from Nevro Corp. Shawn M. Sills has received research support from Nevro Corp. Kasra Amirdelfan has received consulting fees from Biotronik, Medtronic, Nalu Medical, Nevro Corp, and Saluda Medical, as well as research support from Biotronik, IPM Medical Group, Nevro Corp, Saluda Medical, SPR Therapeutics, and Vivex Biologics. Maged N. Guirguis has received consulting fees from Abbott Laboratories, Avanos Medical, Avertis Pharmacy, Boston Scientific, Nevro Corp, and Saluda Medical, as well as research support from Abbott Laboratories, Avanos Medical, Boston Scientific, Nalu Medical, Neuros Medical, Nevro Corp, and Saluda Medical. Jijun Xu has received research support from the Cleveland Clinic Velosano Program, the National Institutes of Health, the Steve and Melody Golding Foundation, and Nevro Corp. Cong Yu has received research support from Nevro Corp. Ali Nairizi has received consulting fees from Aurora Spine, Flowonix, and Nevro Corp as well as research support from Nevro Corp. Denis G. Patterson has received consulting fees from Abbott Laboratories, AIS Healthcare, Allergan, Amgen, Aurora Spine, CornerLoc, Flowonix, Lundbeck, Pajunk Medical, Saluda Medical, Spark Biomedical, and Vertos Medical, research support from Abbott Laboratories, Aurora Spine, Flowonix, Nevro Corp, and Saluda Medical, speakers' bureau or honoraria from Abbott Laboratories, Allergan, Amgen, CornerLoc, Lundbeck, Saluda Medical, and Vertos Medical, and stock options from CornerLoc. Michael J. Creamer has received research support from Nevro Corp. Vincent Galan has received research support from Biotronik, Medtronic, Nevro Corp, PainTEQ, SPR Therapeutics, and St. Jude. Richard H. Bundschu has received research support from Nevro Corp. Neel D. Mehta has received consulting fees from Averitas, Nevro Corp, and Salix Pharmaceuticals, as well as research support from Boston Scientific and Nevro Corp. Dawood Sayed has received consulting fees from Abbott Laboratories, Boston Scientific, Flowonix, Medtronic, Nevro Corp, Vertiflex, and Vertos Medical, as well as research support from Abbott Laboratories, Biotronic, Nevro Corp, Vertiflex, and Vertos Medical. Shivanand P. Lad has received consulting fees from Nevro Corp and research support from Nevro Corp. David J. DiBenedetto has received research support from Nevro Corp, as well as funding for serving as principal investigator of a study supported by SPR Therapeutics paid to his institution. Paul W. Wu has received research support from Nevro Corp. Charles E. Argoff has received consulting fees from AbbVie, Amgen, Biohaven, Clexio Biosciences, Collegium, Eli Lilly, Elsevier, Flowonix, Gene Pharma, Lundbeck, Nevro Corp, Novartis, Pfizer, SK Life Science, Teva Pharmaceutical, and Vertex as well as research support from AbbVie, Allergan, Amgen, Daiichi Sankyo, Eli Lilly, Novartis, Teva Pharmaceutical, and Vertex Pharmaceuticals. Christian E. Nasr has received consulting fees from Exelixis, Neurogastrx, and Nevro Corp as well as research support from Nevro Corp. Rod S. Taylor has received consulting fees from Nevro Corp, Medtronic, and Saluda Medical. David L. Caraway is an employee of Nevro Corp. Nagy A. Mekhail has received consulting fees from Nevro Corp, Relievant Medsystems, Saluda Medical, Sollis Therapeutics, and Vertos Medical, as well as research support from Avanos Medical, Mesoblast, Neuros Medical, and Nevro Corp.

Disclosure: The abstract presents results from a study sponsored by Nevro Corp that evaluated a commercial device manufactured by Nevro Corp. I am an employee of Nevro Corp and have stock in Nevro Corp.

O051

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 02
14-05-2024 16:30 - 18:20

TREATMENT MODALITIES FOR PATIENTS WITH PERSISTENT SPINAL PAIN SYNDROME TYPE II: A NETWORK META-ANALYSIS.

Lisa Goudman, PhD[1], Laure Booghmans, BSc (Hons)[2], Maarten Moens, MD[3]
[1]Laarbeeklaan 103, Stimulus Research Group, Jette, Belgium, [2]Vrije Universiteit Brussel, Stimulus Research Group, Brussel, Belgium, [3]Vrije Universiteit Brussel, Stimulus Research Group, Jette, Belgium

Introduction: To date, appropriate management of patients with Persistent Spinal Pain Syndrome Type 2 (PSPS T2) remains challenging. A broad range of therapeutic options has been proposed, whereby the need for scientific and robust evidence for each treatment modality is urgently pressing. Therefore, the aim of this systematic review and network meta-analysis is to compare the different treatment modalities for patients with PSPS T2 in terms of pain, functionality and quality of life.

Materials / Methods: Four databases were consulted for this systematic literature review: PubMed, Web of Science, Scopus, and Embase. The revised Cochrane Risk of Bias Tool was used to assess the risk of bias. Only RCT's were included, to enable a network meta-analysis. The interventions discussed in this review and meta-analysis comprised any surgical, medical, medicinal or paramedical therapeutic intervention(s); regardless of therapy form, duration, frequency, intensity or setting used. Thereafter, therapeutic interventions are categorized into 4 distinct groups: conservative (C), minimally invasive treatment (M), neurostimulation (N) and re-operation (R), as previously used in a RAND/UCLA Appropriateness Method.

Results: In total, 45 studies were included in the systematic review. A high risk of bias was indicated for the majority of included studies. Random effect models revealed a significant difference between neuromodulation compared to a mixture of conventional and minimal invasive management and compared to sham procedures, in favor of neuromodulation. Additionally, conventional management also outperformed sham treatments.

Discussion: A broad variety in interventions was revealed whereby studies often evaluated efficacy of therapeutic interventions from the same category. Conservative and neuromodulation treatment approaches seem to be the preferred options to reduce pain for patients with PSPS T2.

Conclusions: This systematic review with network meta-analysis provides robust evidence for justified treatment modalities within PSPS T2 patients, whereby neuromodulation is one of the preferred treatment options, based on pooling evidence from published RCT's.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1) To provide innovative & complementary evidence to the letters to the editors for the use of neuromodulation for patients with PSPS T2. 2) To learn the scientific evidence for conservative, minimal invasive, neurostimulation and re-operation for patients with PSPS T2. 3) To critically evaluate and interpret results of a meta-analysis within chronic pain management.

Financial Disclosures: STIMULUS received independent research grants from Medtronic. Lisa Goudman is funded by Research Foundation Flanders (FWO), Belgium (project number 12ZF622N). No specific funding was obtained for this work.

Disclosure: No significant relationships.

O052

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 02
14-05-2024 16:30 - 18:20

COST-EFFECTIVENESS OF MULTIMODAL SPINAL CORD STIMULATION SYSTEMS IN A SWEDISH SETTING

Anna Gustafsson, MSc[1], Emelie Andersson, MSc[1], Kliment Gatzinsky, MD, PhD[2]
[1]The Swedish Institute for Health Economics, Lund, Sweden, [2]Sahlgrenska University Hospital, Gothenburg, Sweden

Introduction: Several cost-effectiveness analyses have established that Spinal Cord Stimulation (SCS) is cost-effective in treatment of patients with persistent spinal pain syndrome type 2 (PSPS2) after lumbar spine surgery. Modern SCS technology has improved the therapy outcomes. The objective of this study was to evaluate the cost-effectiveness of a multimodal SCS system capable of delivering multiple stimulation options (standard rate, burst, high rate, dorsal horn modulation, fast-acting sub-perception, combination therapy).

Materials / Methods: A long-term cost-effectiveness model was developed in Microsoft Excel in two-stages: a decision tree model to reflect the SCS trial and initial response to SCS (the first 6 months), and a Markov process to simulate long-term effects (15-year time horizon). Clinical data (i.e. success rate of SCS trial, response rate in terms of >50% pain reduction, and explant rate) for the rechargeable and non-rechargeable, multimodal WaveWriter Alfa™ SCS systems (Boston Sci, Valencia, CA, USA) were based on a previous observational study [1]. Data reflecting standard care with conventional medical management (CMM), annual rates and costs of SCS complications, and utility data for each health state in the model were obtained from previously published studies, in line with current modelling practice for SCS [2]. Costs related to resource use (pain medication, healthcare visits and rehabilitation) were based on aggregated statistics of Swedish SCS patients in Region Västra Götaland 2013-2020 (n=246) 12 and 24 months pre and post SCS. The rechargeable system was assumed to last throughout the model time horizon of 15 years, and non-rechargeable 5 years.

Results: The analysis suggests that from a health care perspective, the incremental cost-effectiveness ratio (ICER) was approximately SEK 105 000 (USD 9 400) per quality-adjusted life year (QALY) gained for the rechargeable version, and SEK 137 000 (USD 12 300) for the non-rechargeable version. In a societal perspective, including productivity gains, both SCS systems were “dominant”, i.e. more effective and less costly, compared with CMM. Sensitivity analysis indicated that the largest impact was observed for variations in the utility value for optimal pain relief without complication and the probability of achieving optimal pain relief with SCS.

Discussion: The cost-effectiveness acceptability curve suggests a 100% probability of cost-effectiveness for the investigated multimodal SCS systems at a Willingness-to-pay threshold over SEK 200 000 (USD 17 900), based on the results of the probabilistic sensitivity analyses.

Conclusions: This study indicates that rechargeable and the non-rechargeable multimodal SCS systems are cost-effective treatment options for patients with PSPS2 in a Swedish health care perspective.

Supplemental Data:

References: [1] Veizi E, et al. Spinal Cord Stimulation (SCS) with Anatomically Guided (3D) Neural Targeting Shows Superior Chronic Axial Low Back Pain Relief Compared to Traditional SCS-LUMINA Study. Pain Med, 2017;18:1534-48. [2] Taylor RS, et al. The cost-effectiveness of spinal cord stimulation in the treatment of failed back surgery syndrome. Clin J Pain, 2010;26:463-9.

Acknowledgements: The support of Boston Sci for this project is gratefully acknowledged.

Learning Objectives: 1. Long-term cost-effectiveness models are important tools to assess the incremental cost-effectiveness for SCS out of both a health care and a societal perspective. 2. Variations in the utility value for optimal pain relief without complication and the probability of optimal pain relief are the most important factors for SCS cost-effectiveness. 3. Modern SCS technology offering multiple stimulation options from both rechargeable och non-rechargeable pulse generators provides a cost-effective treatment for chronic neuropathic pain.

Financial Disclosures: Dr Gatzinsky reports the following financial disclosures: Abbott, Advisory Board, 501-5000 USD Boston Sci, Advisory Board, 501-5000 USD Medtronic Inc, Advisory Board, 501-5000 USD Nevro Corp, Advisory Board, 501-5000 USD The other authors have no financial disclosures to report.

Disclosure: No significant relationships.

O053

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 02
14-05-2024 16:30 - 18:20

EFFECTS OF SPINAL CORD STIMULATION ON AUTONOMIC DYSFUNCTION IN PATIENTS WITH PAINFUL DIABETIC PERIPHERAL NEUROPATHY: OUTCOMES FROM THE INSPIRE STUDY

Cristian Rizea, MD[1], Jose Paz Solis, MD[2], Javier Díaz De Terán, MD[1], Rafael Martínez-Marín, MD[1], María Román De Aragón, MD[2], Beatriz Mansilla, MD[2], Eva Pérez, MSc[2], Heleen Scholtes, MSc[3], Que Doan, BSc (Hons)[3], Ismael Huertas, PhD[3]
[1]University Hospital La Paz, Neurology, Madrid, Spain, [2]University Hospital La Paz, Neurosurgery, Madrid, Spain, [3]Boston Scientific, Neuromodulation, Valencia, United States of America

Introduction: Autonomic dysfunction is a common but often underappreciated complication in diabetes with a tremendous impact on quality of life and prognosis. Symptoms can affect various vital functions such as gastrointestinal (e.g. constipation), genitourinary (e.g. erectile dysfunction), cardiovascular (e.g. orthostatic intolerance) and sudomotor. Cardiac neuropathy (CAN) is among the most serious and overlooked issues. Unfortunately, besides misdetection, therapeutic options are scarce. In this communication, we will present our findings in the INSPIRE study on the effects of Spinal Cord Stimulation (SCS) to autonomic dysfunction in patients with painful diabetic peripheral neuropathy (pDPN).

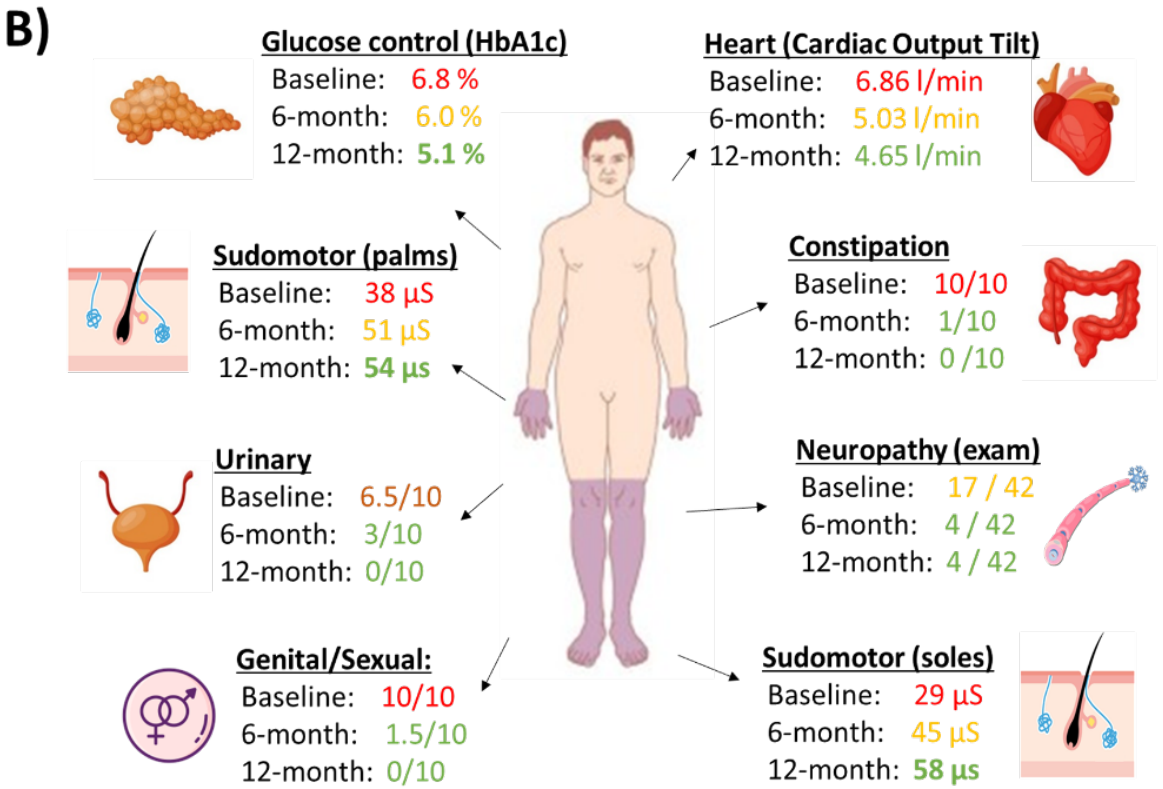
Materials / Methods: Patients with a classical “stocking ang glove” pDPN pain affecting lower (primarily) and upper limbs are being treated with SCS: 4-port system and percutaneous leads at thoracolumbar (T10-T12) and, if necessary, cervical (C5-T1) levels (Alpha-WaveWriter, Boston Scientific). Autonomic function is tested pre- and post-SCS (3-, 6- and 12-months) by the Boston Autonomic Symptoms Questionnaire (BASQ), a sudomotor test (electrochemical skin conductance, ESC), and a complete battery of hemodynamic assessments: deep breath, Valsalva maneuver and tilt test while monitoring key cardiovascular metrics (i.e. heart rate, blood pressure, cardiac output, peripheral resistances).

Results: To date, 18 pDPN subjects have been enrolled and 9 implanted and activated. Significant relief of pain and neuropathic symptoms have been observed in both lower limbs (VRS from 8.6 to 1.7) and upper limbs (from 6.2 to 1.1) at last follow-up (mean of ~4.6 months). Further, in few available long-term subjects, progressive relief in diverse autonomic symptoms is being observed (e.g. BASQ from 34.6 to 10.6), encompassing relief in orthostatic intolerance, cardiorespiratory, gastrointestinal, urinary, and genital/sexual. Sudomotor function is objectively improving after 6-to-12 months (e.g. ESC from 38 to 54µS in palms, and 29 to 58µS in soles). Meaningful changes in hemodynamics are being also observed, such as reduction after tilt in the cardiac output (from to 6.9 to 4.6 l/min), cardiac-index and stroke volume.

Discussion: Early observations indicate that specific approaches to SCS could alleviate autonomic dysfunction at multiple levels in pDPN, including cardiovascular regulation. SCS seems to be relieving both somatic and autonomic peripheral neuropathies via a postulated dual mechanism/pathway.

Conclusions: SCS could offer a solution to holistically treat dysautonomia in pDPN. Screening of these symptoms, including CAN, should not be overlooked in these patients.

Supplemental Data:



References: [1] Vinik et al. Diabetic Autonomic Neuropathy. Diabetes Care 2003 May;26(5):1553-79.

Acknowledgements: The support of Boston Scientific for this project is gratefully acknowledged

Learning Objectives: (1) To enforce adequate clinical instruments to screen for dysautonomia in pDPN (2) To evaluate potential SCS-induced physiological autonomic changes in pDPN (3) To learn specific SCS approaches to treat autonomic dysfunction, including cardiac neuropathy, in pDPN

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O054

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 02
14-05-2024 16:30 - 18:20

ASSESSMENT OF PATIENTS UTILIZING SCS FOR CHRONIC PAIN ASSOCIATED WITH DIABETIC PERIPHERAL NEUROPATHY (DPN) IN A GLOBAL, PROSPECTIVE, MULTICENTER REGISTRY: LONG-TERM OUTCOMES

Anthony Berg, MD[1], John Noles, MD[2], Eric Loudermilk, MD[3], Joseph Hegarty, MD[4], Nathan Harrison, MD[5], Jeff Phelps, MD[6], Richard Rauck, MD[7], Julio Paez, MD[8], Albert Lee, MD[9], Louis Bojrab, MD[10], José Cid, MD[11], Concepción Pérez-Hernández, MD[12], Brett Chandler, MD[13], Binit Shah, MD[14], Todd Turley, MD[15], Mahendra Sanapati, MD[16], Channing Willoughby, MD[17], Simon Thomson, MBBS[18], Stephen Smith, MD[19], Nicolas Varela, MD[20], Anne Christopher, MD[21], Lilly Chen, MD[22], Edward Goldberg, MD[22]
[1]Spine Team Texas, Pain Management, Rockwall, United States of America, [2]Spine and Pain Specialists, Pain Management, Shreveport, United States of America, [3]Piedmont Comprehensive Pain Management Group, Pain Management, Greenville, United States of America, [4]Optim Health System - Tattnall Hospital, Pain Management, Reidsville, United States of America, [5]Ochsner Health Center, Covington, Pain Management, Covington, United States of America, [6]Spine Works Institute, Pain Management, North Richland Hills, United States of America, [7]Carolinas Pain Institute, Pain Management, Winston-Salem, United States of America, [8]South Lake Pain Institute, Pain Management, Clermont, United States of America, [9]Tallahassee Neurological Clinic, Pain Management, Tallahassee, United States of America, [10]Forest Health Medical Center, Pain Management, Ypsilanti, United States of America, [11]Toledo Hospital Complex, Pain Unit, Toledo, Spain, [12]Hospital Universitario de La Princesa, Pain Management, Madrid, Spain, [13]Pain Matrix, Pain Management, Melbourne, Australia, [14]Carolinas Pain Center, Pain Management, Huntersville, United States of America, [15]Advanced Spine and Pain, Pain Management, Phoenix, United States of America, [16]Pain Management Centers of America, Pain Management, Evansville, United States of America, [17]Carolina Orthopaedic & Neurological, Pain Management, Spartanburg, United States of America, [18]Mid & South Essex University Hospitals NHSFT, Pain And Neuromodulation Centre, Basildon, United Kingdom, [19]Ramos Center for Functional Pain Medicine, Pain Management, Clearwater, United States of America, [20]Clínica Universidad de Navarra, Pain Unit, Navarra, Spain, [21]St. Louis Pain Consultants, Pain, Chesterfield, United States of America, [22]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: With the global rise in scale of the incidence of type-2 diabetes mellitus, there exists a growing population of those that will experience Diabetic Peripheral Neuropathy (DPN). Of those that experience DPN, a substantial will experience chronic pain (thought to occur in up to ~26%).[1] As a result of the burgeoning advances in neuromodulatory-based systems, interest has grown in re-assessing this patient population when treated with implanted Spinal Cord Stimulation (SCS) devices. Here, we assessed real-world outcomes from a subset of chronic pain patients diagnosed with DPN as derived from a global, multicenter SCS patient registry who were implanted with contemporary neuromodulation systems capable of more advanced and highly customized approaches to therapeutic neurostimulation.

Materials / Methods: RELIEF (Clinicaltrials.gov identifier: NCT01719055) is a global, multicenter, prospective, single-arm, observational registry designed to collect real-world data for neurostimulation systems utilized for chronic pain indications by patients within routine clinical practice. A sub-set of chronic pain patients with a diagnosis of diabetic peripheral neuropathy were assessed for pain relief (e.g., NRS, Oswestry Disability Index [ODI], Quality-of-Life [EQ-5D]) and other relevant clinical measures, per standard of care.

Results: To date, 43 patients enrolled in the registry for this sub-analysis have now been permanently implanted. In those patients who reached their 12-, 24- and 36-month timepoint, a leg pain responder rate (percent of patients with ≥50% pain relief) of 73 %, 74%, and 85%, respectively, was observed. Correspondingly, the responder rates for targeted pain (i.e., area of pain intended to be treated by SCS) was 78%, 81 %, and 73% at 12-months (n=28), 24-months (n=21), and 36-

months (n=15), respectively. Furthermore, ODI score decreased by -11.48 and -15.81 points (baseline score 47.3 with respective decrease to 37.7 and 32.8), at 24- and 36-months after implant, in accordance with reported minimal clinically important difference (-5 to -10-points or -11 %).[2] At 36-months after implant, EQ5D scores improved by over 33% compared to baseline.

Discussion: These data provide additional support for use of contemporary neuromodulation systems capable of more advanced and highly customized therapeutic neurostimulative approaches for treatment of DPN-diagnosed patients experiencing chronic pain.

Conclusions: Preliminary results demonstrate long-term, sustained clinically significant improvement among patients diagnosed with Diabetic Peripheral Neuropathy (DPN) receiving SCS for treatment of chronic pain.

Supplemental Data:

References: 1. Schreiber AK, Nones CF, Reis RC, Chichorro JG, Cunha JM. Diabetic neuropathic pain: Physiopathology and treatment. World J Diabetes. 2015 Apr 15;6(3):432-44. doi: 10.4239/wjd.v6.i3.432. PMID: 25897354; PMCID: PMC4398900.
2. Hagg O, Fritzell P, Nordwall A; Swedish Lumbar Spine Study Group. The clinical importance of changes in outcome scores after treatment for chronic low back pain. Eur Spine J. 2003 Feb;12(1):12-20.

Acknowledgements:

Learning Objectives: To assess patients diagnosed with DPN in a global registry per the following: 1) responder rate at 12, 24, and 36-month follow-up 2) ODI score at 12, 24, and 36-month follow-up 3) Quality of Life (EQ5D) evaluation at 12, 24, and 36-months follow-up

Financial Disclosures: Dr. Berg has a consulting agreement with Boston Scientific. a) Boston Scientific b) consultant c) 1-5k

Disclosure: This study is sponsored by Boston Scientific. Lilly Chen and Ed Goldberg are employees of Boston Scientific.

O055

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 02
14-05-2024 16:30 - 18:20

PAIN REDUCTION IN PATIENTS UNDERGOING ON-TABLE TESTING FOR SPINAL CORD STIMULATION USING THE FAST-ACTING SUB-PERCEPTION THERAPY

Dimitri Tkatschenko, MD, Simon Bayerl, MD, Peter Vajkoczy, MD
Charité Universitätsmedizin Berlin, Neurosurgery, Berlin, Germany

Introduction: Patients suffering from chronic pain which is therapy-resistant to conservative treatment are evaluated for spinal cord stimulation (SCS) for pain relief. There are several established therapy forms such as tonic stimulation, burst stimulation or high-frequency stimulation. Whereas the tonic and burst stimulations result in paresthesia the high-frequency stimulation is paresthesia-free but has a wash-in phase and result in higher energy consumption of the stimulator. Recently the fast-acting sub-perception therapy (was introduced resulting in straightaway pain relief. The aim of the current work was to evaluate the pain reduction rates in patients undergoing the on-table testing using the fast-acting sub-perception therapy.

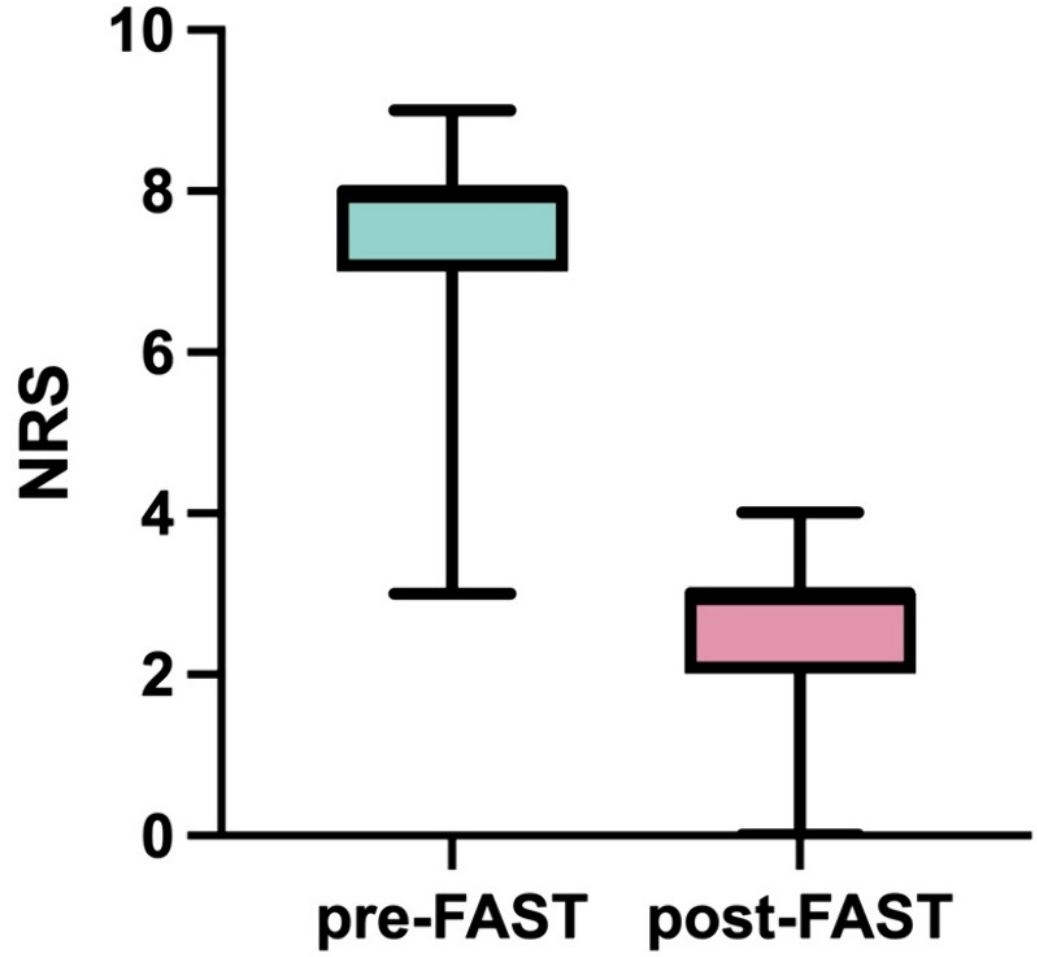
Materials / Methods: After obtaining a positive ethics vote (EA2/093/13) all trails from May 2021 to January 2023 were identified where patients were suitable for on-table testing with the fast-acting sub-perception therapy . NPR scale was used to measure the pain level before and after a 15 minutes on-table testing using the fast-acting sub-perception therapy followed by lead externalization and out-of-hospital trial for at least one week. The reduction of pain was evaluated as well as the correlation of pain reduction and stimulator implantation rate.

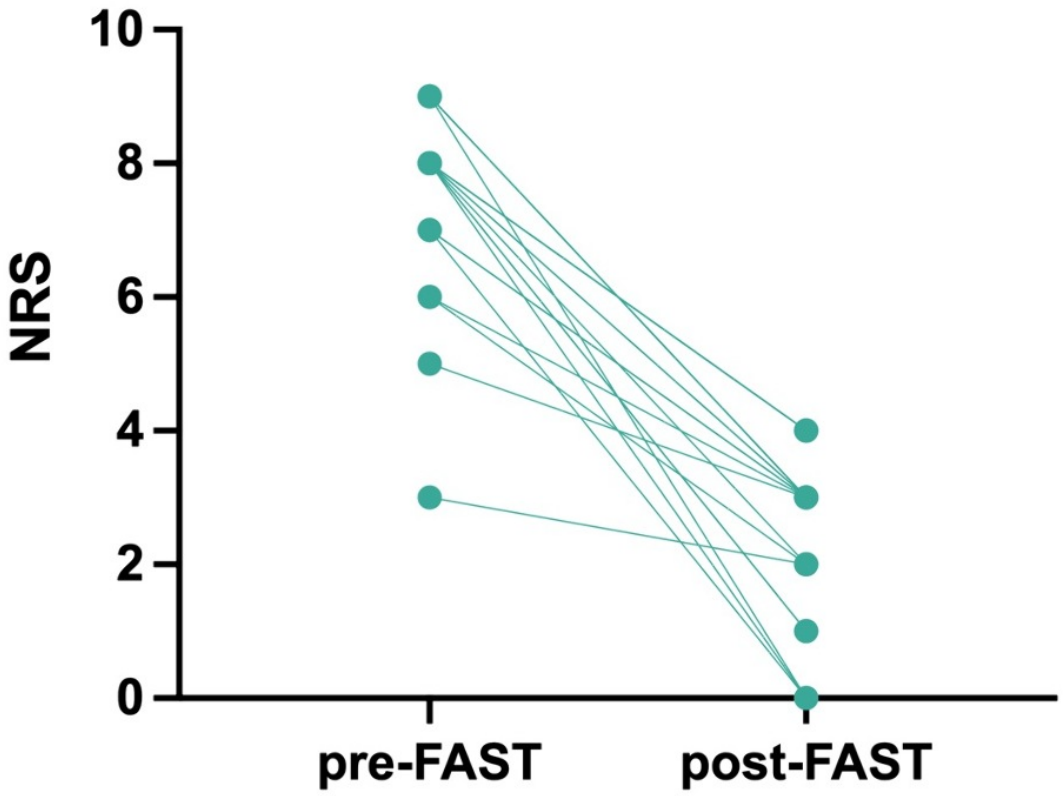
Results: We could identify 23 trials where the fast-acting sub-perception therapy was used. In all trails there was a reduction in NPR scale with mean pain reduction of 5.0 points. In 91.3% of the trials the NPR scale reduction was 50% or more (n=21). In 95.7% of the cases a neurostimulator for permanent SCS therapy was implanted.

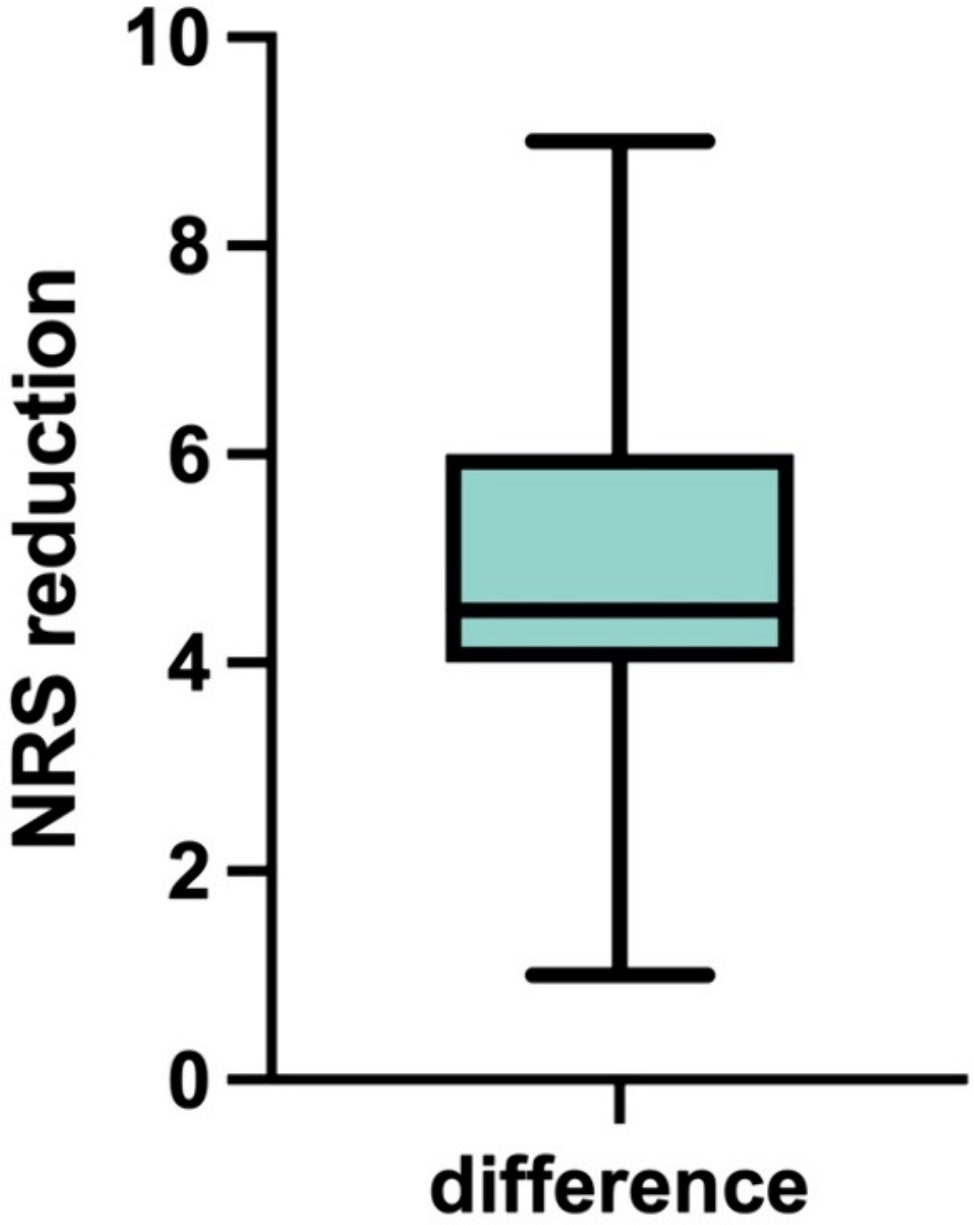
Discussion: We experienced a strong effect in pain reduction when the fast-acting sub-perception therapy was used during on-table testing in patients undergoing a SCS trial. The fast-acting sub-perception therapy combines the advantages of paresthesia free stimulation and instant decrease in pain. The trial-to-implant ratio shows a strong correlation between fast-acting sub-perception therapy testing and SCS therapy efficacy.

Conclusions: The use of the fast-acting sub-perception therapy leads to appreciable pain relief during on-table testing and thus is a useful tool in patients with chronic pain and SCS therapy.

Supplemental Data:


10
8
6
4
2
0
NRS
pre-FAST
post-FAST


10
8
6
4
2
0
NRS
pre-FAST
post-FAST



References: None

Acknowledgements:

Learning Objectives: 1. FAST algorithm is suitable for on-table SCS testing 2. FAST algorithm significantly reduces pain when applied during on-table testing 3. FAST algorithm may be suitable for SCS response prediction

Financial Disclosures: Simon Bayerl, MD: a) Boston Scientific b) education/research c) 501 - 5000 USD Dimitri Tkatschenko, MD and Simon Bayerl, MD: SIlencing Study (NCT05357300) https://clinicaltrials.gov/study/NCT05357300?term=silencing&rank=2 sponsored by Boston Scientific

Disclosure: No significant relationships.

O056

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 02
14-05-2024 16:30 - 18:20

10 KHZ SCS TREATMENT OF PAINFUL DIABETIC NEUROPATHY: RESULTS COMBINING DERMATOMAL DYSESTHESIAS AND LOWER LIMB SENSORY ASSESSMENTS

Charles Argoff, MD[1], Manish Bharara, PhD[2], Michael Jaasma, PhD[3], Zachary Kagan, PhD[3], Kerry Bradley, MSc[3], David Caraway, MD[3], Erika Petersen, MD[4]
[1]Albany Medical Center, Department Of Neurology, Albany, United States of America, [2]Nevro Corp., Redwood City, United States of America, [3]Nevro Corp, Redwood City, United States of America, [4]University of Arkansas for Medical Sciences, Department Of Neurosurgery, Little Rock, United States of America

Introduction: Of the 37 million Americans who have diabetes, approximately 25% will experience painful diabetic neuropathy (PDN), including a variety of dysesthesias[1,2]. Here we report on treatment of PDN with high-frequency (10 kHz) spinal cord stimulation (SCS) and resulting changes in lower limb sensory function through 3 Months (3M).

Materials / Methods: We conducted a multicenter RCT to evaluate 10 kHz SCS in PDN patients[3]. Patients (n=216) were randomized 1:1 to 10 kHz SCS plus CMM or CMM alone, with optional treatment group crossover at 6M. All data were collected at pre-implant and 3M post-implant time points. Numbness dysesthesia drawings were collected from a subset of patients who received 10 kHz SCS. Included patient-provided drawings (n=66) were separated by dermatomes using previously established boundaries[4], quantified by shaded pixel counts, and normalized to total available pixels per dermatome. Lower limb sensory function was assessed by bilateral light touch of L1 through S1 dermatomes.

Results: At 3M, patients who received 10 kHz SCS were significantly less numb based on dysesthesia drawings (12.3% mean shaded area at pre-implant vs 5.9% mean shaded area at 3M, p<.001). When separated by dermatomes, patients reported a significant reduction in numbness in 5 out of 6 dermatomes: L2 (4.9% pre-implant vs 1.5% 3M mean shading, p=.01), L3 (6.6% vs 1.4%, p=.01), L4 (23.0% vs 10.4%, p=.002), L5 (24.7% vs 11.8%, p=.001), and S1 (55.3% vs 35.2%, p<.001). For bilateral light touch assessments, in which each patient had two measures per dermatome (dermatomal N = 132, total N = 792), there were 80 ‘absent’ responses at pre-implant and 34 at 3M. Specifically, L1 and L2 had zero ‘absent’ responses at pre-implant and 3M. The others decreased as follows: L3 (3 absent responses at pre-implant vs 0 at 3M), L4 (15 vs 7), L5 (32 vs 14), and S1 (30 vs 13).

Discussion: While these results are limited to a subset of the patients in the study, there is broad agreement between both methods of data collection used in this analysis. Whereas L3, L4, L5, and S1 dermatomes showed significant reductions after 10 kHz SCS, L1-L2 were predominantly without dysesthesia and normally responsive to light tough at baseline, so there were little improvements to be made.

Conclusions: After 3 months of 10 kHz SCS, patients reported significantly less numbness and improved light touch responses in L3-S1 dermatomes. Furthermore, these results are corroborated by similar trends in light touch assessments of lower limb dermatomes.

Supplemental Data:

References: 1. National Diabetes Statistics Report, CDC 2022
2. Shillo P et al. Curr Diab Rep 2019; 19(6):32
3. Petersen E et al. Diabetes Care 2022; 45(1):e3-e6
4. Downs et al. J Ortho Spor Phys Ther 2011; 41(6):427-434

Acknowledgements:

Learning Objectives: 1. Show reductions in patient-reported dysesthesias and clinician-assessed light touch responses of the lower limbs after 3 Months of 10 kHz SCS. 2. Show agreement between patient-reported dysesthesias and light touch responses of the lower limbs before and after 3 Months of 10 kHz SCS. 3. Demonstrate that while the standard light touch assessment contains useful clinical information, there may be more detailed information in patient-reported dysesthesias.

Financial Disclosures: This research was funded by Nevro Corp.

Disclosure: I am an employee of Nevro Corp.

O057

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 02
14-05-2024 16:30 - 18:20

HIGH-FREQUENCY SPINAL CORD STIMULATION PROVIDES LONG-TERM RELIEF FROM REFRACTORY PAIN OF THE TRUNK AND LIMB

Nick Park, Mr[1], Yong Yie Liew, MSc[1], Richard King, MSc[2], Shibasis Chowdhury, PhD[2]
[1]Lancashire Teaching Hospitals, Neurosurgery, Preston, United Kingdom, [2]Nevro Corp, Redwood City, United States of America

Introduction: Long-term management of chronic neuropathic pain of the trunk and/or limbs presents a significant challenge as many patients are refractory to conventional treatment. High-frequency spinal cord stimulation (10 kHz SCS) provides significant and sustained pain reduction superior to low-frequency SCS[1-2]. Since 2014, we treated >300 patients with 10 kHz SCS and a clinical audit was carried out to evaluate the long-term real-world data from the first 75 patients we implanted with 10 kHz SCS.

Materials / Methods: We analyzed the medical records of the first 75 patients we treated with 10 kHz SCS. Outcomes included self-reported percentage pain relief from which the responder rate (percentage of patients achieving ≥50% pain relief) was calculated. The analyzed population included patients on active 10 kHz SCS therapy with completed baseline and last follow-up data (n=52). There were 23 patients excluded from our preliminary analysis for reasons including device explantation (n=7), device explantation due to infection (n=1), deceased (n=1), device OFF (n=5) and follow-up assessment not complete (n=7). A more conservative secondary analysis based on the assumption patients with the device OFF (n=5) were non-responders (achieved <50% pain relief) was also performed (n=57).

Results: Of the 75 implanted patients, 70 had lower back and/or leg pain, 5 had neck and/or upper limb pain, while 12 had PSPS type I and 63 had PSPS type II. Also, 57 of those 75 patients continue to use their device 9 years following their implantation. In the preliminary analysis population (n=52), the average percentage of pain relief was 60.7%, and the RR was 86.5%. A secondary analysis assuming all patients with devices switched off as non-responders returned a RR of 78.9% (n=57). The mean time between device activation and the last follow-up was 6 years (2.9 - 9 years), and the average annual explantation rate was 1.33/year.

Discussion: The results from this retrospective study are comparable to published evidence[1-2], giving confidence in the clinical application and durability of 10kHz SCS. Our secondary analysis suggests the RR remains high even when potential non-responders are accounted for. Furthermore, 76% (57/75) of our patients were still using SCS up to 9 years after implant, suggesting the perceived utility of the therapy.

Conclusions: This long-term, real-world data provides evidence of the efficacy and durability of 10 kHz SCS for treating refractory pain of the trunk and/or limbs. Further research is needed to evaluate the long-term effect of 10 kHz SCS therapy on function, sleep and quality of life.

Supplemental Data:

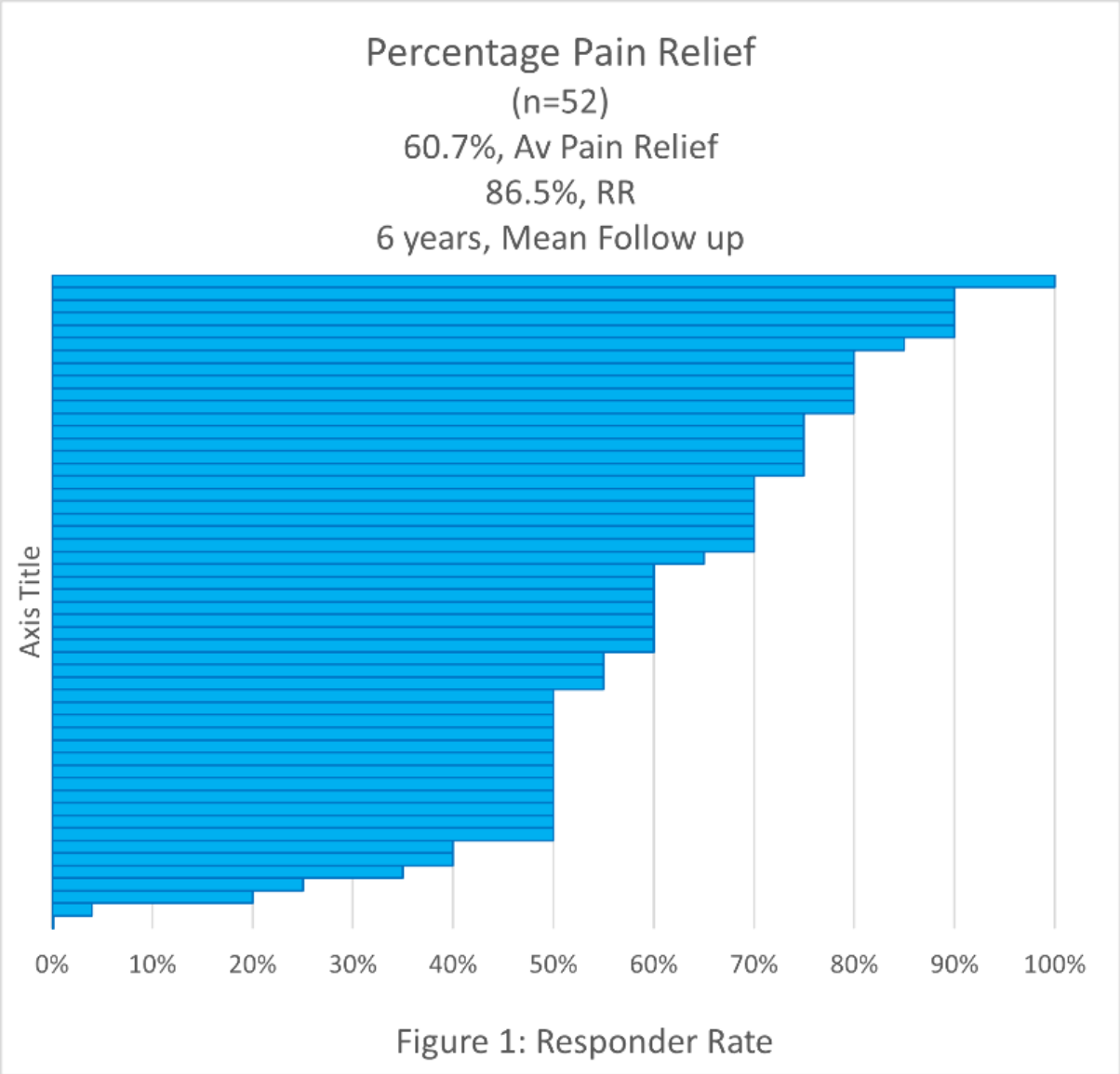


Figure 1: Responder Rate

References: 1. Kapural L, Yu C, Doust MW, et al. Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: The SENZA-RCT Randomized Controlled Trial. *Anesthesiology*. 2015;123(4):851-860. doi:10.1097/ALN.0000000000000774 2. Kapural L, Yu C, Doust MW, et al. Comparison of 10-kHz High-Frequency and Traditional Low-Frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: 24-Month Results From a Multicenter, Randomized, Controlled Pivotal Trial. *Neurosurgery*. 2016;79(5):667-677. doi:10.1227/NEU.0000000000001418

Acknowledgements:

Learning Objectives: Long-term data, Treatment durability, 10 kHz SCS therapy

Financial Disclosures: Dr. Nicholas Park has been involved with Nevro Ltd. in capacities involving consultant/advisory board and education/research. The level of compensation has been in the range 0f $5,001 - $20,000 USD Dr. Yong Yie Liew has no significant financial relationships Mr. Richard King is an employee of Nevro Ltd. and draws a salary from Nevro. He is also awarded restricted Nevro stock units (<5%). The level of compensation for the salary is between >$100,000. Dr. Shibasis Chowdhury is an employee of Nevro Ltd. and draws a salary from Nevro. He is also awarded restricted Nevro stock units (<5%).The level of compensation for the salary is between >$100,000.

Disclosure: No significant relationships.

O058

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 02
14-05-2024 16:30 - 18:20

HEALTH CARE UTILIZATION REDUCTION (HCU) WITH HIGH-FREQUENCY (10 KHZ) SPINAL CORD STIMULATION THERAPY

Vinny Francio, MD, MS[1], John Alm, DO[2], Logan Leavitt, MD[2], Daniel Mok, DO[2], B. Victor Yoon, MD[2], Niaman Nazir, MD[3], Christopher Lam, MD[1], Usman Latif, MD[1], Timothy Sowder, MD[1], Edward Braun, PhD[1], Andrew Sack, MD[4], Talal Khan, MD[4], Dawood Sayed, MD[4]
[1]University of Kansas, Dept Anesthesiology And Pain Medicine, Kansas City, United States of America, [2]University of Kansas, Pm&r, Kansas City, United States of America, [3]University of Kansas, Population Health, Kansas City, United States of America, [4]University of Kansas, Anesthesiology And Pain Medicine, Kansas City, United States of America

Introduction: Chronic low back pain (CLBP) is associated with substantial health care costs exceedingly over $100 billion. Spinal cord stimulation (SCS) is a well-established treatment option with consistent level I-A and I-B evidence that it is effective for reducing pain and disability in CLBP. With increasing health care costs, it is important not to only determine the benefit of SCS therapy in CLBP, but also assess health care utilization (HCU) trends. Therefore, this study analyzed health care utilization (HCU) trends after 10kHz SCS implantation.

Materials / Methods: This was a retrospective single-center observational study of subjects who underwent 10kHz SCS implant for CLBP. IRB approval was obtained. The primary outcome was the rate of HCU, measured by the number of emergency department (ED) visits, the number of interventional pain procedures related to CLBP, and opioid utilization measured by morphine milliequivalents (MME). These outcomes were then compared for the 12 months prior to implant and up to 12-month post-implant. Descriptive statistics and statistical analysis was performed to calculate statistically significance (p value <0.05).

Results: The study population comprised of 160 subjects. We found a statistically significant reduction in HCU from baseline to 12-month follow-up in all domains assessed. On those subjects taking opioids at baseline, 37% completely discontinued and 71% decreased use with a mean average of 78.2% dose reduction. Interestingly, 95.7% reduced their dose to <50 MME and 80.2% reduced to <30MME with 91.5% reaching the minimum clinical important difference (MCID) of 30% decrease dose overall. Likewise, we found statistically significant reduction in ED visits and interventional pain procedures (ESI, facet injections, LMBB, LRFA) up to 12-month follow-up. There was no statistically significant difference in MME, ED and pain procedures visits between the high (>80%) and low responders (50-79%), however all domains demonstrated improvement from baseline to 12-month follow-up.

Discussion: This is the first study to demonstrate statistically significant reduction in daily MME, ED and pain procedure visits following 10kHz SCS implant up-to-12-month follow-up. Our findings are similar to previous studies reporting positive outcomes in HCU reduction with these domains analyzed individually.

Conclusions: This study found that 10kHz SCS resulted in statistically significant decrease in health care utilization trends with reduced number of interventional pain procedures and ED visits up to up to 12-month follow up post-implant, and 91.5% of subjects reaching MCID opioid dose reduction from baseline. These findings corroborate with other studies to indicate that 10kHz SCS therapy is favorable in reducing HCU in the CLBP population.

Supplemental Data:

Table 1. Demographic and patient characteristics at baseline.

Demographics and Characteristics at baseline	Category	N(%)
Gender	Male	69(43.1)
	Female	91(56.9)
Alcohol Use	No	87(54.4)
	Yes	73(45.6)
Tobacco Use	No	100(62.5)
	Yes	60(37.5)
Diabetes	No	110(68.8)
	Yes	50(31.3)
History of Psych Illness	No	73(45.6)
	Yes	87(54.4)
History of Spine Surgery	No	79(49.4)
	Yes	81(50.6)
Level of Disability	Minimal to none	9(6.3)
	Moderate	46(32.2)
	Severe	68(47.6)
	Crippling back pain	19(13.3)
	Bed-bound or symptom	1(0.7)
MME at baseline	<= 50	122(76.7)
	> 50	37(23.3)

Table 2. Changes in health care utilization from baseline and 12-month follow up.

Outcome	Baseline Mean Average (up to 12-month pre)	12-month	Mean Average Reduction	P-value
MME (on those subjects on opioids at baseline)	51.05	26.52	24.53	<0.0001*
ED visits (related to primary diagnosis)	0.12	0.03	0.08	0.01*
Interventional pain procedures	1.39	0.28	1.11	<0.0001*

Table 3. Baseline and 12-month follow up outcomes between low-responders and high-responders.

Outcome	Low Responders (N = 111)	High Responders (N = 49)	P-value
Mean MME at baseline	51.81	49.53	0.78
Mean MME at 12-month	27.97	23.57	0.52
Mean ED visits at baseline	0.11	0.12	0.93
Mean ED visits at 12-month	0.03	0.02	0.56
Mean number of pain procedures at baseline	1.51	1.10	0.17
Mean number of pain procedures at12-month	0.28	0.24	0.62

References: References: Taylor, Rod S. MSc, PhD*,†; Bentley, Anthony MSc‡; Campbell, Bruce MS§; Murphy, Kieran MPH‖. High-frequency 10 kHz Spinal Cord Stimulation for Chronic Back and Leg Pain: Cost-consequence and Cost-effectiveness Analyses. The Clinical Journal of Pain 36(11):p 852-861, November 2020. | DOI: 10.1097/AJP.0000000000000866. Sayed D, Grider J, Strand N, Hagedorn JM, Falowski S, Lam CM, Tieppo Francio V, Beall DP, Tomycz ND, Davanzo JR, Aiyer R, Lee DW, Kalia H, Sheen S, Malinowski MN, Verdolin M, Vodapally S, Carayannopoulos A, Jain S, Azeem N, Tolba R, Chang Chien GC, Ghosh P, Mazzola AJ, Amirdelfan K, Chakravarthy K, Petersen E, Schatman ME, Deer T. The American Society of Pain and Neuroscience (ASPN) Evidence-Based Clinical Guideline of Interventional Treatments for Low Back Pain. J Pain Res. 2022 Dec 6;15:3729-3832. doi: 10.2147/JPR.S386879. Erratum in: J Pain Res. 2022 Dec 24;15:4075-4076. PMID: 36510616; PMCID: PMC9739111. Farrar JT, Young JP Jr, LaMoreaux L, Werth JL, Poole MR. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. Pain. 2001 Nov;94(2):149-158. doi: 10.1016/S0304-3959(01)00349-9. PMID: 11690728. Glassman S, Gornet MF, Branch C, Polly D Jr, Peloza J, Schwender JD, Carreon L. MOS short form 36 and Oswestry Disability Index outcomes in lumbar fusion: a multicenter experience. Spine J. 2006 Jan-Feb;6(1):21-6. doi: 10.1016/j.spinee.2005.09.004. PMID: 16413443. Goudman L, Smedt A, Forget P, Moens M. Determining the Minimal Clinical Important Difference for Medication Quantification Scale III and Morphine Milligram Equivalents in Patients with Failed Back Surgery Syndrome. J Clin Med. 2020;9(11):3747. Published 2020 Nov 21. doi:10.3390/jcm9113747. Patel NP, Wu C, Lad SP, Jameson J, Kosek P, Sayed D, Waldorff EI, Shum LC, Province-Azalde R, Kapural L. Cost-effectiveness of 10-kHz spinal cord stimulation therapy compared with conventional medical management over the first 12 months of therapy for patients with nonsurgical back pain: randomized controlled trial. J Neurosurg Spine. 2022 Oct 21;38(2):249-257. doi: 10.3171/2022.9.SPINE22416. PMID: 36272125. Rajkumar S, Yang LZ, Venkatraman V, Charalambous L, Parente B, Lee HJ, Lad SP. Health Care Resource Utilization of High-Frequency Spinal Cord Stimulation for Treatment of Chronic Refractory Low Back Pain. Neuromodulation. 2023 Jan;26(1):115-123. doi: 10.1016/j.neurom.2022.03.013. Epub 2022 Jul 21. PMID: 35871122. Gupta M, Ray M, Ladesich N, Gupta A. Health-Care Utilization and Outcomes with 10 kHz Spinal Cord Stimulation for Chronic Refractory Pain. *J Pain Res*. 2021;14:3675-3683. Kapural L, Jameson J, Johnson C, Kloster D, Calodney A, Kosek P, Pilitsis J, Bendel M, Petersen E, Wu C, Cherry T, Lad SP, Yu C, Sayed D, Goree J, Lyons MK, Sack A, Bruce D, Rubenstein F, Province-Azalde R, Caraway D, Patel NP. Treatment of nonsurgical refractory back pain with high-frequency spinal cord stimulation at 10 kHz: 12-month results of a pragmatic, multicenter, randomized controlled trial. J Neurosurg Spine. 2022 Feb 11:1-12. doi: 10.3171/2021.12.SPINE211301. Epub ahead of print. PMID: 35148512. Al-Kaisy, A., Van Buyten, JP., Carganillo, R. *et al.* 10 kHz SCS therapy for chronic pain, effects on opioid usage: Post hoc analysis of data from two prospective studies. *Sci Rep*9, 11441 (2019). Kallewaard JW, Gültuna I, Hoffmann V, Elzinga L, Munnikes R, Verbrugge L, Minne V, Reiters P, Subbaroyan J, Santos A, Rotte A, Caraway D. 10 kHz Spinal Cord Stimulation for the Treatment of Failed Back Surgery Syndrome with Predominant Leg Pain: Results from a Prospective Study in Patients from the Dutch Healthcare System. Pain Pract. 2021 Jun;21(5):490-500. doi: 10.1111/papr.12973. Epub 2020 Dec 22. PMID: 33274545; PMCID: PMC8247309. Amirdelfan K, Vallejo R, Benyamin R, Rosen S,

Kosek P, Caraway D, Rotte A, Burgher A. Pain relief and opioid usage in upper limb and neck pain patients after 10-kHz spinal cord stimulation treatment: subanalysis of USA studies. Pain Manag. 2021 Mar;11(2):133-143. doi: 10.2217/pmt-2020-0074. Epub 2020 Nov 13. PMID: 33183130. Feng H, Doherty P, Rotte A. Decreased Opioid Consumption and Durable Pain Relief in Patients Treated with 10 kHz SCS: A Retrospective Analysis of Outcomes from Single-Center. J Pain Res. 2021 Aug 24;14:2593-2600. doi: 10.2147/JPR.S312932. PMID: 34466027; PMCID: PMC8403026.

Acknowledgements: N/A

Learning Objectives: (1) To discuss health care utilization reduction following SCS therapy in a single University based center. (2) To review the current state of the art literature on health care utilization reduction, particular morphine miliequivalent, emergency department visits and additional pain procedure visits domains. (3) To highlight the clinical minimmful importanct difference in opioid utilization on subjects following SCS therapy.

Financial Disclosures: CONFLICTS OF INTEREST: Vinicius Tieppo Francio: receives research funding from Nevro (IIS - investigator-initiated study grant). **Usman Latif:** consultant for Nevro and Nalu. Dr. Latif received research funding from Mainstay Medical unrelated to this study **Dawood Sayed:** reports grants from Boston Scientific, personal fees from Medtronic, Nevro, Saluda, Painteq (with options), Vertos (with options), SPR (with options), Mainstay (with options), and Surgentec, unrelated to this study **Other authors:** The other authors declare no conflicts of interest or funding.

Disclosure: No significant relationships.

O059

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 02
14-05-2024 16:30 - 18:20

HIGH FREQUENCY SPINAL CORD STIMULATION IN PATIENTS WHO PREVIOUSLY FAILED TRADITIONAL SCS: A PROSPECTIVE, MULTICENTER, OBSERVATIONAL STUDY

Saurabh Dang, MD[1], Gladstone McDowell, MD[2], Aaron Calodney, MD[3], George Mandybur, MD[4], Nadeem Moghal, MD[5], Devsmita Das, MBBS[6], Alexios Carayannopoulos, DO, MPH, DABPMR[6]
[1]Garden State Pain & Orthopedics, Clifton, United States of America, [2]Integrated Pain Solutions, Columbus, United States of America, [3]Precision Spine Care, Pain Management, Tyler, United States of America, [4]Mayfield Brain & Spine, Cincinnati, United States of America, [5]Comprehensive Centers for Pain Management, Toledo, United States of America, [6]Nevro Corp, Redwood City, United States of America

Introduction: Low-frequency (typically 40-80 Hz) spinal cord stimulation (SCS) is a well-established treatment option for pain [1,2]. However, limited evidence exists on salvage therapy using high-frequency (10kHz) SCS for subjects who previously failed traditional low-frequency SCS (LF-SCS) therapy or dorsal root ganglion stimulation (DRG) [3]. This post-market study was designed to assess the effectiveness of 10kHz SCS in the treatment of chronic, intractable, neuropathic pain of trunk and/or limbs in patients who previously failed LF-SCS or DRG therapy.

Materials / Methods: A total of 138 patients were enrolled across 34 study centers in United States (Table 1). Data was collected at baseline, and post-implant 3-, 6-, and 12-month (M). Study outcomes included pain (numerical rating scale; NRS), disability (Oswestry Disability Index; ODI), quality-of-life (EQ-5D-5L), patient and clinician global impression of change (PGIC and CGIC), patient satisfaction, and opioid use. Primary endpoint was therapy success at 3M defined as “Clinically Meaningful Responders” (CMR): ≥30% pain relief or ≥2-point NRS change or PGIC of “A little Better” or higher); and “Remitters”: NRS≤3. Missing data was imputed by last observation carried forward method for permanent implanted subset. Changes over time were analyzed using t-test with Bonferroni correction for pain and QoL, and Fisher’s exact test for ODI.

Results: Of the enrolled patients, 92 received permanent implants. Sixty-one percent (61%) of implanted patients completed the study through 12M (56/92). At 3M, 80.4% were CMR and 21.7% were Remitters. At 12M, 68.5% remained CMR and 13% were Remitters. At 12M, there was >20% reduction in number of patients with severe disability on ODI (p-value<0.01; Fig.1) and a greater than MCID improvement in mean EQ-5D-5L index score (p-value<0.001; Fig.2), both significant improvements from baseline. Opioid use either decreased or remained the same for >82% of patients through 12M. Similarly, at 12M, 71% of patients and 79.6% of clinicians reported improvement in GIC. Over 69% of patients reported being “Satisfied” or “Very Satisfied” at each assessment. Among 123 patients who underwent trial and/or permanent implant, 11 adverse events (8.9%) were reported, of which infection (4/123, 3%) was the most common.

Table 1. Demographics and Baseline Characteristics

Characteristics (N=138)	**Number of patients_(%)**
Age in years, median (range)	62.5 years (33-83 years)
Gender	
Female	84 (61.7%)
Male	52 (38.2%)
Race	
White	111 (81.6%)
Black or African American	12 (8.8%)
Other	13 (9.6%)
Baseline pain VAS (cm)	
Mean (SD)	7.4 (1.4)
Median, range	8 (3-10)
Pain Etiology	
Failed back surgery syndrome	75 (60.0%)
Degenerative disc disease	38 (30.4%)
Radiculopathy	63 (50.4%)
Mild / moderate spinal stenosis	23 (18.4%)
Lumber facet-mediated pain	10 (8.0%)
Spondylolisthesis	5 (4.0%)
Spondylosis	32 (25.6%)
Internal disc disruption	6 (4.8%)
Sacroiliac dysfunction	9 (7.2%)
other	38 (30.4%)
Reason for discontinuing previous SCS	
Insufficient therapeutic response	93 (74.4%)
Uncomfortable paresthesia	13 (10.4%)
Other	19 (15.2%)
Time on previous therapy, median (range)	1.5years (1day – 19yrs)

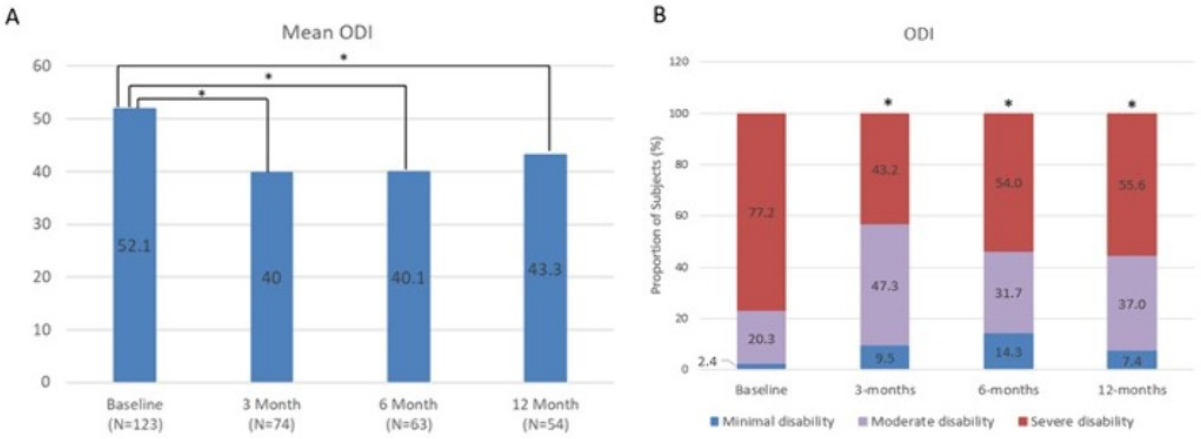


Fig 1. ODI **A]** Mean ODI at baseline and 3- , 6-, and 12- months follow-up (* indicates significant change from baseline ($p<0.0001$), and **B]** Proportion of subjects under each of the disability categories (minimal, moderate or severe) at baseline and follow-up visits (* indicates significant change from baseline in proportion of severe disability ($p<0.01$).

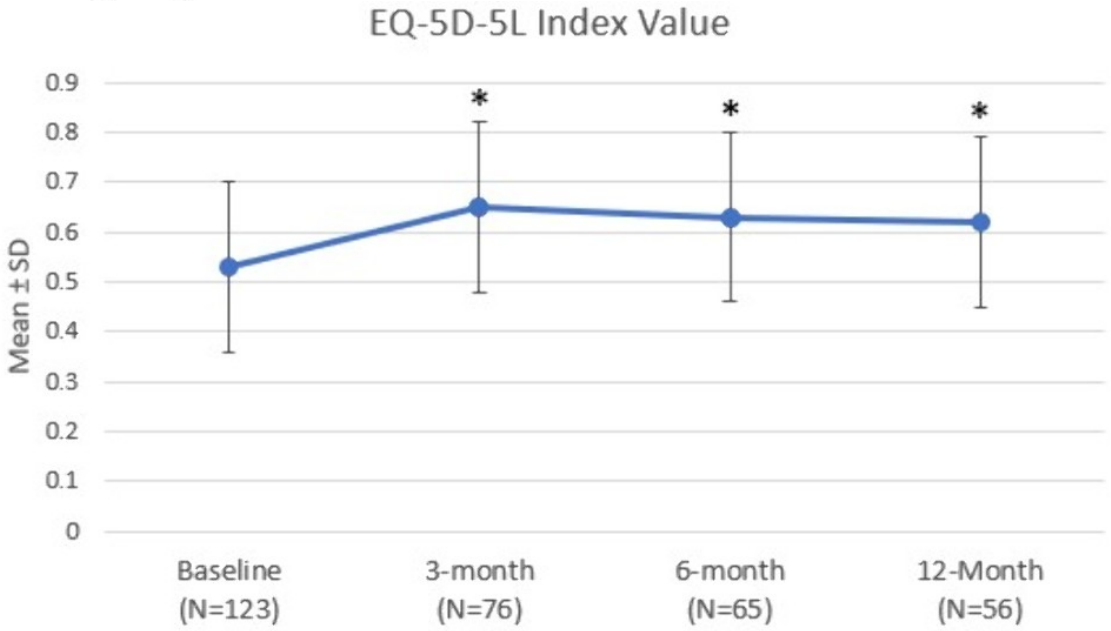


Fig 2. Mean EQ-5D-5L at baseline and 3- , 6-, and 12- months follow-up (* indicates significant change from baseline ($p<0.001$))

Discussion: Few alternative treatment options currently exist in this challenging patient group. Salvaging with 10kHz SCS therapy in patients who previously failed LF-SCS or DRG therapies provides significant pain relief and improvements in functional measures related to activities of daily living, quality-of-life, and opioid use.

Conclusions: Ten kHz SCS is a comprehensive therapy option for patients who failed LF-SCS or DRG.

Supplemental Data:

References: [1] Krames, E.S. Neuromodulatory Devices Are Part of Our “Tools of the Trade”, Pain Medicine, 7 (2006) S3-S5. [2] Vallejo R, Kramer J, Benyamin R. Neuromodulation of the cervical

spinal cord in the treatment of chronic intractable neck and upper extremity pain: a case series and review of the literature. Pain Physician. 2007;10(2):305-311. [3] Kapural L, Sayed D, Kim B, Harstroem C, Deering J. Retrospective Assessment of Salvage to 10 kHz Spinal Cord Stimulation (SCS) in Patients Who Failed Traditional SCS Therapy: RESCUE Study. J Pain Res. 2020;13:2861-2867. Published 2020 Nov 10.

Acknowledgements: The support of Nevro Corp. for this project is gratefully acknowledged.

Learning Objectives: 1. Participants will be able to discuss with their patients with chronic intractable pain of back and/or leg how 10 kHz SCS can lead to clinically meaningful response to therapy. 2. Participants will be able to discuss with their patients with chronic intractable pain of back and/or leg how 10kHz SCS can be an effective treatment option for them especially if they have failed other SCS therapy. 3. Participants will be able to discuss with their patients with chronic intractable pain of back and/or leg how 10 kHz SCS can lead to improved quality of life for them.

Financial Disclosures: **Saurabh Dang, MD 1]** a. Name of the Company- **Medtronic** b. For what role?: Education c. Level of Compensation: $5001 - $20,000 USD **2]** a. Name of the Company- **Boston Scientific** b. For what role?: Education c. Level of Compensation: $5001 - $20,000 USD **Gladstone McDowell, MD 1]** a. Name of the Company- **NEVRO** b. For what role?: Education / Research c. Level of Compensation: $50,000 research grant to my employer **2]** a. Name of the Company- **Medtronic** b. For what role?: Education / Research c. Level of Compensation: $5001 - $20,000 USD to my employer **3]** a. Name of the Company- **Flowonix** b. For what role? Education / Research; Stock Options c. Level of Compensation: $5001 - $20,000 USD to my employer **Devsmita Das, MBBS** a. Name of the Company: **NEVRO CORP** b. For what role? - Company Employee; Stock Options c. Level of Compensation: >$100,000 USD **Aaron Calodney, MD; George Mandybur, MD; and Nadeem Moghal, MD have No Significant Relationships.**

Disclosure: I am the submitter as well as co-author for this abstract. I am a Nevro employee and my financial disclosure is included in the Financial Disclosure Section.

O060

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 02
14-05-2024 16:30 - 18:20

EFFICACY AND SAFETY OF SURGICAL LEADS TO DELIVER 10 KHZ THERAPY FOR THE TREATMENT OF CHRONIC BACK OR LEG PAIN

Dimitri Vanhauwaert, MD[1], Jan Eckermann, MD[2], Julie Pilitsis, MD, PhD[3], Namath Hussain, MD[4], Randall Johnson, MD[5], Michael Dorsi, MD[6], Maarten Moens, MD[7], Johan Vangeneugden, MD[8], Erika Petersen, MD[9], George Mandybur, MD[10], Zaman Mirzadeh, MD[11], Rose Azalde, MSBmE[12], Delea Peichel, BSc (Hons)[12], Frances Rubenstein, PhD[12]
[1]AZ Delta, Neurosurgery, Rumbeke, Belgium, [2]Kern Neurosurgical Institute, Kern Country, United States of America, [3]Florida Atlantic University School of Medicine, Neurosurgery, Boca Raton, United States of America, [4]Loma Linda University Hospital, Loma Linda, United States of America, [5]Neuroscience Group, Neenah, United States of America, [6]Ventura Neurosurgery, Ventura, United States of America, [7]Vrije Universiteit Brussel, Stimulus Research Group, Jette, Belgium, [8]AZ Sint-Maarten, Michelen, Belgium, [9]University of Arkansas for Medical Sciences, Department Of Neurosurgery, Little Rock, United States of America, [10]Mayfield Brain & Spine, Cincinnati, United States of America, [11]Barrow Neurological Institute, Phoenix, United States of America, [12]Nevro Corp., Clinical Research, Redwood City, United States of America

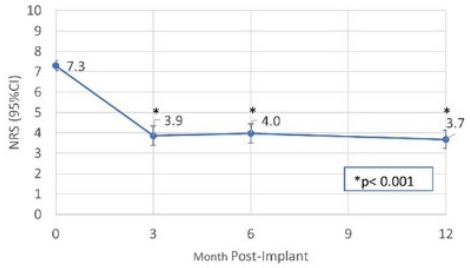
Introduction: Chronic back pain has a major negative impact on mental health and quality-of-life, and can lead to the overuse of opioids.[1] High-frequency (10kHz) SCS has been shown to have superior efficacy in treating chronic pain to traditional stimulation when delivered through percutaneous leads.[2] There are limited studies comparing the efficacy between percutaneous and paddle leads for SCS. This study was designed to assess the clinical performance of 10kHz therapy delivered through paddle leads for the treatment of intractable back and leg pain.

Materials / Methods: Eleven centers from Belgium and the US participated in this post-market, observational study where 10kHz SCS was used to treat back and/or leg pain with a paddle lead placed via a laminectomy procedure. Data was collected at baseline, end of trial, and 3-, 6-, and 12-month(M) follow-up. Outcome data included pain (numerical rating scale, NRS), disability (Oswestry Disability Index, ODI), quality-of-life (EQ5D5L), patient global impression of change (PGIC), patient satisfaction with therapy, and opioid use. The primary pain outcomes were rates of patients meeting a "Clinically Meaningful Responder criteria (≥30% pain relief[3] or PGIC of "A little Better" or higher), and "Substantial Responder" (≥50% pain relief or PGIC of "Moderately Better" or higher) at 3M.

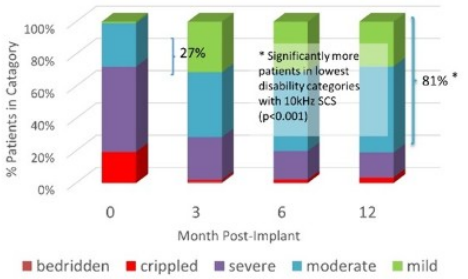
Results: Out of 126 subjects enrolled, 110 received a permanent implant with the paddle lead, and 102 (93.6%) were assessed for the primary endpoints at 3M. Eighty-three percent of patients completed the study to 12 months. The population demographics are shown in Table 1. At 3M, 92% and 76% of patients met the "Clinically Meaningful" and "Substantial" responder rates respectively. The average NRS reduction from baseline was 3.5 pts (Figure 1A), and 72% had a clinically important 30% pain relief[3]. Function (ODI) and quality-of-life (EQ5D5L) were improved significantly through 12M (Figure 1B,C). The percent of patients on opioids decreased from 64% to 44% (p=0.007) with 54% stopping or decreasing use (Fig. 1D). There were 8(7.3%) reported complications, including 2 infections at the lead incision, and no lead migrations. Three (2.7%) of 110 patients were explanted due to therapy inefficacy, while 89% reported being satisfied or very satisfied with the therapy.

Figure 1.

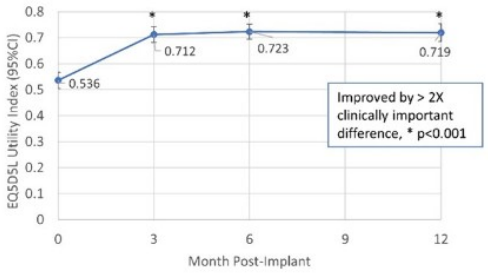
A.



B.



C.



D.

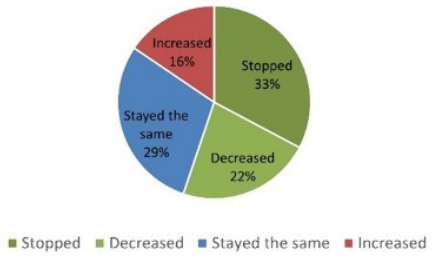


Table 1. Population Demographics of n = 126 enrolled patients.

Age average±SD (range)	56.1±13.1 (23 to 89) years
BMI average±SD	31.1±8.4 kg/m^2
Years Since Diagnosis average±SD	9.0±10.9 years
Characteristics	**N (%)**
Gender	
Female	74 (58.7%)
Male	52 (41.3%)
Pain Diagnosis	
Chronic intractable back pain	114 (95.0%)
Chronic intractable leg pain	93 (77.5%)
Leg pain symmetry	
Bilateral	48 (40.0%)
Unilateral	45 (37.5%)
Pain Etiology	
Failed back surgery syndrome	80 (66.7%)
Degenerative disc disease	29 (24.2%)
Radiculopathy	47 (39.2%)
Mild / moderate spinal stenosis	12 (10.0%)
Lumber facet-mediated pain	1 (0.8%)
Spondylolisthesis	5 (4.2%)
Spondylosis	10 (8.3%)
Internal disc disruption	3 (2.5%)
Sacroiliac dysfunction	1 (0.8%)
Neuropathic	0 (0.0%)
other	27 (22.5%)

Discussion: Similar procedural complication and infection rates to SCS using epidural leads were seen, with no reported lead migration.

Conclusions: This multicenter observational study demonstrates that 10kHz SCS therapy delivered with paddle leads produces clinically important improvements in pain, disability and quality-of-life, while reducing opioid use through 12M.

Supplemental Data:

References: 1) Hong A, Varshney V, Hare GMT, Mazer CD. Spinal cord stimulation: a nonopioid alternative for chronic pain management. *CMAJ*. Oct 19 2020;192(42):E1264-E1267. 2) Kapural L, Yu C, Doust MW, et al. Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: The SENZA-RCT Randomized Controlled Trial. *Anesthesiology*. Oct 2015;123(4):851-60. 3) Dworkin RH, Turk DC, Wyrwich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain*. Feb 2008;9(2):105-21.

Acknowledgements:

Learning Objectives: 1) Similar procedural complication and infection rates to SCS using epidural leads were seen with surgical leads, with no reported lead migrations. 2) This multicenter observational study demonstrates that 10kHz SCS therapy delivered with paddle leads produces clinically important improvements in pain, disability and quality-of-life, while reducing opioid use through 12M

Financial Disclosures: Julie Pilitsis reported fellowship grants from Medtronic, Boston Scientific, and Abbott; and grants from NIH (grant nos. 2R01CA166379, R01EB030324, and U44NS115111) and NIH Blueprint (grant no. 3U54EB015408) outside the submitted work; and medical advisor for and stock equity in Aim Medical Robotics. Erika Petersen reported personal fees from Nevro, Saluda Medical, Presidio Medical, Biotronik, and Medtronic; grants from Nevro and Saluda Medical, and board of directors for and stock options in SynerFuse during the conduct of the study; personal fees from Nalu and grants from Mainstay Medical, Nalu, Neuros Medical, and SPR outside the submitted work; research support from Mainstay, Medtronic, Nalu, Neuros Medical, Nevro Corp, ReNeuron, SPR, and Saluda, personal fees from Abbott Neuromodulation, Biotronik, Medtronic Neuromodulation, Nalu, Neuros Medical, Nevro, Presidio Medical, Saluda, and Vertos; and stock options in neuro42. Michael Dorsi receives consultant fees for scientific advisory from Nevro Crop. Dimitri Vanhauwaert, Jan Eckermann, Namath Hussain, Randall Johnson, Maarten Moens, Johan Vangeneugden, George Mandybur, Zaman Mirzadel received research fees to their institution for the conduct of this research from Nevro Corp. Rose Azalde, DeLea Peichel and Frances Rubenstein are employees of Nevro Corp.

Disclosure: Rose Azalde is an employee of Nevro Corp.

O061

Oral Presentations
NEUROMODULATION FOR REHABILITATION
14-05-2024 16:30 - 18:20

SYSTEMATIC REVIEW AND META-ANALYSIS OF MEDIAL BRANCH STIMULATION IN THE TREATMENT OF CHRONIC LOW BACK PAIN

Sue Copley, MSc[1], Alan Baterham, PhD[2], Anuj Shah, DO[3], Ahmed Foly, MRCA[1], Jonathan Hagedorn, MD[4], Timothy Deer, MD[5], Christopher Gilligan, MD[6], Sam Eldabe, FRCA[7]
[1]South Tees Hospitals NHS Foundation Trust, Pain Management, Middlesbrough, United Kingdom, [2]Teesside University, Middlesbrough, United Kingdom, [3]Detroit Medical Center, Pm&r, Detroit, United States of America, [4]Mayo Clinic, Department Of Anesthesiology And Perioperative Medicine, Rochester, United States of America, [5]The Spine and Nerve Center of the Americas, Pain, Charleston, United States of America, [6]Brigham and Women's Hospital Harvard Medical School, Division Of Pain Medicine, Boston, United States of America, [7]James Cook University Hospital, Department Of Pain Medicine, MIDDLESBROUGH, United Kingdom

Introduction: Chronic low back pain (CLBP) is a leading cause of years lived with disability.[1] MostCLBP is non-specific[2]and is often associated with impaired motor control and atrophy of the lumbar multifidus muscles.[3] Studies have reported on the utility of multifidus stimulation through medial branch stimulation to treat CLBP.[4-8] We present the findings of a systematic review and meta-analysis of studies reporting on the change in low back pain intensity with multifidus/medial branch stimulation.

Materials / Methods: A comprehensive literature search was conducted from 2010-22 for randomised controlled trials or prospective reports of adults with CLBP, treated with multifidus or medial nerve stimulation via an implanted or percutaneous device with usual care, sham, or no control, excluding studies reporting on <10 subjects. Mean change (SE) in pain intensity was extracted from each study and each timepoint reported. Data were synthesised using a mixed effects regression with restricted maximum likelihood, with a random intercept for study to account for repeated timepoints nested within study. We conducted a meta regression with follow-up time as a moderator.

Results: There were 25 effects from 6 studies (1-6 timepoints per study, N=419 participants), with follow-up ranging from 1.5 to 48 months. The weighted pooled mean effect was a reduction in pain intensity (0-10 scale) of 2.9 (95% CI: 2.1 to 3.7) units. The 95% prediction interval – the likely range of true effects in future similar studies - was a reduction in pain intensity of 0.6 to 5.2 units. The estimated probability that reduction in pain intensity in a new similar study would be greater than a clinically relevant difference of 2 points is 0.84 (0.68 to 0.98). The meta-regression revealed that the longer the follow-up, the greater the reduction in pain intensity - approximately 0.25 (0.16 to 0.34) units per 6-month increase. Follow-up time accounted for 16% of the between-trial heterogeneity in effect size.

Discussion: This meta-analysis showed clinically meaningful reductions in pain, though uncertainty exists in the estimates due to the small number of studies, and treatment effects may be exaggerated due to lack of control arms.

Conclusions: Electrical stimulation of the medial branch results in clinically meaningful changes from baseline in pain intensity in single-arm studies. Longer duration of stimulation (longer follow-up) was associated with lower LBP intensities.

Supplemental Data:

References: 1. Maher C, Ferreira G. Time to reconsider what Global Burden of Disease studies really tell us about low back pain. Ann Rheum Dis. 2022;81(3):306-308. 2. Russo M, Deckers K, Eldabe S, et al. Muscle Control and Non-specific Chronic Low Back Pain. Neuromodulation. 2018;21(1):1-9. 3.

Wilke HJ, Wolf S, Claes LE, Arand M, Wiesend A. Stability increase of the lumbar spine with different muscle groups. A biomechanical in vitro study. Spine (Phila Pa 1976). 1995;20(2):192- 198. 4. Gilligan C, Volschenk W, Russo M, et al. An implantable restorative-neurostimulator for refractory mechanical chronic low back pain. Pain. 2021;Publish Ahead of Print. 5. Gilligan C, Volschenk W, Russo M, et al. Long-Term Outcomes of Restorative Neurostimulation in Patients With Refractory Chronic Low Back Pain Secondary to Multifidus Dysfunction: Two-Year Results of the ReActiv8-B Pivotal Trial. Neuromodulation. 2021. 6. Gilligan C, Volschenk W, Russo M, et al. An implantable restorative-neurostimulator for refractory mechanical chronic low back pain: a randomized sham-controlled clinical trial. Pain. 2021;162(10):2486-2498. 7. Gilligan C, Volschenk W, Russo M, et al. Three-Year Durability of Restorative Neurostimulation Effectiveness in Patients With Chronic Low Back Pain and Multifidus Muscle Dysfunction. Neuromodulation. 2022. 8. Deer TR, Gilmore CA, Desai MJ, et al. Percutaneous Peripheral Nerve Stimulation of the Medial Branch Nerves for the Treatment of Chronic Axial Back Pain in Patients After Radiofrequency Ablation. Pain Med. 2021;22(3):548-560.

Acknowledgements:

Learning Objectives: 1. CLBP is associated with Lumbar Multifidus atrophy and functional instability. 2. A number of studies have reported on the treatment of functional instability using electrical stimulation of the lumbar multifidus stimulation or the medial branch of the dorsal ramus. 3. Electrical stimulation of the medial branch is effective in the treatment of CLBP with a high probability of a clinically significant reduction in pain intensity. Longer duration of stimulation was associated with lower LBP intensities.

Financial Disclosures: SC - No significant relationships AB is a consultant to Mainstay Medical AS - No significant relationships AF - No significant relationships JH is a consultant for Abbott, Boston Scientific, Nevro, and Saluda TD is a consultant for SPR Therapeutics and Mainstay Medical CG is a paid consultant for Mainstay Medical and has equity in Mainstay Medical SE is a consultant to Mainstay Medical

Disclosure: No significant relationships.

O062

Oral Presentations
NEUROMODULATION FOR REHABILITATION
14-05-2024 16:30 - 18:20

INTRADURAL IMPLANT FOR DIRECT CURRENT STIMULATION OF SPINAL CORD INJURIES

Lukas Matter, MSc[1], Bruce Harland, PhD[2], Brad Raos, PhD[2], Brittany Hazelgrove, BSc (Hons)[2], Darren Svirskis, PhD[2], Maria Asplund, PhD[1]
[1]Chalmers University of Technology, Electronics Materials And Systems Laboratory, Gothenburg, Sweden, [2]The University of Auckland, School Of Pharmacy, Auckland, New Zealand

Introduction: Spinal cord injuries typically cause long-term neurological impairments such as permanent loss of motor, bladder and bowel function and neuropathic pain. Nerve cells in the central nervous system have a low capacity of regeneration, thus therapies are desperately needed. Direct current electric fields (dcEFs) were shown to act as guidance cues for axonal growth cones, supporting the regeneration of injured axons.[1] The application of dcEFs to the spinal cord is challenging because the current in the tissue is generated by electrochemical redox reactions which can cause toxic concentrations of stimulation by-products.[2] To address this challenge, we have extended an ultra-thin, flexible, and conformable bioelectronic implant made for recordings[3] by leveraging the superior DC capabilities of sputtered iridium oxide film (SIROF) electrodes (Figure 1a).

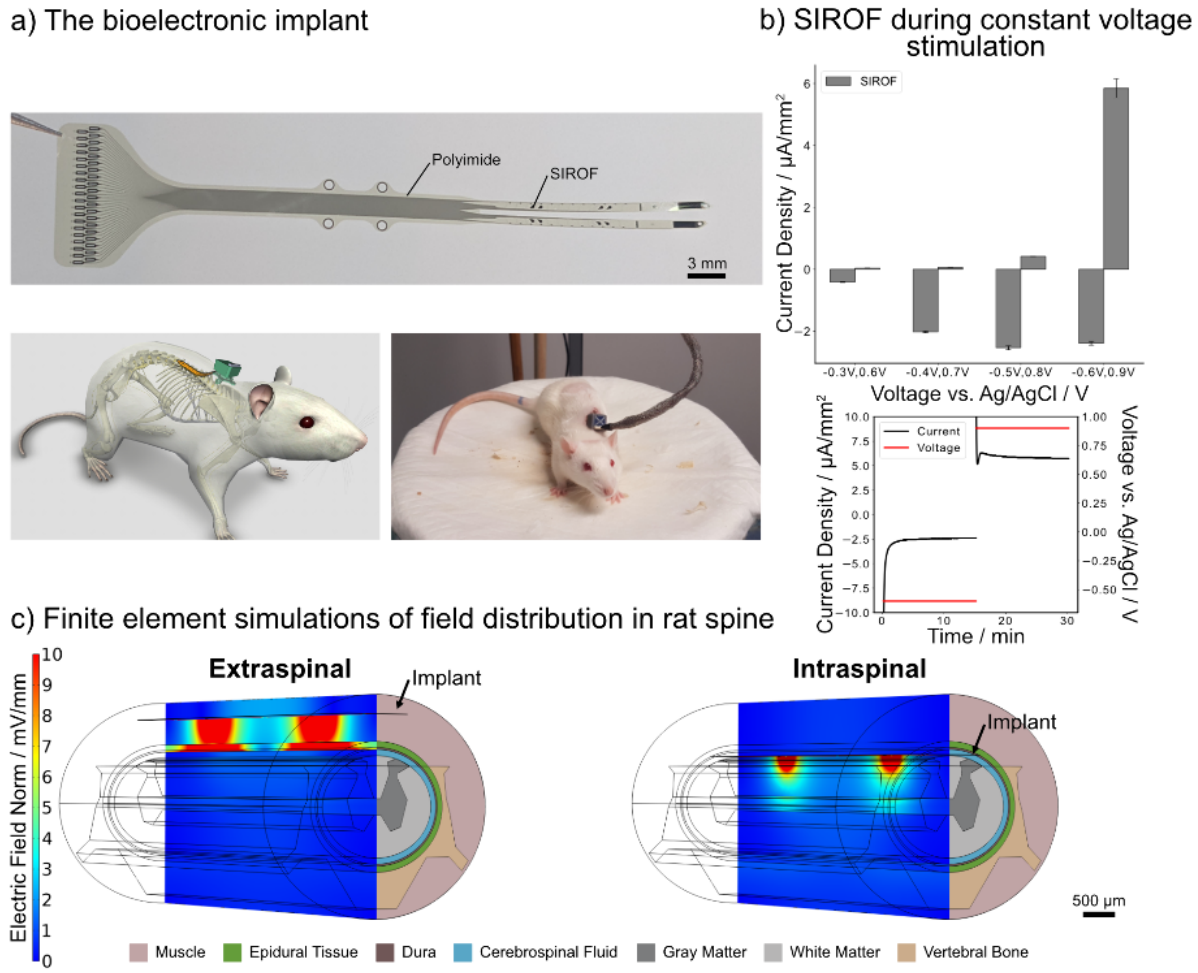


Figure 1. a) The bioelectronic implant. b) Current response of SIROF to constant voltage stimulation. c) Finite element simulation of the field distribution in the rat's spine.

Materials / Methods: The polyimide implant was fabricated in a cleanroom according to thin film microtechnology methods. Finite element model simulations were performed in COMSOL. Electrochemical measurements were done in 1x PBS.

Results: When SIROF is stimulated potentiometrically, the generated current plateaus after 15 min at -2 and 6 μA/mm^2 at the threshold voltage for water splitting reactions in PBS (-0.6 and 0.9 V, Figure 1b). The cerebrospinal fluid (CSF) surrounding the white and grey matter shunts the stimulation current of an extradural implant, which reduces the generated field strength within the cord compared to an intradural implant (Figure 1c).

Discussion: CSF has a high conductivity, which explains its shunting effect. Precision and strength of the EF is thus increased by bringing electrodes close to the white matter, which demands minimizing compression caused by the implant. Several electrochemical reactions happen in parallel to deliver the stimulation current. We found that SIROF is capable to deliver -2 and 6 μA/mm^2 in a voltage window which avoids water splitting and associated toxic changes in surrounding media.

Conclusions: Large SIROF electrodes are necessary to generate dcEFs. Electrodes need to be implanted below the CSF for high spatial resolution and high field strengths.

Supplemental Data:

References: [1] N. A. Silva et al. *Progess in Neurobiology* **114**. 25 (2014). [2] R. J. Hurlbert et al. *J Neurosurg* **79**. 905 (1993). [3] B. Harland et al. *Advanced Science* **9**. 2105913 (2022).

Acknowledgements: This work was supported by the CatWalk Spinal Cord Injury Trust and the Health Research Council of New Zealand (Project grant and HRC/Catwalk Partnership 19/895), and the ERC (No. 759655, SPEEDER).

Learning Objectives: 1. Evaluate the EF distribution by intra- and extraspinal implants 2. Describe the tissue-electrode interface 3. Understand the relationship between current, voltage, and type of electrochemical reaction during stimulation of tissue

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O063

Oral Presentations
NEUROMODULATION FOR REHABILITATION
14-05-2024 16:30 - 18:20

SPATIOTEMPORALLY PATTERNED ACTIVATION USING TRANSCUTANEOUS SPINAL CORD STIMULATION

Conor Keogh, MBBS, James Fitzgerald, MB ChB, PhD
University of Oxford, Nuffield Department Of Surgical Sciences, Oxford, United Kingdom

Introduction: Epidural spinal cord stimulation has emerged as a promising modality for restoring function following spinal cord injury. This is based on the use of spatiotemporally patterned stimulation allowing activation of specific nerve roots at corresponding phases of the gait cycle. Transcutaneous spinal cord stimulation has recently gained attention for its potential applications in improving rehabilitation outcomes. However, its mechanism of action remains unclear, as does the level of selectivity possible. We demonstrate that transcutaneous stimulation mediates its effects by the same mechanism as epidural stimulation. We further show that selective stimulation is possible, allowing for spatially patterned stimulation.

Materials / Methods: We developed a detailed model of the thoracolumbar region using clinical imaging. This included the spinal cord and nerve roots bilaterally at multiple levels. The electric field produced by stimulation was solved using the finite element method. This was coupled with biophysical axon models to determine the effects of stimulation on the spinal cord and nerve roots. We characterized strength-duration curves for the spinal cord and nerve roots and examined the variation in their response with changes in electrode position and stimulation parameters.

Results: We show that the nerve roots are activated at lower amplitudes than the spinal cord for all stimulation parameters and electrode positions. These are consistently the first structures activated and likely mediate the effects of stimulation. The site of initial action potential generation is in the proximal nerve root, at the root entry zone. We further show that it is possible to activate individual segmental nerve roots unilaterally. We characterize the stimulation parameters and electrode positions required to achieve this. This required different electrode configurations than have been used traditionally.

Discussion: Our results suggest that the effects of transcutaneous spinal cord stimulation are mediated by the same mechanisms as epidural stimulation. This suggests that it may be possible to achieve the same benefits non-invasively. We show that greater selectivity can be achieved with transcutaneous stimulation than was thought. We demonstrate that it is possible to achieve spatially precise stimulation. However, this increased selectivity required different electrode configurations than used previously. We characterize the methods for optimally targeting individual nerve roots for precise stimulation.

Conclusions: Transcutaneous spinal cord stimulation mediates its effects via activation of segmental nerve roots, analogous to epidural stimulation. It is possible to target individual nerve roots using transcutaneous stimulation. This allows for spatiotemporally patterned stimulation, opening the possibility of applications in functional restoration.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1. To understand the mechanism of action of transcutaneous spinal cord stimulation 2. To appreciate the selectivity possible using transcutaneous stimulation 3. To understand the applications of transcutaneous stimulation to functional restoration

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O064

Oral Presentations
NEUROMODULATION FOR REHABILITATION
14-05-2024 16:30 - 18:20

COMPUTATIONAL MODELING AND DESIGN OF NOVEL ELECTRODE ARRAYS FOR GENERATING FOCAL SOMATOSENSORY PERCEPTS IN LOWER LIMB AMPUTEES

Sauradeep Bhowmick, PhD[1], Matteo Brocco, MSc[2], Gilgal Ansah, MSBmE[2], Maria Jantz, BSc[2], Robert Gaunt, Associate Professor[2], Lee Fisher, PhD[2], Scott Lempka, Associate Professor[3]
[1]University of Michigan, Ann Arbor, United States of America, [2]University of Pittsburgh, Pittsburgh, United States of America, [3]University of Michigan, Biomedical Engineering, Ann Arbor, United States of America

Introduction: Prosthetic limbs for people with lower-limb amputation lack somatosensory feedback, reducing their effectiveness in restoring gait. Previous research has explored spinal cord and dorsal root stimulation to induce localized sensations in the feet, but unwanted sensations in proximal limb regions remain a challenge. This ongoing computational study aims to design precise electrode arrays to generate targeted sensations in the missing limb regions, enhancing balance control and reducing phantom limb pain.

Materials / Methods: We used a computational framework to analyze the impact of version system design parameters on neural selectivity. We utilized high-resolutions imaging to create a three-dimensional finite element method model of the feline lumbo-sacral spinal cord and multi-compartment models of sensory neurons within the spinal cord. We designed custom 32-contact epidural electrode arrays with varying contact diameters (0.15, 0.5, and 1 mm) that were positioned over the spinal cord. We calculated the electric potential fields and corresponding neural response generated with monopolar and bipolar stimulation configurations to explore the influence of design parameters including contact size and stimulation configuration on stimulation selectivity.

Results: Monopolar stimulation achieved higher selectivity, while bipolar stimulation offered selectivity over a broader range of stimulation amplitudes. Smaller contact sizes had lower activation thresholds, with similar stimulation selectivity across all three contact sizes.

Discussion: Lateral spinal cord stimulation selectively activated dorsal roots. Bipolar stimulation, with reduced contact size and contacts approximately aligned to the orientation of the dorsal roots, provided selective activation over a wider amplitude range, and thereby offers a larger therapeutic window. Smaller contact sizes were more effective in generating neural responses at lower amplitudes with similar selectivity. Selective activation of the roots is necessary to generate focal perceptions in the missing limb to improve prosthetic limb control and functionality.

Conclusions: This computational study offers key insights for optimizing epidural stimulation of lateral spinal cord structures, crucial for restoring sensation in people with lower-limb amputation. The findings advance electrode array design, enabling highly focal somatosensory perceptions and holding promise for enhancing gait and amputees' quality of life.

Supplemental Data:

References: None

Acknowledgements: This work was supported by the National Institute of Neurological Disorders and Stroke of the National Institutes of Health under Award Number 1R01NS121028, and computational resources were provided by Advanced Research Computing (ARC), a division of Information and Technology Services (ITS) at the University of Michigan, Ann Arbor.

Learning Objectives: Objective 1: Validate computational modeling approach with experimental findings. Desired Result: Our aim was to confirm the reliability of our computational modeling

approach by comparing its outcomes with acute experimental data. The successful validation revealed a strong alignment between our model's predictions and the results obtained from experiments conducted on feline subjects. This agreement instilled confidence in the accuracy and applicability of our models. Objective 2: Compare electrode size effect on selectivity. Desired Result: Our goal was to examine how the size of the electrode impacted the selectivity of the stimulation. Surprisingly, our findings indicated that electrode size did not exert a significant influence on selectivity of dorsal roots. This result highlighted that selectivity may be influenced by factors other than electrode size in this context. However, it is to be seen how this varies at the rootlet level. Objective 3: Compare effects of selectivity of monopolar and bipolar stimulation. Desired Result: Our objective here was to assess the effects of selectivity when utilizing monopolar and bipolar stimulations. The desired outcome was to identify which of these stimulation approaches offered a more advantageous therapeutic window. Our study revealed that bipolar stimulation, in fact, provided a significantly larger therapeutic window compared to monopolar stimulation.

Financial Disclosures: Dr. Scott Lempka

a) Abbott Neuromodulation b) Consultant / Advisory Board c) $501 - $5,000 USD a) CereGate b) Consultant / Advisory Board and Stockholder c) $1-500 a) Hologram Consultants, LLC b) Stockholder Stock Value >5% c) $1-500 a) Neuronoff, Inc. b) Stockholder c) $1-500 a) Presidio Medical, Inc. b) Consultant / Advisory Board and Stockholder c) $1-500 Dr. Robert Gaunt a)Blackrock Microsystems b)Consultant c) $1-500 a)Neurowired LLC b)Non-CME/CE Services (e.g. advisor) c) $1-500

Disclosure: No significant relationships.

O065

Oral Presentations
NEUROMODULATION FOR REHABILITATION
14-05-2024 16:30 - 18:20

TACTILE PERCEPT INTEGRATION DURING PERIPHERAL NERVE STIMULATION FOR TOUCH RESTORATION

Leah Roldan, Graduate Student Researcher[1,2], Emily Graczyk, PhD[1,2], Dustin Tyler, PhD[1,2]
[1]Case Western Reserve University, Biomedical Engineering, Cleveland, United States of America, [2]Louis Stokes Cleveland Veterans Affairs Medical Center, Cleveland, United States of America

Introduction: Neural interfaces such as composite flat interface nerve electrodes (C-FINEs) have restored touch to upper and lower extremity amputees, changing how they grab objects, interact with others around them, stand, and walk. The relationship between stimulation paradigms and sensation at a single point of perception with a single channel of stimulation has been extensively studied. There remains a significant gap in understanding of multiple channel stimulation, which is critical to object feature extraction, stereognosis, and improved manual dexterity. We present data from stimulation trials showing integration of multiple perception points, or percepts, to test two main hypotheses: 1) multi-contact stimulation will result in multiple distinct intensities being perceived at once and 2) multi-contact stimulation will result in non-linear addition of the tactile dimensions of sensation.

Materials / Methods: Three unilateral transradial amputees were implanted with 16-channel C-FINEs on the median, ulnar, and radial nerves of their residual limb. Interleaved stimulation was delivered through two contacts at a time, and the stimulation parameters through a single contact were held constant while the pulse amplitude (PA) of a second contact was varied. Participants reported locations of sensation on their perceived hand, a value representing intensity of the sensation, and selected words from a predetermined list to indicate quality of the sensation.

Results: Location and intensity can be varied independently during multi-contact stimulation, with preliminary data showing percept area could be manipulated without a change to percept intensity. When stimulating through multiple contacts, the perceived area elicited by the contact held at a fixed PA decreased as the PA of a second contact was increased. Finally, multiple intensities were capable of being elicited across the hand during multi-contact stimulation.

Discussion: Location and intensity have been shown to trend together during single channel PA modulation, but the ability to vary them independently suggests multi-contact stimulation would allow for increased control over desired sensation outcomes. The decrease in perceived area elicited by a contact held at a fixed PA displays an inhibitory effect that confirms our hypothesis of non-linear addition patterns for both area and intensity. Finally, the ability to elicit multiple intensities indicates this stimulation strategy has the potential to enable feature extraction important for stereognosis.

Conclusions: These results reveal patterns for the integration of multiple percepts in the periphery, and therefore inform the future design of multi-channel stimulation paradigms for a sensory-enabled prosthesis.

Supplemental Data:

References: [1] D.W. Tan, M.A. Schiefer, M.W. Keith, J.R. Anderson, J. Tyler, D.J. Tyler. “A neural interface provides long-term stable natural touch perception.” Science Translational Medicine 6, 257ra138 (2014). [2] A.J. Pruszynski, R.S. Johansson. "Edge-orientation processing in first-order tactile neurons." Nature Neuroscience 17, 1404–1409 (2014). [3] E.L. Graczyk, B.P. Christie, Q. He, D.J. Tyler, and S.J. Bensmaia. “Frequency Shapes the Quality of Tactile Percepts Evoked through Electrical Stimulation of the Nerves.” J Neurosci 42, 2052-2064 (2022).

Acknowledgements: Research supported by the DARPA HAPTIX program Contract No. N66001-15-C-4014, VA Merit Review #I01 RX00133401 and Center #C3819C, and NIH Grant T32EB004314.

Learning Objectives: 1. Evaluate how interleaved multi-contact stimulation affects the different dimensions of tactile sensation, including location, intensity, quality, and temporal properties. 2. Identify tactile percept integration patterns resulting from multi-contact stimulation, so that they can be used to inform future design of multi-channel stimulation paradigms. 3. Assess the potential use of multi-contact stimulation to elicit stereognosis by evaluating if distinct intensities and percepts can be elicted across the hand.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O066

Oral Presentations
NEUROMODULATION FOR REHABILITATION
14-05-2024 16:30 - 18:20

VOLUNTARY LOCOMOTION INTENTION MODULATES MUSCLE ACTIVATION PATTERNS DURING EPIDURAL ELECTRICAL STIMULATION FOR SPINAL CORD INJURY PATIENTS

Xi Zhang, PhD, Xuesong Luo, PhD, Qingyu Yao, MD, Boyang Zhang, MD, Yang Lu, MD, Bozhi Ma, MSc, Luming Li, PhD
Tsinghua University, Beijing, China

Introduction: Epidural Electrical Stimulation (EES) has been validated as a effective method for reinstating voluntary locomotion in patients with spinal cord injury. However, modifications in a patient's gestures could influence the actual stimulation dosage received, thereby blurring the distinction between the impact of electrical stimulation and the patient's voluntary motor control. Evoked Compound Action Potential (ECAP) could be used to disentangle this complex interaction. Therefore, it might help to clarify the significance of voluntary control during motor restoration.

Materials / Methods: Multi-modal signal recording, including ECAP and EMG signals, were recorded during patient's voluntary movement and resting states. ECAP signal was extracted using curve fitting method. EMG signal was filtered using 3rd order Butterworth bandpass filter with the cut-off frequency of 25 to 250Hz and RMS value was used to quantify the task-specific muscle activation patterns.

Results: ECAP signal was proved to be an effective marker of stimulation dosage change induced by different postures. It was subsequently employed as an indicator to disentangle the effect of posture change and voluntary locomotion intention on muscles activation patterns. We show that the muscle activation patterns differ between posture alteration and voluntary motion control. With EES, patient regains task-specific spinal cord neural control capacity not via posture change but through voluntary movement control intention. Various motor tasks (knee extension, hip flexion, ankle plantarflexion) tested demonstrated that the EES enables SCI patients to regain task-specific muscle control capacity. Techniques utilizing ECAP signal that decouples actual received stimulation dosage and voluntary control intention could effectively prove the significance of voluntary locomotion intention for SCI patients' motor restoration. Fig1: Experiment set up and baseline
control

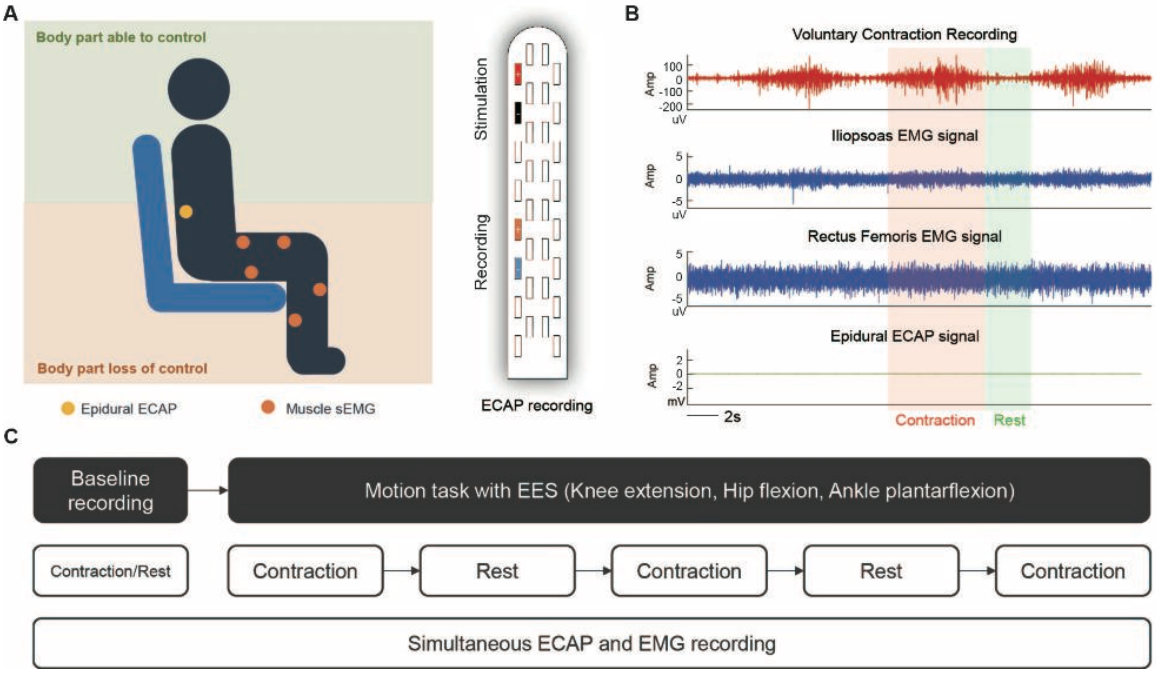


Fig2: Prouf of effectiveness using ECAP signal as a marker of stimulation dosage

change

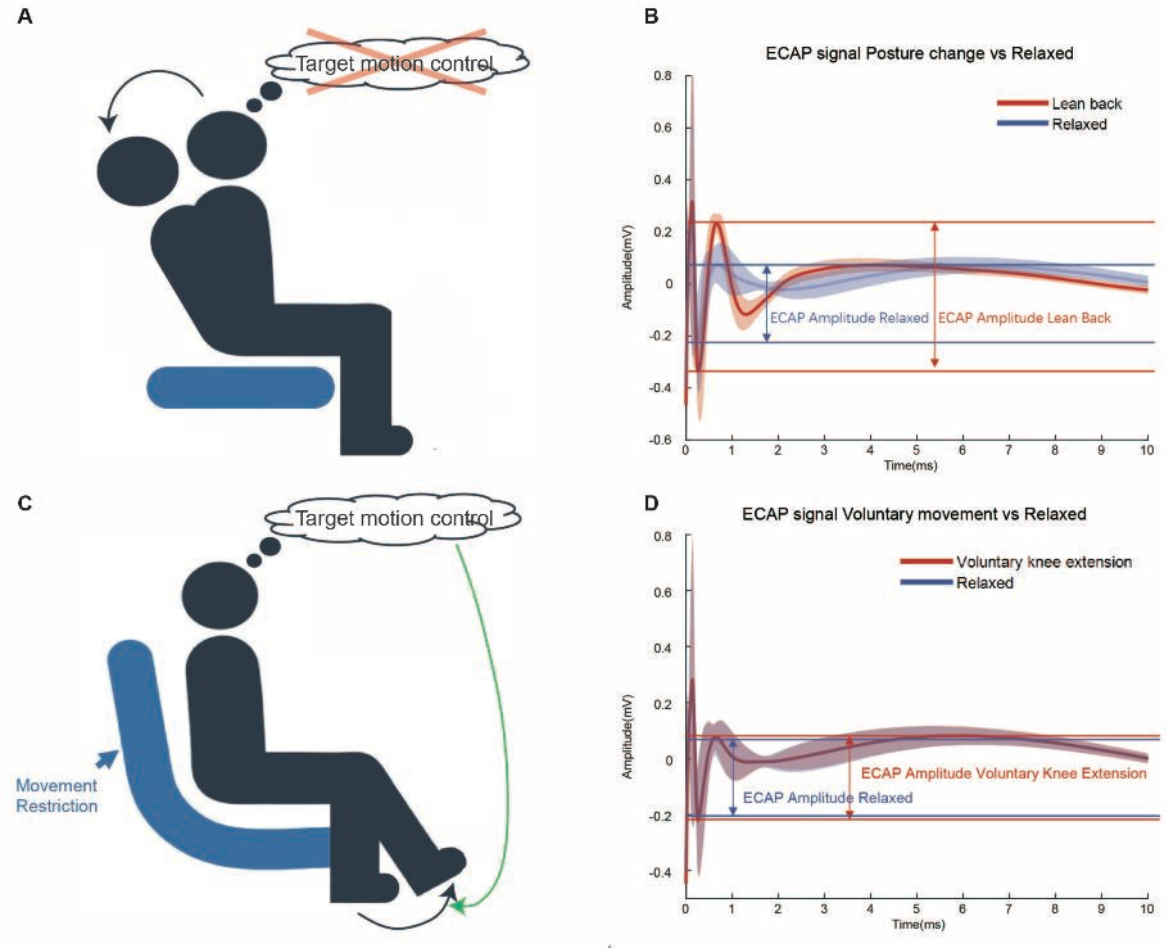
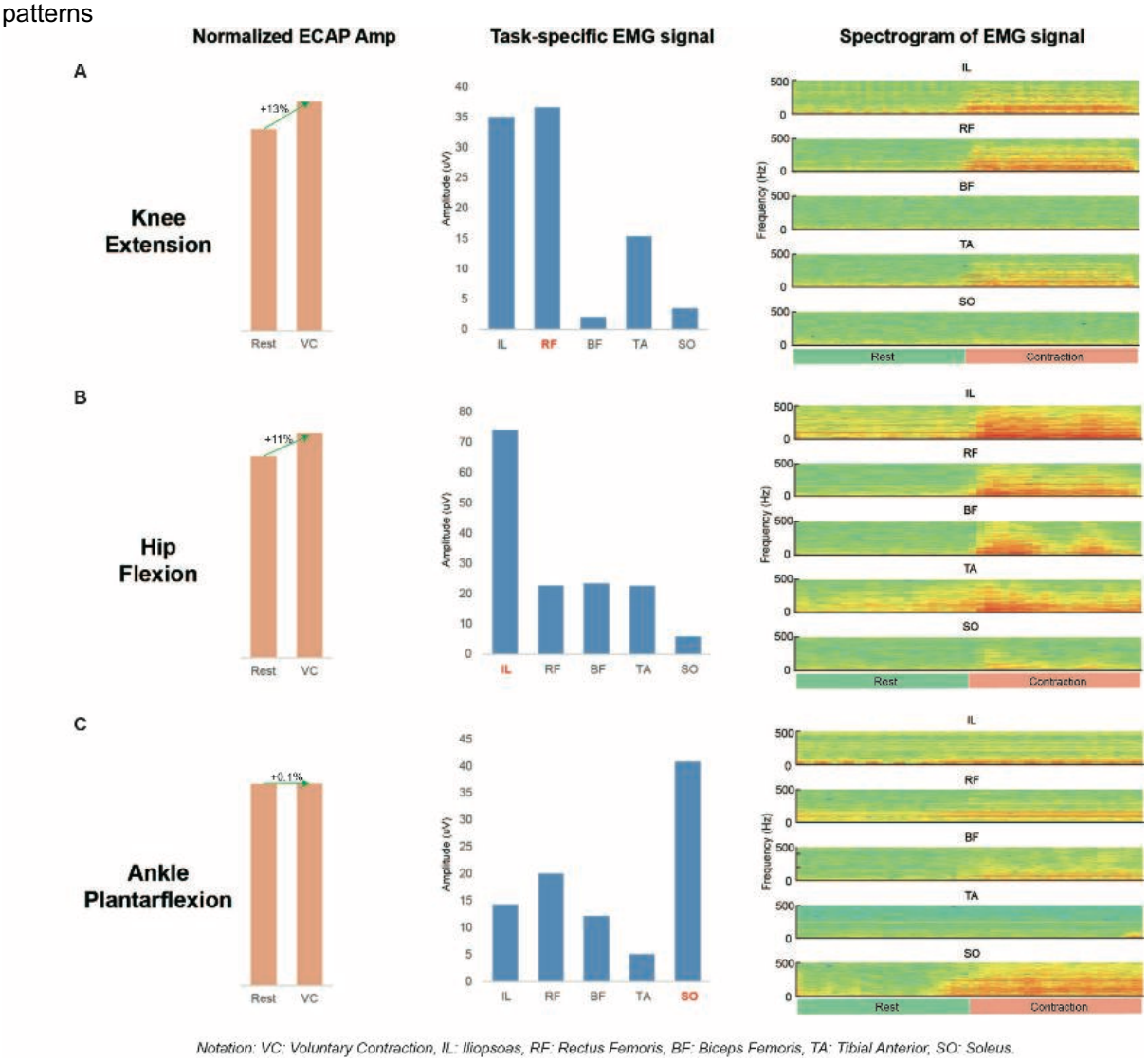


Fig3: Task-specific muscle activation

patterns



Notation: VC: Voluntary Contraction, IL: Iliopsoas, RF: Rectus Femoris, BF: Biceps Femoris, TA: Tibial Anterior, SO: Soleus.

Discussion: Our research unveiled that spinal cord injury patients could voluntarily stimulate targeted muscle activity with the assistance of epidural electrical stimulation, irrespective of real-received stimulation dosage alterations. The proportionate contribution of posture modification and voluntary movement intent, along with the underlying mechanisms of these phenomena, should be studied in future studies.

Conclusions: This study found that while the same ECAP signal, that is, the actual stimulation intensity received by the spinal cord is unchanged, the patient could perform task-specific activation of the specified exercise-related muscle groups, which means that the myoelectric activation with the involvement of voluntary motor intention is ordered and task-specific. This phenomenon has been verified in lower limb during different movements.

Supplemental Data: Videos that patients conduct different motor tasks during EES.

References: 1. Wagner F B, Mignardot J B, Le Goff-Mignardot C G, et al. Targeted neurotechnology restores walking in humans with spinal cord injury[J]. Nature, 2018, 563(7729): 65-71. 2. Mekhail N, Levy R M, Deer T R, et al. Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial[J]. The Lancet Neurology, 2020, 19(2): 123-134. 3. Darrow D, Balser D, Netoff T I, et al. Epidural spinal cord stimulation facilitates immediate restoration of dormant motor and autonomic supraspinal pathways after chronic neurologically complete spinal cord injury[J]. Journal of neurotrauma, 2019, 36(15): 2325-2336. 4. Calvert J S, Grahn P J, Zhao K D, et al. Emergence of epidural electrical stimulation to

facilitate sensorimotor network functionality after spinal cord injury[J]. Neuromodulation: Technology at the Neural Interface, 2019, 22(3): 244-252. 5. Zhou A, Johnson B C, Muller R. Toward true closed-loop neuromodulation: artifact-free recording during stimulation[J]. Current opinion in neurobiology, 2018, 50: 119-127. 6. Gill M L, Linde M B, Hale R F, et al. Alterations of spinal epidural stimulation-enabled stepping by descending intentional motor commands and proprioceptive inputs in humans with spinal cord injury[J]. Frontiers in Systems Neuroscience, 2021, 14: 590231.

Acknowledgements: Support for this work was provided by the Changping Laboratory, National Engineering Research Center of Neuromodulation, Beijing PINS Medical Co., Ltd and Beijing Tsinghua Changgung Hospital. The authors would like to thank the patients for their generous time and dedication to this study.

Learning Objectives: 1. The ECAP signal used in this study to decouple the effects of posture change and voluntary locomotion control is original. It could serve as a marker to indicate the real-received stimulation dosage thus the posture changes. 2. The voluntary locomotion control is essential for motor restoration since it provides task-specific muscle control. Furthermore, the task-specific rehabilitation promotes plasticity of neural system. 3. The different muscle activation patterns quantified by the RMS value of EMG signal, could serve as biomarkers to indicate the outputs of voluntary locomotion intention in the aid of epidural electrical stimulation for spinal cord injury patients.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O067

Oral Presentations
NEUROMODULATION FOR REHABILITATION
14-05-2024 16:30 - 18:20

SPINAL CORD DTI SHOWS IMPROVED AND RETAINED METRICS FOR ACTIVITY-BASED TRAINING PAIRED WITH SPINAL CORD TRANSCUTANEOUS STIMULATION FOR INDIVIDUALS WITH SCI

Mehmed Bayram, PhD[1,2], Nabila Brihmat, PhD[1,2], Soha Saleh, PhD[3,4], Guang Yue, PhD[2,3], Gail Forrest, PhD[1,2,3]
[1]Kessler Foundation, Tim And Caroline Reynolds Center For Spinal Stimulation, West Orange, United States of America, [2]Rutgers, the State Univ. of New Jersey, Physical Medicine And Rehabilitation, Newark, United States of America, [3]Kessler Foundation, Center For Mobility And Rehabilitation Engineering Research, West Orange, United States of America, [4]Department of Rehabilitation and Movement Sciences, School of Health Professions, Department Of Neurology, Robert Wood Johnson Medical School (rwjms), Newark, United States of America

Introduction: Spinal cord transcutaneous stimulation (scTS) combined with activity based training (ABT), notably exoskeleton and overground gait training for individuals with a chronic spinal cord injury (SCI) can improved independent gait(1),(2). Diffusion tensor imaging (DTI) is a dependable imaging method with significant histological and functional correlations of spinal cord damage; therefore, DTI can be used to comprehend underlying microstructural changes in the cord (3). In this pilot study, we analyzed spinal cord DTI for individuals with motor incomplete SCI, KS1 and KS2 who both completed ABT interventional training to see the anatomical changes along the cord and especially around the site of the injury. KS1 completed ABT-alone intervention while KS2 completed scTS+ABT.

Materials / Methods: For both subjects, a pre- and a post-intervention spinal cord DTI were acquired, whereas KS2 had an additional 3.5-year follow-up DTI. Each ABT training session was 2-hr long, with the interventional period being 1 hour and comprised of exoskeleton and overground gait training. 100 sessions and 34 training sessions were completed, for KS1 and KS2, respectively. KS2 added a targeted scTS during ABT. Parameters for scTS were based on systematic spinal mapping sessions at vertebral sites: frequency, amplitude, and site locations were modulated. Spinal cord DTI were analyzed for metrics included fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD) and axial diffusivity (AD).

Results: DTI along the cord showed improvement on FA, for KS2. The following values are depicted as mean±SD, for pre- vs post- and for KS1 and KS2, respectively: FA were 0.4408±0.0362 vs 0.4583±0.0368 and 0.3235±0.0910 vs 0.4154±0.0481. MD were 0.0015±0.0002 vs 0.0015±0.0002 and 0.0018±0.0002 vs 0.0017±0.0001. RD were 0.0011±0.0001 vs 0.0011±0.0001 and 0.0015±0.0003 vs 0.0013±0.0001. AD were 0.0022±0.0002 vs 0.0022±0.0002 and 0.0024±0.0002 vs 0.0024±0.0002. KS2 shows a retained FA value of 0.4141±0.0855 for follow-up.

Discussion: Neuromodulation of the spinal circuity via scTS+ABT training had positive and retained anatomical changes along the cord for SCI, especially for FA.

Conclusions: Analysis of scTS+ABT is being performed with additional subjects to see if observed effect would continue.

Supplemental Data:

References: 1) Ramanujam, A. et al. (2017). Training Response to Longitudinal Powered Exoskeleton Training for SCI. In: González-Vargas, J., Ibáñez, J., Contreras-Vidal, J., van der Kooij, H., Pons, J. (eds) Wearable Robotics: Challenges and Trends. Biosystems & Biorobotics, vol 16. Springer, Cham. https://doi.org/10.1007/978-3-319-46532-6_59 2) Shapkova EY, Pismennaya EV, Emelyannikov DV and Ivanenko Y (2020) Exoskeleton Walk Training in Paralyzed Individuals Benefits

From Transcutaneous Lumbar Cord Tonic Electrical Stimulation. Front. Neurosci. 14:416. doi: 10.3389/fnins.2020.00416 3) Vedantam A, Jirjis MB, Schmit BD, Wang MC, Ulmer JL, Kurpad SN. Diffusion tensor imaging of the spinal cord: insights from animal and human studies. Neurosurgery. 2014;74(1):1-8. doi:10.1227/NEU.0000000000000171

Acknowledgements: The study received funding from the Tim Reynolds Foundation. The authors would like also to thank the center research staff and the study participants for their involvement in the study.

Learning Objectives: 1) ABT combined with scTS might have a positive impact as neuromodulatory intervention for SCI rehabilitation. 2) Spinal cord DTI could show the microstructural changes along the spinal cord following a training intervention. 3) FA might be the most sensitive metric to microstructural changes in SCI.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O068

Oral Presentations
NEUROMODULATION FOR REHABILITATION
14-05-2024 16:30 - 18:20

MODELING THE DYNAMICS BETWEEN SINGLE-PULSE EPIDURAL SPINAL STIMULATION AND TRUNK MUSCLE ACTIVITY: A SYSTEM IDENTIFICATION STUDY

Kira Wedemeier, BSc (Hons)[1], Abdul Shaik Gadda, BSc (Hons)[1], Sydney Schadan, BSc (Hons)[1], Alexander Steele, PhD[2], Amir Faraji, MD[2], Dmitry Sayenko, MD, PhD[2], Albert Vette, PhD[1,3]
[1]University of Alberta, Department Of Mechanical Engineering, Edmonton, Canada, [2]Houston Methodist Hospital / Research Institute, Houston, United States of America, [3]Glenrose Rehabilitation Hospital, Research And Technology Development, Edmonton, Canada

Introduction: Impaired trunk control is a serious problem for individuals with spinal cord injury as it can lead to mobility limitations and secondary health concerns. In this context, epidural spinal stimulation (ESS) has been used to activate relevant trunk muscles and enhance trunk stability. One of the ultimate goals of ESS is to embed it in a closed-loop control scheme that regulates stimulation level (e.g., amplitude) based on wearable biomechanical measurements (e.g., center of pressure during sitting). However, such control scheme generally requires the knowledge of the underlying 'dynamic model' capturing the dynamics between ESS and muscle activity – since it can be used to regulate, in real-time, the required time-dependent ESS variation based on the biomechanical measurements. **The objective of this work was to quantitatively model the dynamics between single-pulse ESS and trunk muscle activity using system identification.**

Materials / Methods: Experimental data from five adults undergoing pain treatment and electrode implantation (16- or 32-channel array) above the eighth thoracic vertebra have been analyzed to date. During ESS, surface electromyography (EMG) was collected bilaterally from the external and internal obliques and the rectus abdominis. Single-pulse ESS at varying amplitude and 300-500 µs pulse width was applied via the two most lateral columns of the electrode array (3 trials each). The ESS pulse and EMG response served as input and output, respectively, for the system identification ('tfest' function in Matlab). Two experimental trials were used for model identification, and one for model validation.

Results: Our results demonstrate that a converging dynamic model from ESS to EMG response can be identified for each participant and trunk muscle, and that the validation trials resulted in a model fit of up to 85% across participants. The identified model represents a stable, eighth order system with low-pass behaviour.

Discussion: Our results suggest that a quantitative dynamic model from ESS to trunk muscle response can be identified, which will be especially valuable for closed-loop control efforts that require an "internal model" of the stimulation to muscle activity relationship. However, it should be noted that such model should be quantified for a given individual since confounding factors affecting, for example, the EMG recordings have a considerable effect on the system identification.

Conclusions: In conclusion, we were able to quantify the dynamic model from ESS to trunk muscle response. In future work, this approach will be used in closed-loop control studies to regulate time-varying spinal stimulation and counteract postural perturbations during sitting.

Supplemental Data: None

References: None

Acknowledgements: None

Learning Objectives: Educational Objective (1): Characterize the effect of single-pulse epidural spinal stimulation on trunk muscle activity. **Desired Result (1):** Attendants understand how epidural

spinal stimulation can be used to activate trunk muscles. **Educational Objective (2):** Explain how system identification can be used to quantify the dynamics between epidural spinal stimulation and trunk muscle activation. **Desired Result (2):** Attendants are exposed to the technique of system identification and understand its purpose in closed-loop control of trunk stability. **Educational Objective (3):** Explain how a dynamic model can be used in closed-loop control of trunk stability to guide the desired stimulation variation over time. **Desired Result (3):** Attendants understand the value of obtaining a quantitative dynamic model (from stimulation to trunk muscle activity) in closed-loop control efforts.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O069

Oral Presentations
NEUROMODULATION FOR REHABILITATION
14-05-2024 16:30 - 18:20

THE SHORT-TERM EFFECT OF COMBINED CEREBELLUM AND SPINAL CORD DIRECT CURRENT STIMULATION ON PROMOTING LEARNING RETENTION IN WALKING: A PILOT STUDY

Jui-Te Lin, PhD, PT, Tamara Shields, BSc (Hons), Haley Dennerlein, BSc (Hons), Andrew Lenneper, BSc (Hons), Andrew Ruggiero, BSc (Hons), Lauren Snowdon, PT
Seton Hall University, Physical Therapy, Nutley, United States of America

Introduction: Walking is a complex movement that necessitates precise regulation of neural circuitry within the cerebellum and spinal cord. Specifically, the cerebellum can modulate motor behavior by integrating motor commands and sensory feedback, while the spinal cord carries somatosensory inputs and motor outputs. Non-invasive transcranial and transcutaneous direct current stimulation (tDCS and tsDCS, respectively) have emerged as promising tools for modulating the neural excitability of the underlying neural tissues. Although tDCS and tsDCS have been intensively studied with encouraging findings, few studies have investigated the combined stimulation effects on motor learning, particularly in walking. Therefore, the study aims to explore the combined stimulation effect on improving motor learning in walking.

Materials / Methods: The study follows a randomized repeated-measures crossover design with two visits. Five healthy young adults (aged 24-25 y/o) participated in the study, and they were naïve to interventions (active vs. sham) during each visit. Direct current stimulators for tDCS and tsDCS were set at an intensity of 2.5 mA with 2×2 pads. The anodal tDCS electrode was placed over the cerebellar hemisphere on the side where participants had a longer step length. The cathode tDCS electrode was placed on the ipsilateral buccinator muscle. An anodal tsDCS electrode was positioned on T11, whereas a cathodal tsDCS electrode was placed over the right shoulder. A new walking pattern was introduced using a split-belt walking protocol. During the asymmetry walking section, belt speeds were set faster on the side where participants had a shorter step length. The treadmill protocol began with 2 minutes of comfortable walking, followed by 15 minutes of learning (i.e., the asymmetry walking section) with active/sham stimulation, and concluded with 5 minutes of comfortable walking. Over-ground walking parameters were collected before, immediately after, and 15 minutes after the treadmill walking. The primary outcome of the study is the symmetry index.

Results: Participants demonstrated comparable learning responses when introduced to the new walking pattern ($p > .05$). Interestingly, with active stimulation, participants exhibited greater retention of the new walking patterns compared to sham conditions immediately after treadmill training ($p = .004$) and after 15 minutes of rest ($p = .121$).

Discussion: These preliminary findings support our hypothesis that combined anodal tDCS and tsDCS may excite neural circuitry necessary for motor learning and thus retain learning in walking.

Conclusions: The pilot results with a healthy young population could provide alternative insights into rehabilitating individuals with neurological disorders (e.g., stroke) who face challenges in re-learning to walk.

Supplemental Data:

References:

Acknowledgements: The study was funded by University Research Council Research Grant from Seton Hall University

Learning Objectives: 1. Understand the impact of transcranial and transcutaneous direct current stimulation on motor learning and retention 2. Evaluate the role of the cerebellum and spinal cord in regulating walking 3. Explore the potential applications in correcting gait symmetry for individuals with neurological disorders

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O070

Oral Presentations
NEUROMODULATION FOR REHABILITATION
14-05-2024 16:30 - 18:20

IMPROVEMENTS IN SOMATOSENSATION AND DYNAMIC BALANCE DURING POSTURAL TRANSITIONS USING STOCHASTIC RESONANCE STIMULATION IN AN INDIVIDUAL WITH CEREBRAL PALSY – AN ONGOING STUDY

Khushboo Verma, BPT[1], Ashwini Sansare, PhD[1], Eman Alsaqabi, PT[2], Hendrik Reimann, PhD[2], Samuel Lee, PT[1]
[1]University of Delaware, Department Of Physical Therapy, Newark, United States of America, [2]University of Delaware, Department Of Kinesiology And Applied Physiology, Newark, United States of America

Introduction: Cerebral Palsy (CP) is characterized by asymmetrical muscle tone, abnormal posture, and movement disorders. People with CP have a high risk of falls, leading to serious injuries. Recent research in CP suggests sensory deficits contribute to balance impairments. Falls occur due to deficits in the motor system, i.e., failures in generating appropriate motor responses, and or deficits in the sensory system, i.e., somatosensory impairments preventing accurate feedback of position and movements of the body in space. Multiple interventions focus on improving motor responses in CP, however, sensory modulation approaches that may enhance proprioception are currently under-explored. Providing background noise or stochastic resonance (SR) stimulation has shown promising results in populations with sensory deficits, such as individuals with diabetic neuropathy and stroke. The potential for SR use in neurodevelopmental conditions, such as CP, is comparatively under-explored. SR is a phenomenon in which random, sub-sensory noise improves the sensitivity of the sensory system to detect a weak signal. The present research hypothesizes that SR stimulation may enhance sensory detection and sensorimotor processing to improve balance control in people with CP.

Materials / Methods: One individual with CP and one typical developing peer (TD) performed somatosensation tests: vibration sense, joint position sense, two-point discrimination, and light touch pressure, followed by postural transitions such as sit-to-stand and gait initiation and instrumented Timed up-and-go test. SR stimulation was applied to muscles and ligaments of the ankle and hip joints on both sides.

Results: SR improved vibration and joint position sense for the individual with CP, whereas the TD participant showed slightly better performance in vibration and worse performance in joint position sense. The individual with CP, having better baseline two-point discrimination scores than the TD individual, showed a slight decline, while the individual with TD showed an improvement with SR. No changes were detectable for light touch pressure for either of the subjects. During postural transitions, SR stimulation reduced the total time and anteroposterior center of pressure excursions during sit-to-stand and gait initiation in CP, while TD showed little to no change. Moreover, the mediolateral center of mass variability decreased, and the anteroposterior and mediolateral center of mass velocity increased with SR in CP during the instrumented timed up-and-go test, indicating better locomotor planning and balance control.

Discussion: SR stimulation appears to improve somatosensation and balance control during postural transitions and timed up-and-go tests in CP, which may be more prevalent when tested on a larger group. The data collection is ongoing.

Conclusions: We will better understand the efficacy of SR stimulation to improve balance control strategies during postural transitions and timed up-and-go test, which may be a critical factor in advancing combined sensory-motor rehabilitation techniques for CP.

Supplemental Data:

References: None

Acknowledgements: The support of the University of Delaware's Graduate College for this project is gratefully acknowledged.

Learning Objectives: 1. Stochastic resonance stimulation may improve somatosensation in individuals with cerebral palsy. 2. Stochastic resonance stimulation may improve balance control during postural transitions in individuals with cerebral palsy. 3. A combined sensory- motor approach may serve as a better rehabilitation approach.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O071

Oral Presentations
NEUROMODULATION FOR REHABILITATION
14-05-2024 16:30 - 18:20

RESTORATIVE NEUROSTIMULATION FOR MECHANICAL CHRONIC LOW BACK PAIN – A DISEASE MODIFYING PAIN MEDICINE THERAPY

Marc Russo, MBBS
Hunter Pain Specialists, Hunter Pain Specialists, Broadmeadow, Australia

Introduction: Debilitating chronic low back pain (CLBP) experiences are suffered by roughly 43 million people in the United States (US) today.[1,2] Unfortunately, patients with CLBP find inadequate symptom relief with conservative care. Restorative neurostimulation aims to treat pain and neuromuscular control impairments involving impaired multifidus function in patients with mechanical CLBP (having no radicular symptoms or need for surgery). This study aims to aggregate analyses across three clinical studies with a significant volume of published clinical data incorporating all pertinent demographics and outcomes from pre- and post-implantation of restorative neurostimulation.

Materials / Methods: Data from clinical trials in the US, United Kingdom (UK), Europe, Australia were aggregated (N=204, Clinicaltrials.gov Identifier: NCT02577354[3–5], N=87, Clinicaltrials.gov Identifier: NCT03255200, Germany[6], and N=42, Clinicaltrials.gov Identifier: NCT01985230, UK)[7]. All consented patients received implanted restorative neurostimulation devices (ReActiv8®, Mainstay Medical, Inc., Dublin, Ireland). Inclusion and exclusion criteria were varied across studies, therefore, the minimum requirements for inclusion were identified. A cohort of 261 (78% of total) had complete assessments pre-operatively, and at six, 12, and 24 months post-operatively. Pain ratings (Numeric Pain Rating Scale (NPRS)/Visual Analog Scale (VAS)), disability (Oswestry Disability Index (ODI)), and quality of life (EuroQol 5-Dimension 5-Level (EQ-5D-5L)) were evaluated.

Results: At baseline, patients (mean ± standard deviation: N=261; age=49.1±0.7yrs; F=51%; BMI=28.4±0.3kg/m^2) ODI ratings were 40.6±0.8 and EQ-5D-5L were 0.544±0.013. At the 2-year follow-up, 65% reported greater than 50% pain reduction, and 60% were classified as remitters (less than or equal to 2.5 and 3 for VAS and NRS, respectively) and 60% had greater than 15-point reduction in ODI. By 2 years, 74% of patients reported 50% reduction in pain and / or a 15-point reduction in ODI and 51% of patients experienced both. Effects of demographics on outcomes were also assessed.

Discussion:

Conclusions: Restorative neurostimulation is developing a significant evidence base to support safety, efficacy, and durability of this technique in mechanical CLBP patients with multifidus dysfunction.

Supplemental Data:

References: 1. Shmagel, A., Foley, R. & Ibrahim, H. Epidemiology of Chronic Low Back Pain in US Adults: Data From the 2009-2010 National Health and Nutrition Examination Survey. Arthritis Care Res. 68, 1688–1694 (2016).
2. US Census Bureau. United States Government. https://www.census.gov/popclock/ https://www.census.gov/popclock/.
3. Gilligan, C. et al. An implantable restorative-neurostimulator for refractory mechanical chronic low back pain: a randomized sham-controlled clinical trial. Pain 162, 2486–2498 (2021).
4. Gilligan, C. et al. Long-Term Outcomes of Restorative Neurostimulation in Patients With Refractory Chronic Low Back Pain Secondary to Multifidus Dysfunction: Two-Year Results of the ReActiv8-B Pivotal Trial. Neuromodulation 26, 87–97 (2021).
5. Gilligan, C. et al. Three-Year Durability of Restorative Neurostimulation Effectiveness in Patients

With Chronic Low Back Pain and Multifidus Muscle Dysfunction. Neuromodulation 26, 98–108 (2023).
6. Ardeshiri, A., Shaffrey, C., Stein, K.-P. & Sandalcioglu, I. E. Real-World Evidence for Restorative Neurostimulation in Chronic Low Back Pain-a Consecutive Cohort Study. World Neurosurg. 168, e253–e259 (2022).
7. Thomson, S. et al. Restorative neurostimulation for chronic mechanical low back pain – Three year results from the United Kingdom post market clinical follow-up registry. British Journal of Pain 20494637231181496 (2023).

Acknowledgements: The support of Mainstay Medical, Inc. for this project is gratefully acknowledged.

Learning Objectives: Objective 1: Recall the studies in the field of multifidus neurorestoration therapy. Desired result: There are 3 studies, with 261 subjects with complete data for 2-year outcomes. Objective 2: List the outcome measures that were recorded for these subjects. Desired result: Pain ratings (Numeric Pain Rating Scale (NPRS)/Visual Analog Scale (VAS)), disability (Oswestry Disability Index (ODI)), and quality of life (EuroQol 5-Dimension 5-Level (EQ-5D-5L)) were evaluated. Objective 3: Demonstrate knowledge of the outcomes achieved at 2 years in these subjects. Desired result:ODI. By 2 years, 74% of patients reported 50% reduction in pain and / or a 15-point reduction in ODI. 51% of patients experienced both.

Financial Disclosures: This project was supported by Mainstay Medical. Dr Marc Russo discloses the following: Non-paid consultancies (nil income for term of INS presidency) to Boston Scientific, Mainstay Medical, Medtronic, Nevro, Presidio Medical, and Saluda Medical. Research (income paid to research institution) for Boston Scientific, Mainstay Medical, Medtronic, Nevro, Presidio Medical, and Saluda Medical. Stock options in Presidio Medical and Saluda Medical.

Disclosure: Dr Russo discloses non-paid consultancies to Boston Scientific, Mainstay Medical, Medtronic, Nevro, Presidio Medical, and Saluda Medical. He discloses research activities for Boston Scientific, Mainstay Medical, Medtronic, Nevro, Presidio Medical, and Sal

O072

Oral Presentations
NEUROMODULATION: ENGINEERING AND AI
14-05-2024 16:30 - 18:20

SINGLE-AXIS INTERFERENTIAL NEUROSTIMULATION: SAIF-STIM

Thomas Yearwood, MD, PhD[1], William Carroll, BSc (Hons)[2], Scott Lempka, Associate Professor[3], Keith Cobry, PhD[4]
[1]Guy's and St Thomas Hospitals NHS Trust, Pain Management & Neuromodulation Centre, London, United Kingdom, [2]Neuromodulation Specialists LLC, Biomedical Engineering, Fairhope, United States of America, [3]University of Michigan, Biomedical Engineering, Ann Arbor, United States of America, [4]Xi Engineering Consultants, Edinburgh, United Kingdom

Introduction: Single-axis Interferential Neurostimulation Interferential (IF) neurostimulation is a technique that involves the constructive or destructive interference of two or more high-frequency waveforms with slightly different frequencies [1]. The resulting low-frequency beat component pulses sinusoidally with a frequency equal to the difference between the contributing carrier frequencies. This technique aims to penetrate neural tissues more intensely than conventional low-frequency neurostimulation approaches [2]. In a recent first-in-human study, a dual lead system using steerable parallel and cross-bias configurations [3] demonstrated the short-term safety and efficacy of IF spinal cord stimulation (SCS) to treat chronic pain [4]. However, the optimal stimulation parameters for neural recruitment during IF SCS are unknown. Therefore, in this study, we implemented a computational approach to investigate using a novel single-axis interferential (SAIF) stimulation configuration in which the active electrodes were on a single linear electrode array.

Materials / Methods: We developed a finite element model (FEM) of the spinal cord and surrounding anatomy along with two eight-contact, parallel percutaneous electrode arrays within the epidural space on either side of the physiological midline, as for conventional dual-axis stimulation. Active contacts were confined to only one laterally placed lead to test our SAIF FEM. We assigned conductivity and permittivity values for the different tissues, including the white matter, gray matter, cerebrospinal fluid, dura, epidural tissue, bone, thorax, and superficial tissues. We then calculated the time-dependent electric potential fields generated within the spinal cord.

Results: Our results predicted that the SAIF configuration could be used to steer the maximal modulation region along the lead's axis. Higher frequencies penetrated the gray matter more effectively, suggesting the possibility of increased polarization within the dorsal horn at these higher frequencies. However, as noted in our first-in-human dual-axis clinical trial, higher frequencies required higher amplitudes to achieve meaningful field strengths within the spinal cord. We also tested additional stimulation configurations to reduce the current densities generated within the superficial spinal cord at the higher carrier frequencies.

Discussion: Computational modeling suggests that novel programming scenarios are possible for high-frequency sinusoidal stimulating currents in the thoracic spinal cord using an epidural SAIF platform.

Conclusions: These findings will be instrumental in planning an upcoming clinical trial of SAIF stimulation for chronic pain patients.

Supplemental Data:

References: Agharezaee, M and Mahnam, A. 2015. A computational study to evaluate the activation pattern of nerve fibers in response to interferential currents stimulation. Medical, and Biological Engineering, and Computing 53: 713-720. doi: 10.1007/s11517-015-1279-6. https://doi.org/10.1007/s11517-015-1279-6 Ariel, E; Ratmansky, M; Levkovitz, Y; Goor-Aryeh, I. 2019. Efficiency of Tissue Penetration by Currents Induced by 3 Electrotherapeutic Techniques: A Comparative Study Using a Novel Deep-Tissue Measuring Technique. Phys Ther 99: 540–548.

Yearwood TL, Carroll WJ, Keith D. (2016) The Effects of cross-bias and parallel-bias on Dorsal Column Targeting in High-Frequency Interferential-Spinal Cord Stimulation. Neuromodulation, 2016; 19:e42. https://doi.org/10.1111/ner.12428 Yearwood T, Lazzari Z, Carroll W. Safety and Efficacy of Dynamic Interferential Spinal Cord Stimulation System for Pain Relief: First-In-Human Trial. Abstract Pain Practice. P- 089, page 87, Volume 22, Issue S1, 2022. https://doi.org./10.1111/papr.13148

Acknowledgements: The support of Neuromodulation Specialists LTD, London, UK for this project is gratefully acknowledged.

Learning Objectives: Computational modeling of spinal cord stimulation can significantly aid the design and development of clinical testing for new devices and waveforms in neuromodulation.

Financial Disclosures: Thomas L Yearwood, MD Ph.D. is a major owner of Neuromodulation Specialists Ltd in London, UK William J Carroll is a part owner of Neuromodulation Specialists LLC, USA Scott F Lempka, Ph.D. has received research funds from Neuromodulation Specialists LLC, USA Keith Cobry, Ph.D. is an employee of Xi Engineering Consultants, Edinburgh, UK

Disclosure: I am a majority owner of Neuromodulation Specialists, Ltd in London, UK, a start-up neuromodulation device company in the early phases of development and clinical trials. Currently, there are no commercially available products related to this start-up bus

O073

Oral Presentations
NEUROMODULATION: ENGINEERING AND AI
14-05-2024 16:30 - 18:20

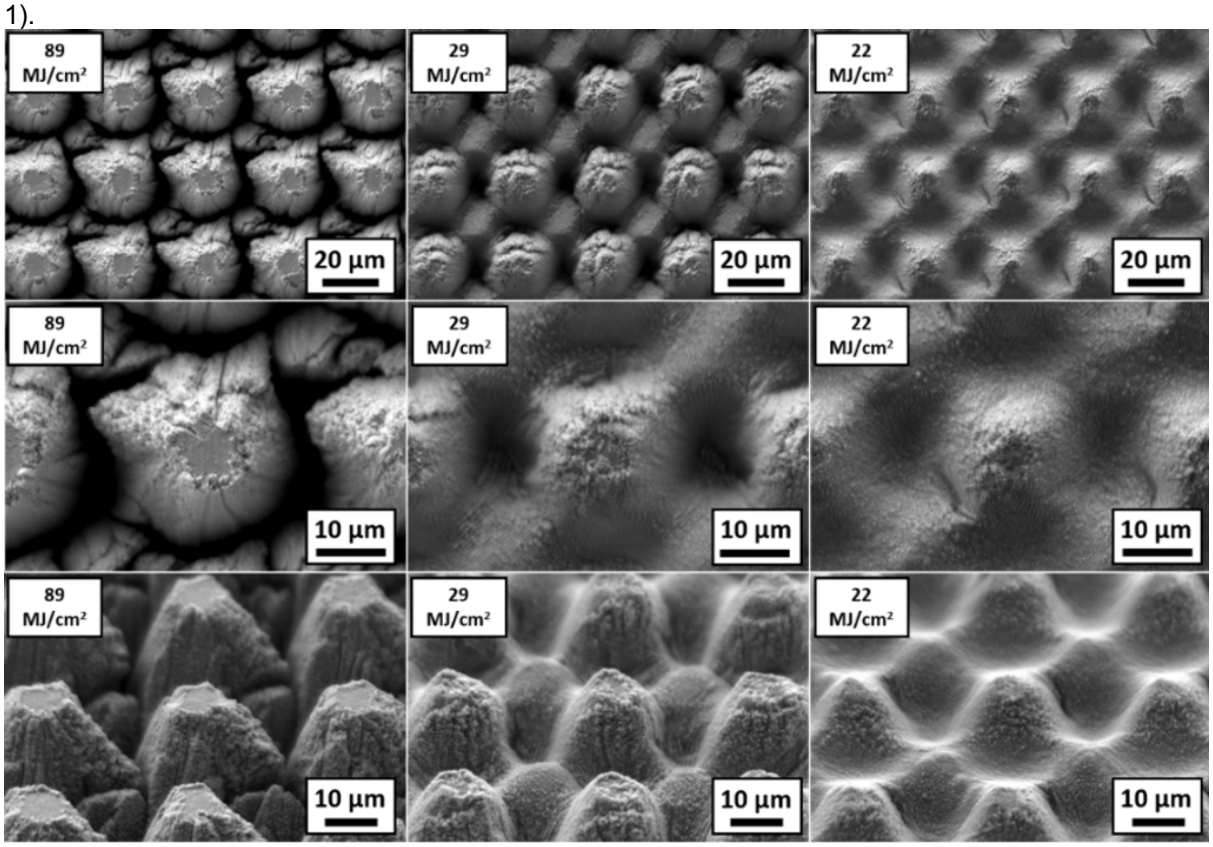
REACTIVE HIERARCHICAL SURFACE RESTRUCTURING TECHNOLOGY FOR NEXT GENERATION, LOW-COST, SUSTAINABLE, AND HIGH-PERFORMING NEUROSTIMULATION ELECTRODES

Shahram Amini, VP of R&D
Pulse Technologies Inc., Quakertown, United States of America

Introduction: Over the last two decades, Platinum group metals (PGMs) and their alloys have been the most common choice for electrode materials in neurostimulation devices due to their excellent conductivity, mechanical and chemical stability, biocompatibility, corrosion resistance, radiopacity, and inherent electrochemical performance. However, PGM manufacturing processes are extremely expensive, complex, and challenging with possible health hazards. Additionally, PGMs are associated with high supply risk and significant economic importance due to their price volatility. Therefore, substitution of PGM-based electrodes with other biocompatible materials that can yield electrochemical performance values equal or greater than PGMs is the only viable and sustainable solution to reduce and ultimately substitute the use of PGMs in neurostimulation devices. In this work, we demonstrate for the first time how the novel technique of “reactive hierarchical surface restructuring” can be utilized on titanium — that is widely used in many non-stimulation medical device and implant applications — to manufacture low-cost, sustainable, and high-performing neural stimulation electrodes.

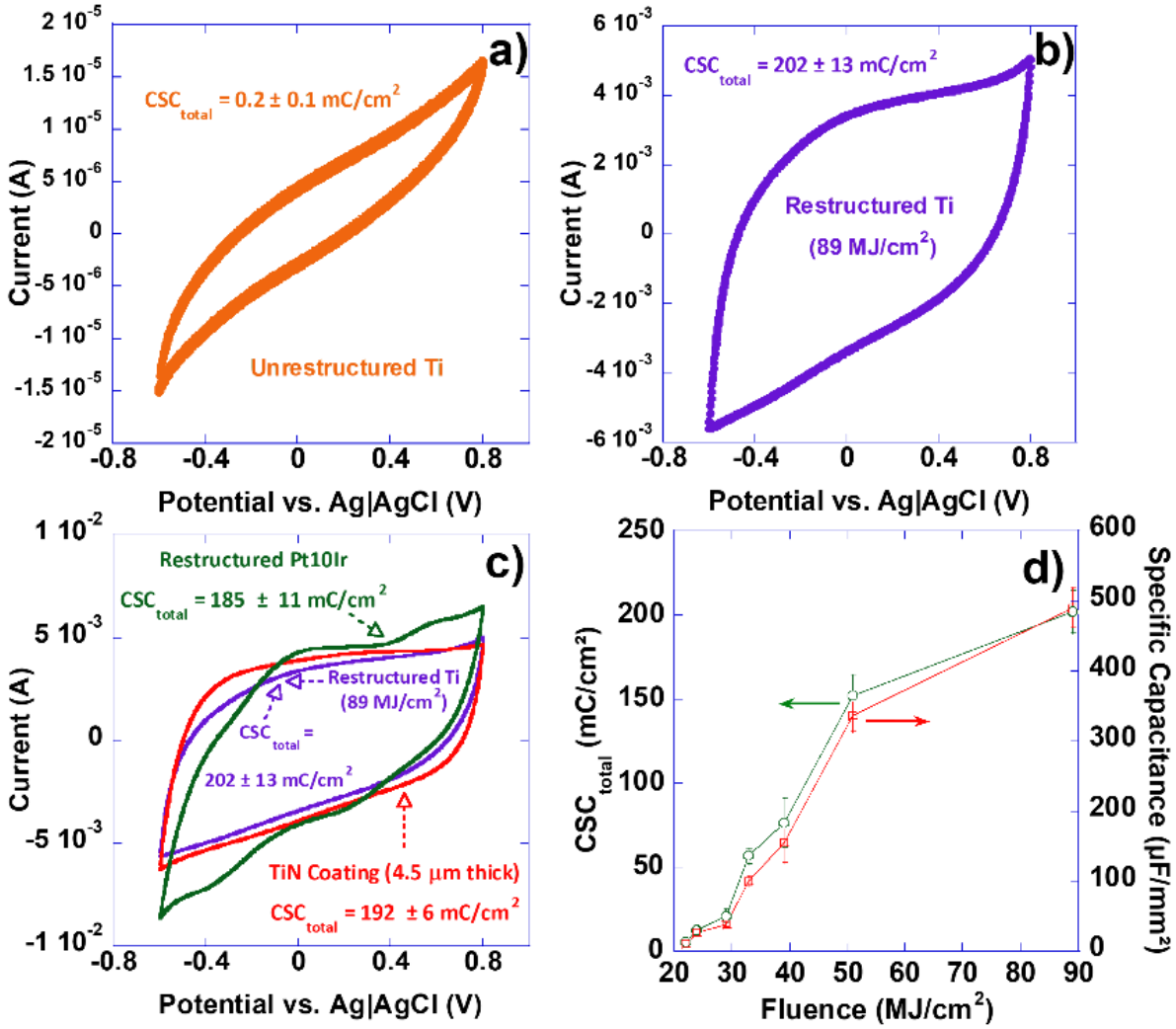
Materials / Methods: In this work, it was demonstrated that Ti – similar to Pt10Ir – can be hierarchically restructured by femtosecond lasers in the presence of nitrogen to promote reactive synthesis of electrochemically stable TiN on the surface of the electrodes. We have shown how the surface of titanium electrodes with extremely poor electrochemical performance undergoes compositional and topographical transformations that will result in electrodes with superior electrochemical performance (Figure

1).



Results: The electrochemical performance of reactively restructured Ti electrodes can be comparable or superior to hierarchically restructured Pt10Ir electrodes. Figure 2 displays representative cyclic voltammograms of an un-restructured Ti electrode and a restructured Ti electrode. To provide a better context and for the sake of comparison, Figure 2 compares cyclic voltammogram of the restructured Ti electrode with the cyclic voltammograms of a restructured Pt10Ir electrode as well as a 4.5 µm thick TiN

coating.



Discussion: Restructured Ti electrodes not only showed over three orders of magnitude increase in their total charge storage capacity compared to their un-restructured Ti electrode counterparts, but also their total charge storage capacity exceeds those of restructured Pt10Ir electrodes.

Conclusions: The “reactive hierarchical surface restructuring” technology introduced for the first time in this work would lead to reduction in the amount of PGM used in long-term implantable neural stimulation applications, which in turn ensures sustainability and security of PGM supply chain for the future of our planet.

Supplemental Data:

References:

Acknowledgements: This work was carried out in part at the Singh Center for Nanotechnology, part of the National Nanotechnology Coordinated Infrastructure Program, which is supported by the National Science Foundation grant NNCI-2025608.

Learning Objectives: 1) Electrode surface treatment technology and miniaturization 2) Improvement in electrodes’ electrochemical performance 3) Cost reduction and sustainability in neurostimulation electrode manufacturing

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O074

Oral Presentations
NEUROMODULATION: ENGINEERING AND AI
14-05-2024 16:30 - 18:20

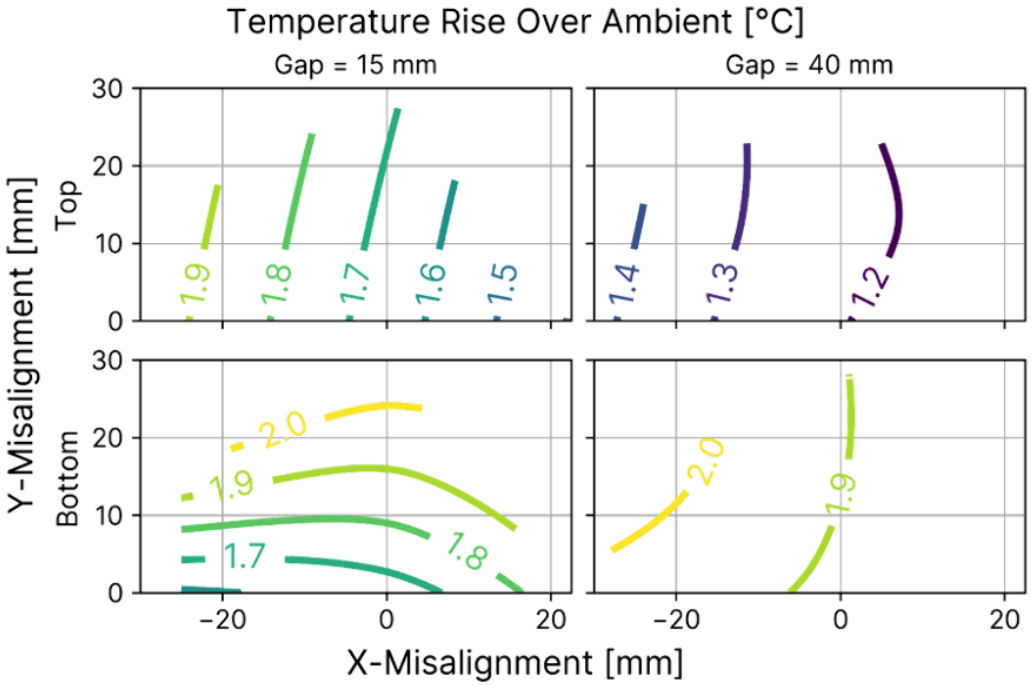
WIRELESS TRANSCUTANEOUS ENERGY TRANSFER AND CONTROL SYSTEM FOR POWERING TITANIUM-ENCASED IMPLANTABLE PULSE GENERATORS

Jessica Humphrey, BSc (Hons)[1], Phyo Aung Kyaw, Ph.D.[1,2], Kyle Goodrick, PhD[1], Scott Warren, BSc (Hons)[1], Panteleimon Papamanolis, PhD[1], Aaron Stein, PhD[1], Milovan Kovacevic, PhD[1]
[1]Resonant Link, Engineering, South Burlington, United States of America, [2]Resonant Link, R&d, South Burlington, United States of America

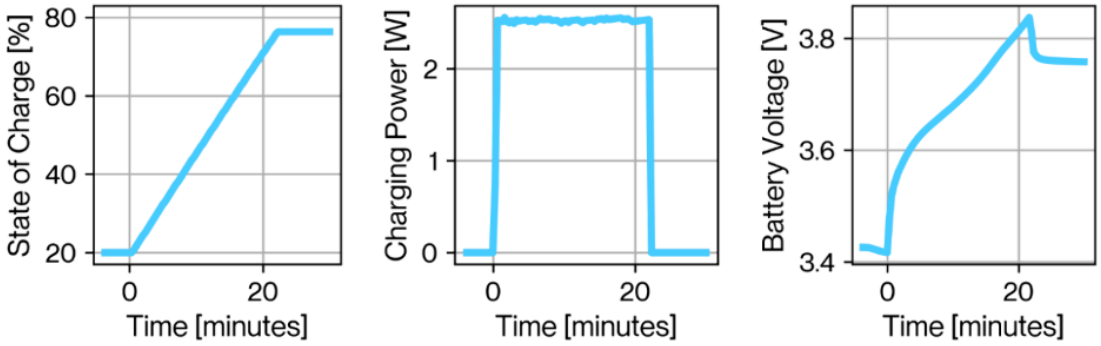
Introduction: Clinicians and patients want to be able to recharge active implantable medical devices like neurostimulators and other implantable pulse generators (IPGs), to eliminate the need for battery replacement surgeries and improve the recharging experience; however, most of these devices are built inside a titanium case, called a can, because of titanium's strength, durability, and biocompatibility. Despite these desirable properties, titanium presents challenges for wireless power transmission due to its relatively low electrical conductivity, including low efficiency, high heating, and precise alignment requirements, limiting the devices that can be recharged and causing a frustrating patient experience when recharging is possible.

Materials / Methods: To overcome these challenges, Resonant Link optimized wireless power transmission (WPT) for titanium-encased medical devices, enhancing efficiency and minimizing heat generation to enable fast charging that's consistent even during dynamic movement. Resonant Link's WPT allows for high efficiency transcutaneous energy transfer via magnetic coupling. The system delivers 2.5 W of continuous power with a high misalignment tolerance to recharge a 440 mAh implanted battery from 20% to 80% SOC in 21 minutes. Charging stays constant during dynamic movement, while meeting regulatory limits of <2 degree C tissue temp rise, <43 degree C max skin temp, and <48 degree C max touch temp. To accomplish this, a WPT innovation, the Multilayer Self-Resonant Structure (MSRS), which has previously been shown to have 6x lower losses (Q > 1200) than conventional wireless coils, was adapted to work with a form factor representative of titanium-encased IPGs on the market today. The high-efficiency MSRS integrated into the header portion of the IPG, with electromagnetic field shaping, results in minimum heat generation, keeping the total implant temperature rise under the acceptable limit.

Results: In vitro gelatin test results show: - A 440 mAh battery charges from 20% to 80% SOC in 21 minutes - Thermal measurement of the RX coil @ 2.5W: < 2 deg C rise - High spatial performance simulating body motion at up to 40 mm gap between the two coils, with 3 cm radial misalignment in all directions



Charge speed and power:



Discussion: See the Methods and Results sections.

Conclusions: Resonant Link's WPT allows for fast charging of titanium-encased IPGs during dynamic movement, while meeting thermal requirements. With this innovation, patients who use titanium-encased devices like neurostimulators, ICDs, and pacemakers can have a faster recharging experience that's safe and allows them to move around while recharging, increasing the appeal of rechargeable IPGs.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1. To optimize wireless power transmission (WPT) for titanium-encased medical devices, enhancing efficiency and minimizing heat generation to enable fast charging that's consistent even during dynamic movement. Our goal was to reduce the charge time as much as

possible from what is today usually a 2-3 hour charge time, for titanium-encased medical devices like spinal cord stimulators, and to ensure charging can happen as patients move around, as opposed to sitting or lying still to charge which is what's required today.
2. To determine the best form factor for WPT in a titanium can to optimize charge speed and spatial freedom while minimizing heat generation. We evaluated multiple designs for the implant, including placing the wireless power receiver in the can and in the header, or the top, portion of the device.
3. To provide a path to improve outcomes and quality of life for every patient who needs an implanted medical device. By enabling fast, safe wireless charging of titanium-encased medical devices, we hoped to show recharging is possible even using challenging materials like titanium and there's no need for battery replacement surgeries which create unnecessary risk for patients and burden our healthcare system.

Financial Disclosures: Disclosures: the authors have financial and commercial interests from their employment and due to the commercial nature of the product. Jessica Humphrey, Resonant Link, Company Employee, Stock Options, > $100,000 USD Kasthuriramanan Sivaguru, Resonant Link, Company Employee, Stock Options, > $100,000 USD Kyle Goodrick, PhD, Resonant Link, Company Employee, Stock Options, > $100,000 USD Scott Warren, Resonant Link, Company Employee, Stock Options, > $100,000 USD Panteleimon Papamanolis, PhD, Resonant Link, Company Employee, Stock Options, > $100,000 USD Aaron Stein, PhD, Resonant Link, Company Employee, Stock Option Value >5%, > $100,000 USD Milovan Kovacevic, PhD, Resonant Link, Company Employee, Stock Options, > $100,000 USD Phyo Aung Kyaw, PhD, Resonant Link, Company Employee, Stock Option Value >5%, > $100,000 USD

Disclosure: Disclosures: the authors have financial and commercial interests from their employment and the commercial nature of Resonant Link's wireless power systems.

O075

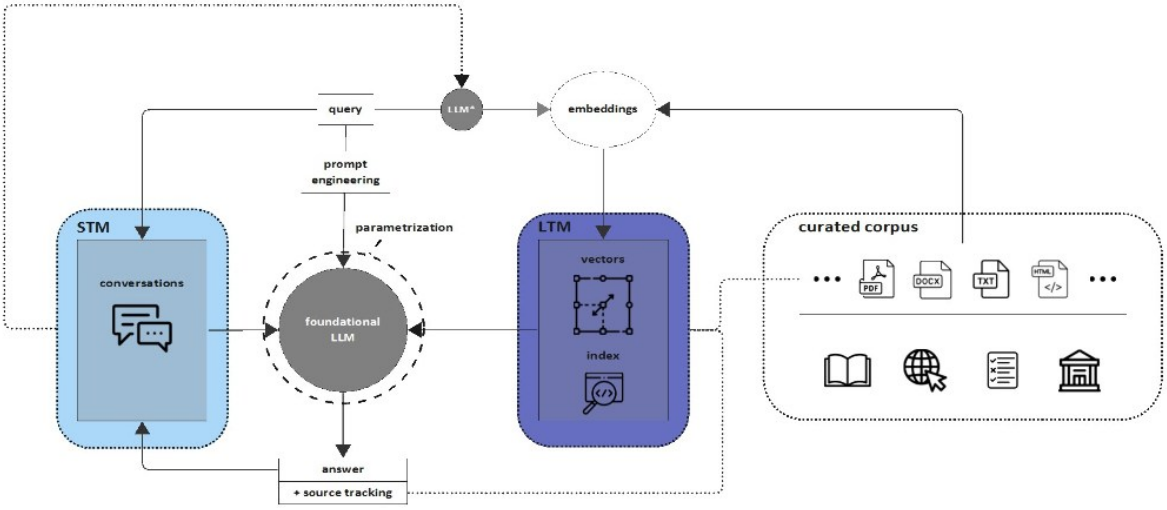
Oral Presentations
NEUROMODULATION: ENGINEERING AND AI
14-05-2024 16:30 - 18:20

AI INTERFACING PHYSICIANS WITH NEUROMODULATION INFORMATION: AUGMENTED INTERACTION THROUGH A SPECIALIZED LARGE LANGUAGE MODEL ON VAGUS NERVE STIMULATION

Sami Barrit, MD[1], Maxine Dibue-Adjei, PhD[2], Steffen Fetzer, PhD[3], Romain Carron, MD, PhD[4]
[1]Université Libre de Bruxelles, Neurosurgery, Brussels, Belgium, [2]Brandenburg Medical School — Berlin Campus, Centre For Palliative And Neuro-palliative Care, Brandenburg, Germany, [3]LivaNova, Medical Affairs Neuromodulation, London, United Kingdom, [4]Aix-Marseille University/INSERM — APHM — Timone Hospital, Functional, And Stereotactic Neurosurgery,, Marseille, France

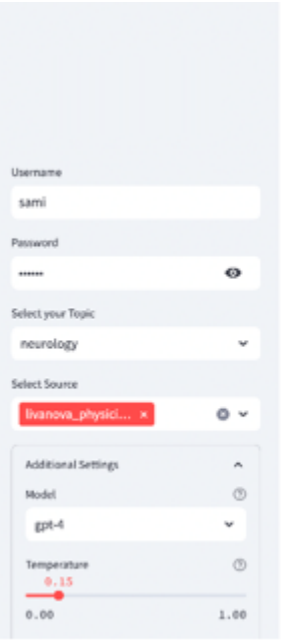
Introduction: Neuromodulation in healthcare settings necessitates rapid, precise access to a plethora of technical and clinical information that is both accurate and verifiable. Traditional information retrieval methods are often cumbersome, time-consuming, and unreliable. Recently, large language models (LLM) have garnered attention for their proficiencies in broad applications of natural language processing. However, their application in medical domains poses challenges due to their opaque information generation (often incongruent with stringent regulatory constraints) and to their operation within highly specific, data-rich environments. Here, we explore the potential of a specialized LLM solution to enhance and accelerate physicians' interaction with curated vagus nerve stimulation (VNS) -related information.

Materials / Methods: We implemented Neura, a specialized LLM solution for neuroscience, built on the Eunoia infrastructure (Sciense Labs, New York City, U.S.). Eunoia's architecture integrates a dual-database system comprised of 'long-term memory' (LTM) and 'short-term memory' (STM) components, each equipped to precisely trace the source of utilized information for generation purposes. The LTM is a domain-specific knowledge corpus, while the STM captures conversational history, adding contextual understanding. The LTM was populated with curated VNS-related information, endorsed by the manufacturer (LivaNova PLC, London, UK), submitted to regulatory agencies, and subjected to quality control by one clinician and one technical expert in VNS.



Results: The solution was integrated into a web chatbot interface with extended cross-platform compatibility. Employing a user-centric design, its interface streamlines physician access to the curated VNS-specific knowledge base, focusing on usability and information retrieval. While intuitive for novice users, it also offers advanced options to cater to seasoned

users.



Discussion: Applying a specialized LLM in the context of VNS management exemplifies the transformative potential of AI in healthcare. The framework enhances information retrieval efficiency and introduces a layer of contextual understanding that is notably absent in traditional knowledge management systems. The solution embodies advanced information traceability and quality control, not only affording citations but also pinpointing exact source locations, such as document sections or pages, all while being deployed on a curated information corpus. Consequently, it streamlines the verification of information in line with explainable AI (XAI). This is particularly crucial in the fast-paced, high-stakes environment of neuromodulation therapies such as VNS, where rapid access to accurate information can substantially impact clinical workflow and patient care.

Conclusions: We introduce an AI solution to augment interaction between physicians and neuromodulation information. Specialized LLM may enhance information management in complex clinical settings, setting the stage for broader applications in healthcare.

Supplemental Data:

References: 1. Yu, K.-H., Beam, A. L. & Kohane, I. S. Artificial intelligence in healthcare. Nature biomedical engineering 2, 719–731 (2018). 2. Xu, Y. et al. Artificial intelligence: A powerful paradigm for scientific research. The Innovation 2 (2021). 3. OpenAI. GPT-4 Technical Report. arXiv: 2303.08774 [cs.CL] (2023). 4. Devlin, J., Chang, M.-W., Lee, K. & Toutanova, K. BERT: Pre-training of Deep Bidirectional Transformers for Language Understanding. arXiv: 1810.04805 [cs.CL] (2019). 5. Beam, A. L. et al. Artificial intelligence in medicine 2023. 6. Ling, C. et al. Domain Specialization as the Key to Make Large Language Models Disruptive: A Comprehensive Survey. arXiv: 2305.18703 [cs.CL] (2023). 7. Singhal, K. et al. Large Language Models Encode Clinical Knowledge. arXiv: 2212.13138 [cs.CL] (2022). 8. Gabriel, I. Artificial intelligence, values, and alignment. Minds and machines 30, 411–437 (2020). 9. London, A. J. Artificial intelligence in medicine: Overcoming or recapitulating structural challenges to improving patient care? Cell Reports Medicine 3 (2022).

Acknowledgements: The support of LivaNova PLC (London, United Kingdom) for this project is gratefully acknowledged.

Learning Objectives: 1. To understand the unique challenges and requirements in information retrieval and management within the domain of vagus nerve stimulation (VNS) in healthcare settings. This encompasses considerations for rapidity, precision, and reliability, especially in light of existing traditional methods that may be cumbersome and time-consuming. 2. To explore the architecture and

functionalities of specialized Large Language Models (LLMs) in addressing these challenges. This involves a particular focus on the dual-database system of 'long-term memory' (LTM) and 'short-term memory' (STM), their roles in information sourcing and contextual understanding, and how these elements contribute to efficient and reliable information retrieval for physicians. 3. To evaluate the implications of employing specialized LLMs for VNS management on healthcare delivery, including the impact on clinical workflow and patient care. This objective will also encompass a critical examination of the model's adherence to Explainable AI (XAI) principles, particularly in the realm of information traceability and quality control.

Financial Disclosures: Concerning authors: BARRIT Sami; CARRON, Romain a) LivaNova PLC b) For what role? Consultant & Education / Research c) Level of Compensation? $501 - $5,000 USD Concerning authors: DIBUE-ADJEI, Maxine; FETZER, Steffen a) LivaNova PLC b) For what role? Company Employee c) Level of Compensation? $501 - $5,000 USD (monthly wage)

Disclosure: No significant relationships.

O076

Oral Presentations
NEUROMODULATION: ENGINEERING AND AI
14-05-2024 16:30 - 18:20

NEW METHOD FOR OPTIMIZING MULTI-CHANNEL TRANSCRANIAL ELECTRICAL STIMULATION TO IMPROVE ROBUSTNESS TO ELECTRODE DISPLACEMENT: A SIMULATION STUDY

Jaehoon Jeong, MS student, Sangwoo Lee, Undergraduate, Chang-Hwan Im, PhD
Hanyang University, Seoul, Korea, Republic of

Introduction: In the conventional transcranial electrical stimulation (tES) with a pair of electrodes, small drift of electrode locations could alter the pattern of electric field inside the brain [1]. In this paper, we hypothesized that the similar problem might arise when a commercialized tES system with multiple electrodes mounted on an elastic cap is used. Therefore, the influence of the electrode displacement on the electric field was investigated. In addition, a new optimization method considering the possible displacements of the electrodes was proposed to improve the robustness to the electrode displacement during the repeated use of the tES system.

Materials / Methods: A digitizer is used to estimate the average displacement of electrodes during repeated self-wearing of the electrode cap. Ten participants tried on a cap by themselves a total of 25 times. We generated five models for finite element method (FEM) based on the electrode locations of the international 10-10 EEG system: the original location, forward shift, backward shift, rightward shift, and leftward shift. Left hand motor cortex (HM), right intraparietal sulcus (ISC), left dorsolateral prefrontal cortex (DLPFC), and visual cortex (VC) were set as the regions of interest (ROIs). We optimized the input current distributions for each of the five electrode locations using the FEM-based field simulation and the least squares algorithm to best modulate the designated ROIs. We then generated a new current distribution by averaging the five optimization results. We compared how the intensity of electric field (from the mean value within the ROI) and the focality of electric field (from the maximum value outside the ROI divided by the minimum value within the ROI) decreased when the electrode locations were shifted.

Results: The average displacement of electrodes was 1.08 cm, based on which the electrode locations were shifted. Our method showed higher intensity and focality in all ROIs, exhibiting the superiority of the proposed method.

Discussion: Even when assuming that channel positions would not change, our method showed increased intensity of the electric field in all ROIs. Further studies might be necessary to generalize the superiority of our method with more numbers of head models.

Conclusions: In this study, we improved the robustness of tES to the electrode shift by employing a new optimization method that averages optimization results for five FEM models with different electrode displacements. It is expected that the proposed optimization method can be a useful tool to improve the robustness and reliability of tES in practical scenarios.

Supplemental Data:

Table: Performance comparison between conventional and new optimization methods

	Ratio of intensity to original location of the channels (%)		Ratio of focality to original location of the channels (%)	
	Conventional optimization	New optimization	Conventional optimization	New optimization
Left HM	80.41	83.45	72.26	77.81
Right ISC	79.90	82.62	54.10	57.60
Left DLPFC	90.52	91.88	74.53	80.13
VC	87.45	87.90	81.96	88.51
Average	84.57	**86.46**	70.71	**76.01**

HM: hand motor cortex / ISC: intraparietal sulcus / DLPFC: dorsolateral prefrontal cortex / VC: visual cortex

References: [1] Woods, A.J., et al., *Effects of electrode drift in transcranial direct current stimulation.* Brain stimulation, 2015. **8**(3): p. 515-519.

Acknowledgements: This research was supported by the National Research Foundation of Korea (NRF), funded by the Korea government (MSIT). (No. RS-2023-00266075)

Learning Objectives: 1. The influence of the electrode displacement on the electric field delivered to the target brain areas was investigated. 2. A new optimization method considering the possible displacements of the electrodes was proposed to improve the robustness to the electrode displacement during the repeated use of the tES system. 3. Our method outperformed the conventional approach in terms of the electric field intensity and focality of electric field.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O077

Oral Presentations
NEUROMODULATION: ENGINEERING AND AI
14-05-2024 16:30 - 18:20

A PROSPECTIVE CASE-CONTROL EVALUATION OF SELECTIVITY IN A HIGH-RESOLUTION SPINAL CORD STIMULATION PADDLE

Deepak Berwal, PhD[1], Alejandra Quintero, BS[1], Ilknur Telkes, MSN, PhD[1], Marisa Dimarzio, PhD[1], Tessa Harland, MD[2], Steven Paniccioli, BS, CNIM[3], Bryan McLaughlin, PhD[4], Yohannes Iyassu, PhD[4], John Dalfino, MD[2], Julie Pilitsis, MD, PhD[1]
[1]Florida Atlantic University, Boca Raton, United States of America, [2]Albany Medical College, Albany, United States of America, [3]NuVasive Clinical Services, San Diego, United States of America, [4]Micro-Leads Inc, Somerville, United States of America

Introduction: Spinal cord stimulation (SCS) offers significant pain relief for many patients. However, often discrete painful regions are left untreated. Whether these areas can be selectively targeted by modulating structures lateral to the dorsal columns has not been studied. Here we investigate whether a high-resolution spinal cord stimulation (HR-SCS) paddle with greater medio-lateral coverage offers greater selectivity to commercially available devices.

Materials / Methods: In this prospective study (clinicaltrials.gov NCT05459324), we compare evoked EMG responses from 9 muscle groups obtained during intraoperative neuromonitoring (IONM) between HR-SCS (8 columns) and commercially paddles (2-4 columns). Column locations were normalized by overlaying fluoroscopic images of both paddles. Medial contacts were considered the 3 contacts closest to midline and presumably those that modulate the dorsal columns. There were varied number of recordings at each thoracic level T9,T10>T7,T6>T8. There was not enough data at T8 to perform statistical analysis.

Results: Our study included 21 patients (14F:7M; mean age 56). 11 patients were diagnosed with neuropathic pain, 8 with failed back surgery syndrome, and 2 with complex regional pain syndrome. At stimulation amplitudes $\leq$ 6mA and at 10mA, the max root mean-square value (RMS) % change was greater across all contacts with HR-SCS as compared to commercial paddles. % max RMS for HR-SCS was significantly higher in both distal and proximal leg muscle groups with activation of medial contacts at T6 and T9. Lateral contact stimulation resulted in additional muscle group activation both distally and proximally not only at T6 and T9 but also at T7 and T10 (Table 2).

Discussion: Our findings demonstrate that HR-SCS is able to selectively stimulate muscles throughout the lower extremities at lower amplitudes than often required for evoked EMG responses from commercial paddles during IONM. Further stimulation of lateral contacts offered greater muscle activation in proximal and distal muscle groups at all thoracic levels.

Conclusions: We are hopeful that this improved selectivity will correlate with improved pain relief for patients who undergo SCS for FBSS and chronic neuropathic pain.

Supplemental Data: Table 1: For normalization, HR SCS and commercial paddle columns were aligned with fluoroscopy. The contact corresponding to the paddle's column at anatomical midline was labeled Contact 0. Recordings were taken from 21 patients. The number of recordings for each contact at each paddle varied from 0 to 12. Maximum root-mean-square (RMS) group averages of evoked EMG responses with stimulation at amplitudes of 0.5-6mA were compared using Kruskal Wallis with Bonferroni corrections. $P < 0.0056$ denotes where greater RMS were seen in HR SCS compared to commercial paddles.

Spine Level	Left Lateral Contacts			Medial Contacts			Right Lateral Contacts		
	-4	-3	-2	-1	0	1	2	3	4
T6		0.015	<0.001	0.894	<0.001	0.003	0.627	0.001	
T7		0.17	0.79	0.96	0.12	0.45	0.62	<0.001	
T8		0.015		<0.001	0.353		0.002		
T9		<0.001		0.003	<0.001	0.005	<0.001	0.046	0.69
T10			0.96	0.89	0.5	0.015	0.2	0.5	

Table 2: HR SCS and commercial paddles were aligned with fluoroscopy. The contacts corresponding to anatomical midline column were labeled Contact 0. Contacts 0 and |1| were considered medial and to correlate with dorsal column stimulation. Contacts |2| and |3| were assumed to stimulate lateral structures. Recordings were taken from 21 patients. The number of recordings for each contact at each paddle varied from 0 to 12. Maximum root-mean-square (RMS) group averages of evoked EMG responses with stimulation at amplitudes of 0.5-6mA were calculated. A linear mixed-effects model test determined when RMS at each level and for each muscle group was greater with HR-SCS as compared to commercial paddles. (AH= abductor hallucis, MG- medial gastrocnemius, BF- biceps femoris, GLUT- gluteus, QUAD- quadriceps, ADD= adductors).

Spine Level	Medial Contacts (0 and |1|)		Lateral Contacts (|2| and |3|)	
	Distal Lower Extremities (AH, TA, MG)	Proximal Lower Extremities (GLUT, QUAD, BF, ADD)	Distal Lower Extremities (AH, TA, MG)	Proximal Lower Extremities (GLUT, QUAD, BF, ADD)
T6	AH	BF, GLUT	AH, TA, MG	GLUT, QUAD, BF
T7	AH	-	AH	GLUT, QUAD, BF
T8	-	-	-	-
T9	MG	QUAD, BF, ADD	TA, MG	GLUT, QUAD, BF, ADD
T10	-	-	AH, MG	ADD

References: None

Acknowledgements: N/A

Learning Objectives: 1. Learn if high-resolution spinal cord stimulation (HR-SCS) has greater selectivity in eliciting evoked electromyography (EMG) responses in an intraoperative setting. 2. Understand that HR-SCS offers recruitment of muscle groups at lateral contacts. 2. Understand that targeting the involved dermatome with spinal cord stimulation is a crucial step toward personalized treatment.

Financial Disclosures: Dr. Pilitsis receives grant support from Medtronic, Boston Scientific, Abbott, NIH 2R01CA166379and NIH U44NS115111. She is the medical advisor for Aim Medical Robotics and has stock equity. Dr. Telkes receives grant support from NIH R00NS119672, NIH U44NS115111, and FAU COECS/I-SENSE. Dr. McLaughlin is CEO of Micro-Leads, Inc. Steven Paniccioli is an employee of NuVasive Clinical Services.

Disclosure: No significant relationships.

O078

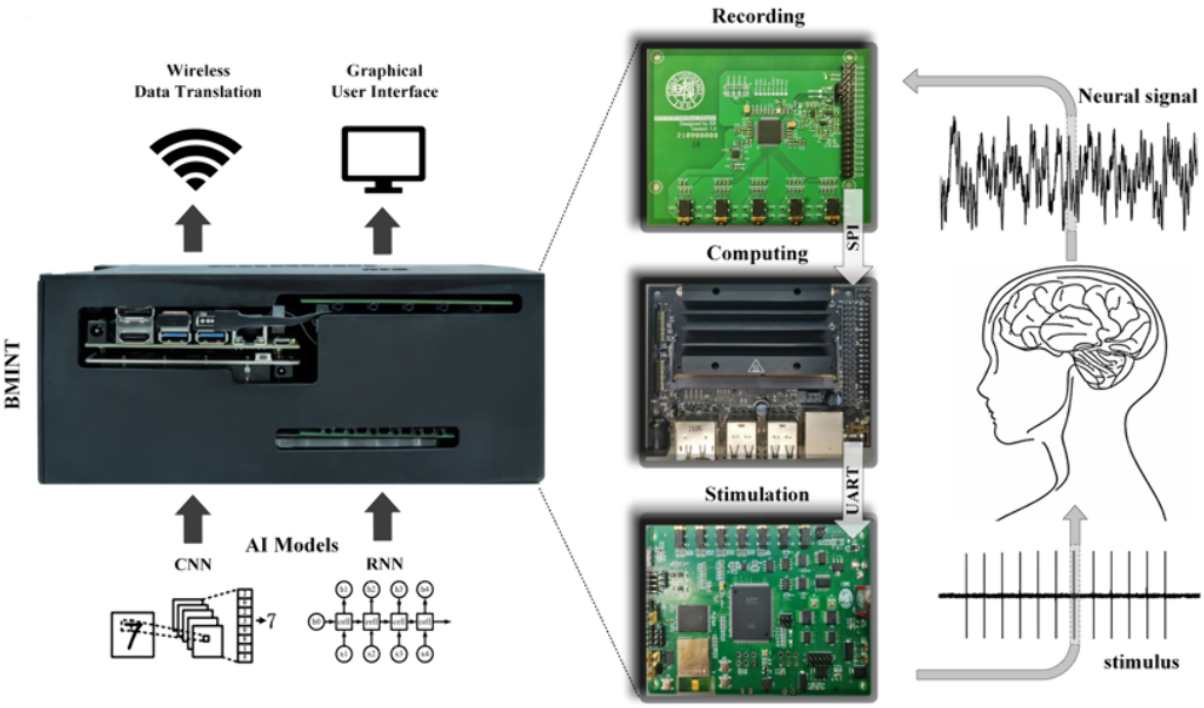
Oral Presentations
NEUROMODULATION: ENGINEERING AND AI
14-05-2024 16:30 - 18:20

BRAIN-MACHINE INTERACTIVE NEUROMODULATION RESEARCH TOOL WITH EDGE AI COMPUTING

Yan Li, MSBmE, Shouyan Wang, PhD
FUDAN UNVIVERSITY, Istbi, Shanghai, China

Introduction: Intelligent neuromodulation has shown great potentials in providing novel neuro-technology for treating neurological and psychiatric diseases. Development of brain-machine interactive neuromodulation strategies could lead to breakthroughs in precision and personalized electronic medicine. The neuromodulation research tool integrating artificial intelligent computing and performing neural sensing and stimulation in real-time could accelerate the development of intelligent neuromodulation strategies and translational research into clinical application.

Materials / Methods: We developed a brain-machine interactive neuromodulation research tool (BMINT) with careful hardware and software architecture design. The hardware consists of a recording module with 8 channels and a 2000Hz sample rate, a computational module with 921 MHz GPU power and 1.3 GHz CPU power, and a stimulation module with 2 channels of constant current outputs. The software architecture named Intelligent computing frameworks embedded in the BMINT enables real-time closed-loop neuromodulation developed with mainstream AI ecosystem resources.



Results: The BMINT research tool achieved system time delay under 3 ms. The utilization of GPU for acceleration enables the research tool to perform calculations on 256*256 size data using a deep learning model with 11.7 million parameters in just 24ms. Three commonly used machine learning algorithms of SVM, CNN and RNN were developed and deployed into the research tool and performed a simulation seizure detection task.

Discussion: The machine learning has showed great potentials to the development of intelligent neuromodulation strategies . Recent research has suggested that personalized neuromodulation

approaches may lead to better treatment outcomes, not only for individual patients but also for specific targets of brain regions in each patient. The brain-machine interactive neuromodulation tool has been developed in this study and the key performance of real-time processing and the computing capabilities was evaluated. The system time delay was stably controlled within 3 ms in the closed-loop system with variation less 0.5 ms. This delay time guarantees the ability to intervene in a single cycle of neural oscillations below 100 Hz. This performance allows to intervene each single cycle of the most important theta, alpha, beta and gamma oscillations related to brain diseases and brain functions. The research tool can assist researchers to efficiently deploy machine learning algorithms from pre-trained models to implementation of closed-loop neuromodulation in real-time environment.

Conclusions: The BMINT could provide timely contribution to accelerate the translational research of intelligent neuromodulation by integrating neural sensing, edge AI computing and stimulation with AI ecosystems.

Acknowledgements:

Learning Objectives: 1. Understand the potential of intelligent neuromodulation in advancing the treatment of neurological and psychiatric diseases. Desired Result: Participants will gain insight into the promising role of intelligent neuromodulation. 2. Recognize the importance of brain-machine interactive neuromodulation strategies for achieving precision and personalized electronic medicine. Desired Result: Attendees will understand how the development of such strategies can lead to breakthroughs in medical treatment. 3. Learn about the capabilities of the Brain-Machine Interactive Neuromodulation Research Tool (BMINT), including neural sensing, real-time computing with machine learning, and precise electrical stimulation. Desired Result: Participants will be informed about the technology and features of BMINT and how it accelerates neuromodulation research.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O079

Oral Presentations
NEUROMODULATION: ENGINEERING AND AI
14-05-2024 16:30 - 18:20

ESTABLISHING BIDIRECTIONAL BRAIN/NEURAL COMPUTER INTERACTION (BNCI) USING TRANSCRANIAL ALTERNATING CURRENT STIMULATION (TACS)

Mareike Vermehren, MSc, Marian Wiskow, MSc, Annalisa Colucci, MSc, Niels Peekhaus, MSc, David Haslacher, MSc, Surjo Soekadar, MD
Charité - Universitätsmedizin Berlin, Berlin, Germany

Introduction: Up to date, bidirectional brain/neural-computer interaction (BNCI) that builds on the ability to simultaneously record and stimulate brain activity was restricted to implantable devices. The main reason for this limitation relates to stimulation artifacts impeding reliable assessment of brain signals when using transcranial stimulation that spreads electric fields over very large cortical areas. However, establishing non-invasive bidirectional BNCI would be critical to improve versatility of BNCI control, e.g., to control a prosthetic device delivering direct sensory feedback to the brain, or to specifically modulate brain dynamics in various brain disorders, such as epilepsy, stroke, or depression. Building on a real-time compatible stimulation artifact source separation (SASS) algorithm (Haslacher et al., 2021) combined with spatio-temporal decomposition (SSD) (Nikulin et al., 2011), we show that a bidirectional BNCI using transcranial alternating current stimulation (tACS) targeting sensorimotor m-oscillations is feasible.

Materials / Methods: Five healthy participants were invited to engage in motor-imagery based BNCI using 32-channel electroencephalography (EEG). During the task, either amplitude-modulated tACS or sham was applied near the sensorimotor cortex for the same number of trials. During the stimulation ON condition, m-rhythm oscillations were recorded simultaneously to stimulation and translated into contingent visual feedback displayed on a computer screen.

Results: All participants could successfully establish BNCI control in absence and during stimulation. Single-trial m-rhythm-based BNCI control in the stimulation ON condition was comparable with the stimulation OFF condition.

Discussion: By applying a novel artifact suppression approach embedding SSD, we achieved reliable bidirectional BNCI control using amplitude-modulated tACS. This new approach paves the way to improve versatility and scope of non-invasive BNCI, e.g., to deliver sensory feedback to the brain or interfere with aberrant brain dynamics.

Conclusions: This is the first study that shows successful combination of a motor imagery-based BNCI with tACS targeting sensorimotor oscillations. Larger studies are needed to confirm generalizability of our findings.

Supplemental Data:

References: 1. Haslacher, D., Nasr, K., Robinson, S. E., Braun, C., & Soekadar, S. R. (2021). Stimulation artifact source separation (SASS) for assessing electric brain oscillations during transcranial alternating current stimulation (tACS). *NeuroImage*, *228*, 117571. https://doi.org/10.1016/j.neuroimage.2020.117571 2. Nikulin, V. V., Nolte, G., & Curio, G. (2011). A novel method for reliable and fast extraction of neuronal EEG/MEG oscillations on the basis of spatio-spectral decomposition. *NeuroImage*, *55*(4), 1528–1535. https://doi.org/10.1016/j.neuroimage.2011.01.057

Acknowledgements: This study was supported by the European Research Council (ERC) under the project NGBMI (759370), the Deutsche Forschungsgemeinschaft (DFG), Germany, under the project SO932/7-1, and the Federal Ministry of Research and Education (BMBF) under the projects SSMART (01DR21025A) and NEO (13GW0483C).

Learning Objectives: 1.Understand innovative neuromodulation technologies and techniques, in particular non-invasive ones, that hold promise for treatment of stroke. 2. Learn how translation of neuromodulation techniques to clinical practice can be facilitated. 3. Present and critically discuss my work with colleagues working on related topics. I would particularly like to learn from researchers with experience on conducting clinical studies about challenges that come from translating methodology from the lab to a patient population.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O080

Oral Presentations
NEUROMODULATION: ENGINEERING AND AI
14-05-2024 16:30 - 18:20

A FEASIBILITY STUDY OF AN ENDOVASCULAR STENT ELECTRODE ARRAY FOR CORTICAL RECORDING IN SHEEP

Zheshan Guo, PhD[1], Feng Shi, Engineer[1], Yan Jiang, Engineer[1], Shijie Fan, Engineer[1], Wei Gao, Engineer[1], Meixian Wang, Engineer[1], Kun Zhao, Engineer[1], Gengshen Xiao, Engineer[1], Sheng Xin, Engineer[1], Chuanwei Yin, Engineer[1], Xiaoyi Min, PhD[2]
[1]Amygdala Neuro Technologies Co., Ltd, Shenzhen, China, [2]Amygdala Neuro Technology, santa rosa va, United States of America

Introduction: Utilizing MEMS technology, the endovascular stent electrode achieved success in a clinical trial, enabling computer communication for patients [1]. This accomplishment has spurred the innovation of another technology, incorporating a braided stent as a base with embedded insulated DFT wires. Each DFT wire carries a tiny electrode (Fig. 1A left), and the stent connects via a transvascular lead to an external device. The study aims: 1) to assess the stent-electrode's deliverability, release, and extraction at the transverse sinus (TS) and superior sagittal sinus (SSS); 2) to evaluate signal quality collected by the new system.

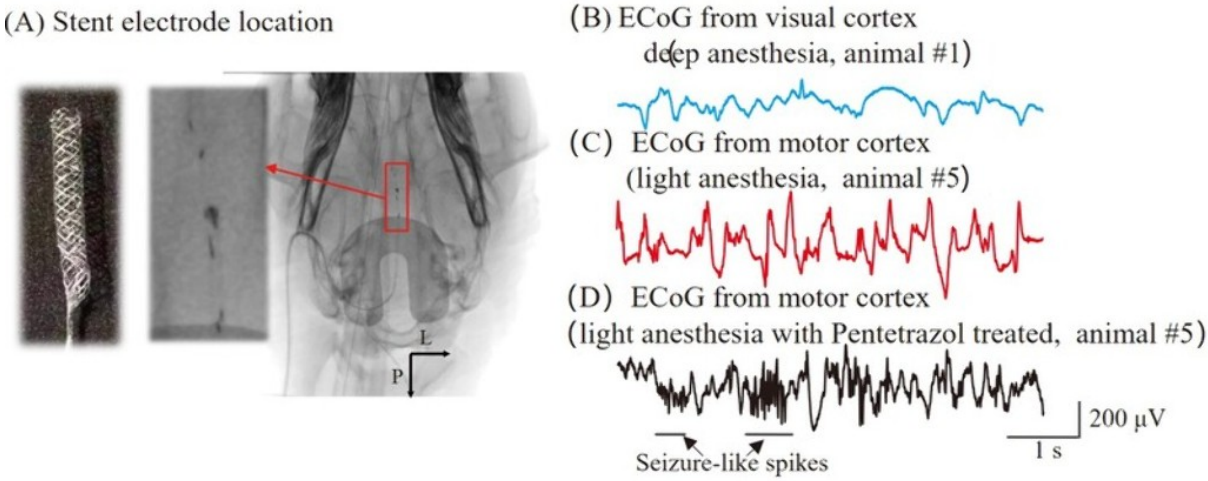


Figure 1. Stent electrode location and transvascular recorded ECoG during different states and positions. (A) Stent electrode placed in SSS; (B) ECoG from TS; (C) from SSS; (D) from SSS with Pentetrazol treated. 0.1 - 200 Hz bandpass filter and 50 Hz notch filter were applied.

Materials / Methods: To assess the system, vascular stent electrodes were implanted in five female sheep weighing between 70-75 kg. The electrodes were placed within the TS or distal ends of SSS to record ECoG signals in the visual or motor cortex. The stent establishes a connection through a transvascular lead to an external device, which could be either the commercial signal acquisition system (Apollo I 32-channel, Bio-Signal Technologies, Nanjing, Jiangsu, China) or an in-house recording/stimulation unit. The procedures were performed according to regulations and the Animal Welfare Act, with preoperative planning through MRI venous vascular enhancement scans and 3D reconstructions. The surgery was performed under general anesthesia with vital signs monitored. The implantation technique required a learning curve and multiple catheters and guide wires were used before success.

Results: Design modifications were made to the stent electrode, which allowed it to be successfully placed in the TS position, collecting signals up to 200 μV from the visual cortex (Fig. 1B). However, accessing SSS was initially challenging. Lessons from the first attempts improved techniques for the

next two animals, successfully reaching SSS (Fig. 1AC). Using Pentetrozol to induce seizures, seizure-like spikes were observed in all sensing channels, confirmed by body twitching (Fig. 1D). The single electrode pathway's impedance at 1 kHz was 1092 Ω ± 194.6 Ω.

Discussion: The successful implantation of the stent-electrode system in animals opens up possibilities for further research and, potentially, clinical applications in humans. However, several technical and ethical considerations must be addressed before this technology can reach its full potential.

Conclusions: This study demonstrated the feasibility of the newly proposed stent electrode system, successfully implanting it in the SSS and TS to record high-quality brain signals. The approach presents a potential alternative for lower electrode impedance and reduced product cost. Future efforts will focus on chronic studies using an updated system.

Supplemental Data:

References: [1] Oxley T J, Opie N L, John S E, et al. Minimally invasive endovascular stent-electrode array for high-fidelity, chronic recordings of cortical neural activity[J]. Nature Biotechnology, 2016, 34(3): 320-327.

Acknowledgements: The support of Amygdala Neuro Technologies Co., Ltd, Shenzhen, China, for this project is gratefully acknowledged.

Learning Objectives: Learning Objective 1: By the end of this study, learners will be able to evaluate the feasibility and success of implanting the braided stent electrode system in the transverse sinus (TS) and superior sagittal sinus (SSS) for the purpose of recording brain signals, and assess the techniques required for the deliverability, release, and extraction of these stent-electrodes. Learning Objective 2: After engaging with this study, participants will gain the ability to analyze and compare the signal quality collected by the new braided stent electrode system in the transverse sinus (TS) and superior sagittal sinus (SSS) for electrocorticography (ECoG) recording, with a specific focus on its application in the visual or motor cortex. Learning Objective 3: Upon completion of this study, learners will be capable of discussing the implications of the design modifications made to the stent-electrode system and their impact on signal quality, electrode impedance, and potential cost reduction, as well as recognizing the potential of this system as an alternative for future brain signal recording studies.

Financial Disclosures: 1) Xiaoyi Min; a) Amygdala Neuro Technologies Co., Ltd, Shenzhen, China; b) Role: Company Employee; c) Level of Compensation: >$100,000 USD 2) Zheshan Guo; a) Amygdala Neuro Technologies Co., Ltd, Shenzhen, China; b) Role: Consultant; c) Level of Compensation: $501 - $5,000 USD 3) Feng Shi; a) Amygdala Neuro Technologies Co., Ltd, Shenzhen, China; b) Role: Company Employee; c) Level of Compensation: $20,001 - $100,000 USD 4) Yan Jiang; a) Amygdala Neuro Technologies Co., Ltd, Shenzhen, China; b) Role: Company Employee; c) Level of Compensation: $20,001 - $100,000 USD 5) Shijie Fan; a) Amygdala Neuro Technologies Co., Ltd, Shenzhen, China; b) Role: Company Employee; c) Level of Compensation: $20,001 - $100,000 USD 6)Wei Gao; a) Amygdala Neuro Technologies Co., Ltd, Shenzhen, China; b) Role: Company Employee; c) Level of Compensation: $20,001 - $100,000 USD 7) Meixian Wang; a) Amygdala Neuro Technologies Co., Ltd, Shenzhen, China; b) Role: Company Employee; c) Level of Compensation: $20,001 - $100,000 USD 8) Kun Zhao; a) Amygdala Neuro Technologies Co., Ltd, Shenzhen, China; b) Role: Company Employee; c) Level of Compensation: $20,001 - $100,000 USD 9) Gengshen Xiao; a) Amygdala Neuro Technologies Co., Ltd, Shenzhen, China; b) Role: Company Employee; c) Level of Compensation: $20,001 - $100,000 USD 10) Sheng Xin; a) Amygdala Neuro Technologies Co., Ltd, Shenzhen, China; b) Role: Company Employee; c) Level of Compensation: $20,001 - $100,000 USD 11)Chuanwei Yin; a) Amygdala Neuro Technologies Co., Ltd, Shenzhen, China; b) Role: Company Employee; c) Level of Compensation: $20,001 - $100,000 USD

Disclosure: No significant relationships.

O081

Oral Presentations
NEUROMODULATION: ENGINEERING AND AI
14-05-2024 16:30 - 18:20

ROBUST AND HETEROGENEOUS CELLULAR RESPONSES TO 40-1000HZ DEEP BRAIN STIMULATION ACROSS BRAIN REGIONS

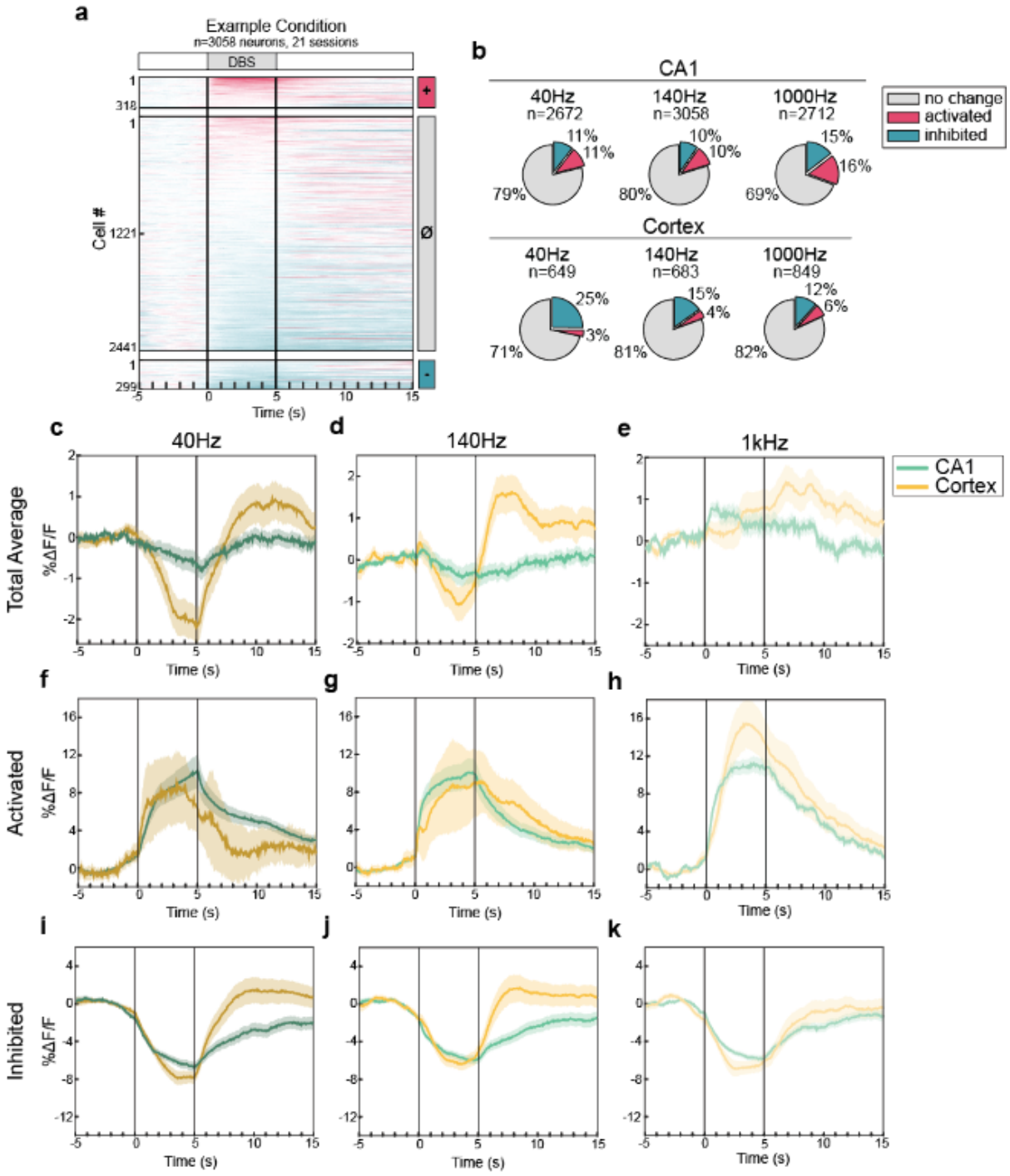
Cara Ravasio, MSc, Krishnakanth Kondabolu, PhD, Eric Lowet, PhD, Samuel Zhou, BSc (Hons), Rebecca Mount, BSc (Hons), MSc, PhD, Xue Han, PhD
Boston University, Biomedical Engineering, Boston, United States of America

Introduction: The therapeutic outcome of deep brain stimulation (DBS) depends on electrical pulse patterns, particularly frequencies. Clinical DBS is typically administered around 140Hz, as lower frequencies are generally ineffective[1]. Interestingly, recent clinical studies demonstrated that ultrahigh frequency DBS in the kilohertz range was also effective[2,3], despite evidence that kilohertz stimulation does not effectively modulate neurons[4,5].

Materials / Methods: To probe the cellular and circuit effects of DBS at different frequencies, we performed widefield cellular calcium imaging using syn-jGCaMP7f on over 10,000 individual neurons in the hippocampus and the sensorimotor cortex of awake mice while delivering local electrical stimulation at 40Hz, 140Hz, or 1kHz. Each imaging session included 10-20 trials; each trial was 20 seconds long (5 seconds baseline, 5 seconds DBS, and 10 seconds post-DBS). We included an 18 second intertrial interval to prevent photobleaching. DBS pulses were current-controlled cathode leading biphasic square wave pulses and were delivered at 40Hz (200μs/phase), 140Hz (200μs/phase), or 1kHz (90μs/phase).

Results: We found that 1kHz DBS robustly modulates intracellular calcium and is equally effective as 40Hz and 140Hz DBS. During DBS, modulated neurons exhibit heterogeneous responses; some display activation and others inhibition (Figure1a-b). Regardless of stimulation frequency, in the hippocampus the ratio of activated to inhibited neurons is roughly equal, but in the cortex, there are more inhibited neurons (Figure1b). Interestingly, 40Hz and 140Hz, but not 1kHz DBS, evoked prominent inhibitory responses at the population level in both CA1 and cortex (Figure1c-e). Furthermore, we found that increasing stimulation frequency increased the strength of activation within a brain region, but had no or negligible effects on the strength of inhibition (Figure1f-k). Finally, 40Hz and 140Hz evoked distinct calcium temporal profiles in the CA1 and cortex for both activated and inhibited neurons, while 1kHz did not evoke or evoked a negligible temporal difference (Figure1f-k). All p-values are summarized in Supplemental Tables 1-3. For all significant p-values, Cliff's δ is included to quantify the effect

size.



Discussion: All three tested frequencies had consistent activation and inhibition suggesting that DBS effectively alters intracellular signaling. Following DBS offset, modulated neurons showed rapid recovery, suggesting a transient DBS effect without prolonged compensatory response. The lack of region-dependent effects during 1kHz DBS suggests that supraphysiological DBS alters neural activity through a distinct mechanism from the physiological 40Hz and 140Hz DBS.

Conclusions: Our results demonstrate brain-region dependent DBS effects across stimulation frequencies, and that ultrahigh frequency DBS modulates neural activity through a distinct mechanism from lower frequency DBS.

Supplemental Data: Supplemental Table 1: Kruskal-Wallis test within the CA1 across frequencies

Comparing within CA1	40Hz vs 140Hz	40Hz vs 1kHz	140Hz vs 1kHz
Activated Neurons: AUC	p = 0.063	p = 3.36×10^{-14} δ = -0.344, medium	p = 1.61×10^{-7} δ = -0.228, small
time to peak	p = 6.27×10^{-9} δ = 0.284, small	p = 2.23×10^{-10} δ = -0.285, small	p = 1
Inhibited Neurons: AUC	p = 1	p = 1	p = 1
time to peak	p = 0.101	p = 7.14×10^{-4} δ = 0.169, small	p = 0.375

Supplemental Table 2: Kruskal-Wallis test within cortex across frequencies

Comparing within Cortex	40Hz vs 140Hz	40Hz vs 1kHz	140Hz vs 1kHz
Activated Neurons: AUC	p = 0.844	p = 0.003 δ = -0.470, medium	p = 2.24×10^{-5} δ = -0.604, large
time to peak	p = 0.034 δ = -0.404, medium	p = 1	p = 0.005 δ = 0.424, medium
Inhibited Neurons: AUC	p = 0.026 δ = -0.028, negligible	p = 0.980	p = 0.1219
time to peak	p = 5.83×10^{-5} δ = 0.318, small	p = 0.031 δ = 0.180, small	p = 0.340

Supplemental Table 3: Wilcoxon rank-sum test for 40Hz, 140Hz, and 1kHz across brain regions and sign-rank at a population level DBS effect.

Comparing CA1 and Cortex	40Hz	140Hz	1kHz
Activated Neurons: AUC time to peak	p = 0.331	p = 0.505	p = 0.058
	p = 0.003 δ = 0.383, medium	p = 0.005 δ = -0.318, small	p = 0.902
Inhibited Neurons: AUC time to peak	p = 0.014 δ = 0.140, negligible	p = 0.384	p = 4.23×10^{-4} δ = 0.228, small
	p = 7.60×10^{-4} δ = 0.192, small	p = 5.83×10^{-6} δ = 0.299, small	p = 0.046 δ = 0.129, negligible
Population level DBS effect CA1	p = 7.14×10^{-36} δ = -0.222, small	p = 2.80×10^{-28} δ = -0.225, small	p = 0.011 δ = -0.114, negligible
Population level DBS effect cortex	p = 1.91×10^{-15} δ = -0.264, small	p = 7.32×10^{-7} δ = -0.204, small	p = 0.663

References: 1. Ushe, M. *et al.* Effect of stimulation frequency on tremor suppression in essential tremor. *Mov. Disord.* **19**, 1163–1168 (2004). 2. Neudorfer, C. *et al.* Kilohertz-frequency stimulation of the nervous system: A review of underlying mechanisms. *Brain Stimulat.* **14**, 513– 530 (2021). 3. Harmsen, I. E. *et al.* Ultra-high-frequency deep brain stimulation at 10,000 Hz improves motor function. *Mov. Disord. Off. J. Mov. Disord. Soc.* **34**, 146–148 (2019). 4. Grossman, N. *et al.* Noninvasive Deep Brain Stimulation via Temporally Interfering Electric Fields. *Cell* **169**, 1029-1041.e16 (2017). 5. Couto, J. & Grill, W. M. Kilohertz Frequency Deep Brain Stimulation Is Ineffective at Regularizing the Firing of Model Thalamic Neurons. *Front. Comput. Neurosci.* **10**, 22 (2016).

Acknowledgements: XH acknowledges funding from NIH 5R01MH122971. 1RF1NS129520, 1R01NS119483. El acknowledges support from the Boston University Center for Systems Neuroscience. RAM acknowledges funding from NIH NRSA fellowship (F31MH123008). CRR acknowledges funding from NSF GRFP (2021324226) and support from the Boston University Neurophotonics Center.

Learning Objectives: 1. Determine whether kilohertz DBS alters neural activity. 2. Examine whether different frequency DBS evoked distinct cellular changes across different brain regions. 3. Gain

insight into potential differences in therapeutic mechanisms for physiological vs supraphysiological DBS frequencies.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O082

Oral Presentations
NEUROMODULATION: ENGINEERING AND AI
14-05-2024 16:30 - 18:20

ELECTRICAL STIMULATION CREATES INFORMATIONAL LESION IN CORTICAL PV NEURONS THROUGH ALTERING MEMBRANE VOLTAGE

Pierre Fabris, MSc[1], Eric Lowet, BSc (Hons), MSc, PhD[2], Krishnakanth Kondabolu, BSc (Hons), MSc, PhD[1], Xue Han, PhD[2]
[1]Boston University, Boston, United States of America, [2]Boston University, Biomedical Engineering, Boston, United States of America

Introduction: DBS has been suggested to create informational lesion[1], and recent evidence in hippocampal pyramidal cells suggests that electrical stimulation-evoked membrane depolarization is critical for DBS effects[2]. To understand whether membrane depolarization-mediated informational lesion occurs in other neuron types, we performed voltage imaging from individual cortical parvalbumin-positive (PV) interneurons, while delivering electrical stimulation at 40Hz or 140Hz.

Materials / Methods: To perform optical voltage imaging from PV interneurons, we transduced them with the voltage indicator SomArchon[3], through injection of AAV-CAG-FLEX-SomArchon-GFP in the motor cortex of PV-cre transgenic mice (Fig 1A). Membrane voltage (Vm) fluctuations, measured as SomArchon fluorescence changes, were optically imaged with simultaneous electrical stimulation at 40Hz and 140Hz, while mice were awake and head fixed. Single neurons were recorded with multiple 3 second trials including 1 second baseline, 1 second stimulation, and 1 second post-stimulation period.

Results: We found that electrical stimulation at both 40Hz and 140Hz effectively altered Vm and spike timing in PVs. While DBS-evoked membrane voltage changes were heterogeneous across individual neurons, at a population level, 40Hz DBS led to persistent increase in spike rate throughout the entire 1 second DBS period, whereas 140Hz DBS only transiently increased spike rate within ~100ms of DBS onset. Furthermore, 40Hz stimulation produced temporally precise pacing of Vm and spiking to individual electrical pulses, whereas 140Hz stimulation evoked Vm and spiking largely failed to follow stimulation pulses (Fig 1B-C). Finally, stimulation at both frequencies interfered with cellular informational processing by disrupting timed spiking output in response to intrinsic rhythmic circuit
inputs.

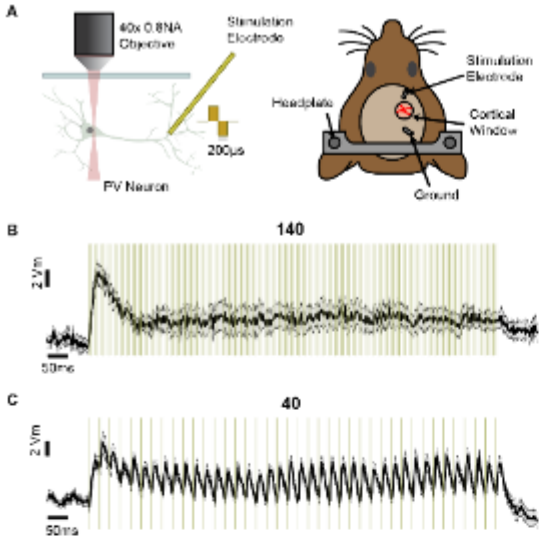


Figure 1: A) Illustration of the optical imaging window and animal preparation. B) Population average Vm of PVs before, during, and after 140Hz stimulation. Individual DBS pulses shown in gold. Gray area indicates standard error of the mean (SEM). C) Same as b, but with 40Hz stimulation.

Discussion: These results highlight the similarity between the DBS effects on hippocampal pyramidal neurons and cortical interneurons. Since membrane voltage dynamics ultimately dictate spike timing, DBS-evoked Vm changes thus underlie the observed spike timing disruption to intrinsic rhythmic inputs. Even though both 40Hz and 140Hz DBS alters membrane voltage, it is more difficult for neurons to follow 140Hz stimulation, and thus less likely to induced undesired circuit entrainment effect.

Conclusions: DBS-evoked effects on cortical interneurons largely resemble that observed in the hippocampal pyramidal cells, suggesting that membrane voltage perturbation-mediated informational lesion represents a general cellular mechanism of DBS.

References: 1. Grill, W. M., Snyder, A. N., & Miocinovic, S. (2004). Deep brain stimulation creates an informational lesion of the stimulated nucleus. *Neuroreport*, *15*(7), 1137-1140. 2. Lowet, E., Kondabolu, K., Zhou, S., Mount, R. A., Wang, Y., Ravasio, C. R., & Han, X. (2022). Deep brain stimulation creates informational lesion through membrane depolarization in mouse hippocampus. *Nature Communications*, *13*(1), 7709. 3. Piatkevich, K. D., Bensussen, S., Tseng, H. A., Shroff, S. N., Lopez-Huerta, V. G., Park, D., ... & Han, X. (2019). Population imaging of neural activity in awake behaving mice. *Nature*, *574*(7778), 413-417.

Acknowledgements: Funding from NIH 5R01MH122971. 1RF1NS129520, 1R01NS119483

Learning Objectives: 1. Examine whether DBS directly alters membrane voltage across cell types and brain regions. 2. Determine whether electrical stimulation-mediated membrane voltage change interferes with neuronal response to inputs. 3. Evaluate whether informational lesion hypothesis of DBS represents a general cellular mechanism of therapeutic DBS.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O083

Oral Presentations
NEUROSTIMULATION FOR PAIN - CLINICAL UPDATE 03: CLOSED LOOP SCS
14-05-2024 16:30 - 18:20

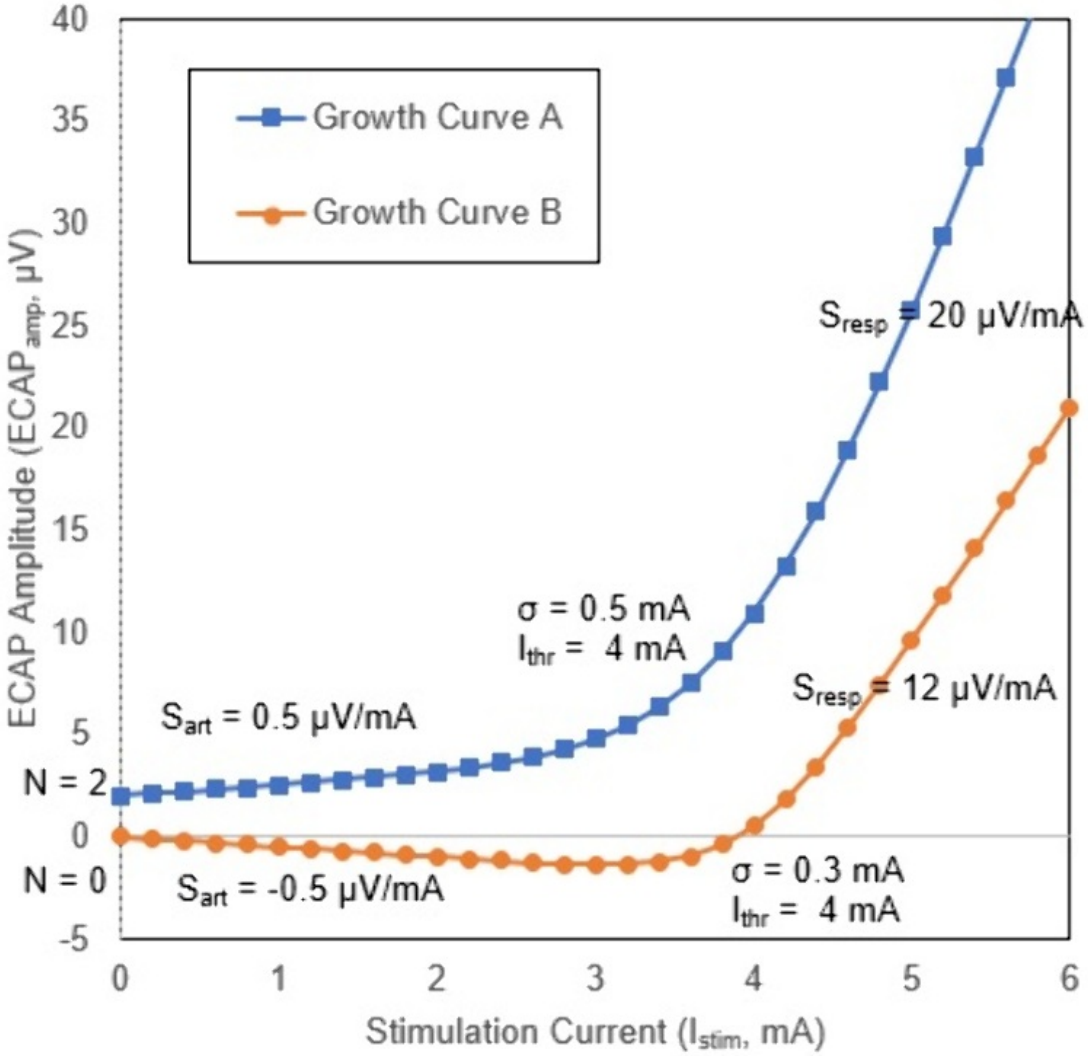
EVOKED COMPOUND ACTION POTENTIAL GROWTH CURVES WITH AND WITHOUT CONCURRENT HIGH-RATE PROGRAMMING

Ashish Gulve, MD[1], David Dinsmoore, MS[2], Malgorzata Straka, PhD[3]
[1]James Cook University Hospital, Pain Management, Middlesbrough, United Kingdom, [2]Medtronic plc, Minneapolis, United States of America, [3]Medtronic, Minneapolis, United States of America

Introduction: The spinal evoked compound action potential (ECAP) is a biopotential resulting from the synchronized activation of dorsal column fibers in response to spinal cord stimulation (SCS). The ECAP is often triphasic, with a first peak (P1), a trough (N1), and a second peak (P2). Assuming the ECAP has been appropriately processed to remove stimulation artifacts, the ECAP amplitude may be described as the voltage difference between P2 and N1[1]. The ECAP amplitude—which grows linearly once the stimulation current (I_{stim}) exceeds the neural threshold for activation—may be plotted with respect to the stimulation current on the so-called *growth curve*. Characteristics of the growth curve, such as ECAP threshold (ECAPT), may be assessed to provide electrophysiologic insight into the state of the spinal cord[2]. While some ECAP sensing SCS systems are constrained to deliver only low-rate programs (LRP) when sensing[3], other systems can also deliver concurrent high-rate programs (HRP). In this study, we will assess growth curves from 14 patients implanted with a novel implantable neurostimulator, or INS (Inceptiv™, Medtronic plc) and receiving SCS both with and without the HRP characteristics of differential target, multiplexed (DTM™) programming[4].

Materials / Methods: During implantation, growth curves in response to 50Hz LRP was collected, and the presence of ECAPs was evaluated for each of the two stimulation quadrants available per lead. Approximately 3 weeks after implantation, patients were programmed with a 50 Hz LRP and a 900 Hz HRP. With both the HRP enabled and disabled, the LRP amplitude was incremented through the perception threshold (PT) and up to the discomfort threshold (DT). ECAPT was extracted from each patient's growth curve. We provide representative growth curves in **Fig. 1**. We present interim results on the first 14 patients

implanted.



Results: We found that across 52 total quadrants tested intraoperatively, 77% of all quadrants had an ECAP present. Approximately three weeks later, we collected growth curves across in 21 quadrants. Comparing the LRP growth curves taken in an upright position to those collected during implantation in a prone position, the ECAPTs increased for 76% of stimulation quadrants (16 of 21 quadrants). Next, we compared the ratio of ECAPTs for growth curves without HRP to those taken with HRP at the 3 weeks visit, both in the seated position. Across 18 quadrants tested, the average ratio was 1.0 +/- 0.1 mA (mean +/- std), or within 1 amplitude step of parity.

Discussion: The impact of high-rate programming on ECAPS generated by low-rate programs has not been assessed in humans. Here we demonstrate that HRPs have minimal direct clinical effects into ECAPs elicited with an LRP. Moreover, we demonstrate changes in the neural interface from implantation to 3 weeks later due to electrode tissue maturation.

Conclusions: The contemporary practice of SCS—including DTM™, among others—includes HRPs. The ECAP is a powerful tool for gaining direct clinical insight into the effect of HRPs, if any, on the ECAPs elicited with an LRP.

Supplemental Data:

References: 1. Chakravarthy K, FitzGerald J, Will A, Trutnau K, Corey R, Dinsmoor D, Litvak L. A Clinical Feasibility Study of Spinal Evoked Compound Action Potential Estimation Methods.

Neuromodulation. 2022 Jan;25(1):75-84 2. Pilitsis JG, Chakravarthy KV, Will AJ, Trutnau KC, Hageman KN, Dinsmoor DA, Litvak LM. The Evoked Compound Action Potential as a Predictor for Perception in Chronic Pain Patients: Tools for Automatic Spinal Cord Stimulator Programming and Control. Front Neurosci. 2021 Jul 12;15:673998. 3. Saluda Medical Evoke® SCS System Clinical Manual, https://www.accessdata.fda.gov/cdrh_docs/pdf19/P190002D.pdf 4. Cedeño DL, Vallejo R, Kelley CA, Platt DC, Litvak LM, Straka M, Dinsmoor DA. Spinal Evoked Compound Action Potentials in Rats With Clinically Relevant Stimulation Modalities. Neuromodulation. 2023 Jan;26(1):68-77.

Acknowledgements:

Learning Objectives: 1. Assess growth curves from patients implanted with a novel implantable neurostimulator receiving SCS both with and without the HRP characteristics of differential target, multiplexed programming (DTMP)

Financial Disclosures: Dr Ashish Gulve: Medtronic Advisory Board & Speaker Program: $501 - $5,000 USD
Boston Scientific: Speaker Program $501 - $5,000
NEVRO: Speaker Program $501 - $5,000
Dr. Straka, and Mr. Dinsmoor are employees of Medtronic plc.

Disclosure: No significant relationships.

O084

Oral Presentations
NEUROSTIMULATION FOR PAIN - CLINICAL UPDATE 03: CLOSED LOOP SCS
14-05-2024 16:30 - 18:20

OBJECTIVE NEURAL INSIGHTS TO PREDICT SCS TRIAL RESPONDERS & NON-RESPONDERS

Jason Pope, MD[1], Erika Petersen, MD[2], Ajay Antony, MD[3], Steven Rosen, MD[4], Abeer Khurram, BSE, MS[5], Ian Gould, MSc, PhD[5], Dean Karantonis, MSBmE, MSBmE[5]
[1]Evolve Restorative Center, Santa Rosa, United States of America, [2]University of Arkansas for Medical Sciences, Little Rock, United States of America, [3]The Orthopaedic Institute, Gainesville, United States of America, [4]Delaware Valley Pain and Spine Institute, Trevose, United States of America, [5]Saluda Medical, Macquarie Park, Australia

Introduction: Drawbacks with traditional spinal cord stimulation (SCS) trials include extended onset of pain relief (hours-days), lead migrations, and compromised outcomes due to medications[1–4]. Additionally, programming optimization becomes challenging as each program/setting evaluation takes ~1-2 days[2-5]. Evoked compound action potential (ECAP)-controlled closed-loop (CL) SCS allows objective confirmation of therapeutic neural activation[5]. We evaluated the feasibility of incorporating ECAPs in SCS trial evaluation at the earliest stages. Here, we report on the immediate trial-phase treatment response post-physiologic ECAP-controlled CL-SCS and feasibility of early SCS trial responder prediction.

Materials / Methods: Participants with chronic, intractable trunk and/or limb pain were enrolled in the prospective, multicenter ECAP study (NCT04319887). For a subset of patients (N=140), an objective SCS evaluation (Saluda Medical, USA) was performed immediately after a traditional trial procedure to confirm neural activation and stable closed-loop therapy. Patient-reported pain relief (PPR), functional improvement assessment while performing previously pain inducing activities, and willingness to proceed to permanent implant were collected on same day (Day-0) and end of trial (EOT). Patients were defined as passing the Day-0 evaluation if they reported PPR≥50%, functional improvement, and willingness to proceed to permanent implant. Day-0 results were compared to EOT outcomes for patients without mid-trial lead migration (N=2). Neurophysiological responses from the trial were analysed for responder groups.

Results: Of the 132/140 patients in stable closed-loop therapy at the time of the Day-0 evaluation, 106 (80%) reported immediate pain response (PPR≥50%) and 120 (91%) reported immediate pain response or functional improvement. A high positive predictive value (PPV) was achieved with 98% (60/61) of patients passing the overall Day-0 evaluation also responding at EOT. The false positive rate (FPR) of this assessment was 6% (1/18); one cervical CRPS patient was a EOT pain and function responder at EOT but did not wish to proceed to permanent implant. 13% (17/132) of patients reported taking anticoagulant/antiplatelet medications. Neurophysiological insights into the profiles and predictors of Day-0 and EOT responders will be presented later.

Discussion: Most patients were rapid pain and/or function responders. The high Day-0 evaluation PPV and low FPR provides confidence in the ability of a same day trial evaluation to predict traditional trial outcomes when objective ECAP measures are considered.

Conclusions: Same day trials may be beneficial for patients using anti-coagulants and for reducing trial complication rates associated with extended trials. Physiologic ECAP-controlled CL therapy may provide objective data to improve prognostic ability of SCS trials in predicting outcomes and reducing associated patient burden.

Supplemental Data:

References: 1. Shealy, C. N., Mortimer, J. T. & Hagfors, N. R. Dorsal Column Electroanalgesia. *J. Neurosurg.* **32**, 560–564 (1970). 2. Thomson, S. J. *et al.* Effects of Rate on Analgesia in Kilohertz Frequency Spinal Cord Stimulation: Results of the PROCO Randomized Controlled

Trial. *Neuromodulation J. Int. Neuromodulation Soc.* **21**, 67–76 (2018). 3. Metzger, C. S. *et al.* A novel fast-acting sub-perception spinal cord stimulation therapy enables rapid onset of analgesia in patients with chronic pain. *Expert Rev. Med. Devices* **18**, 299–306 (2021). 4. Chakravarthy, K., Richter, H., Christo, P. J., Williams, K. & Guan, Y. Spinal Cord Stimulation for Treating Chronic Pain: Reviewing Preclinical and Clinical Data on Paresthesia-Free High-Frequency Therapy: HIGH-FREQUENCY THERAPY FOR CHRONIC PAIN. *Neuromodulation Technol. Neural Interface* **21**, 10–18 (2018). 5. Falowski, S. M., Kim, C. H., Obradovic, M. & Parker, J. L. A Prospective Multicenter Case Series Utilizing Intraoperative Neuromonitoring With Evoked Compound Action Potentials to Confirm Spinal Cord Stimulation Lead Placement. *Neuromodulation J. Int. Neuromodulation Soc.* **25**, 724–730 (2022).

Acknowledgements: Trial sponsored by Saluda Medical.

Learning Objectives: 1. The prognostic value and cost utility of traditional open-loop spinal cord stimulation (SCS) trials is debatable. 2. ECAP-controlled closed-loop SCS allows objective confirmation of therapeutic neural activation from the earliest stages of the trial. 3. ECAP-controlled closed-loop SCS may provide objective data to improve prognostic ability of SCS trials in predicting outcomes and reducing associated patient burden.

Financial Disclosures: Jason Pope, Saluda Medical, Consultant/Advisory Board, >$100,000 USD Erika Petersen, Saluda Medical, Consultant/Advisory Board, $20,001-$100,000 USD Ajay Antony, Saluda Medical, Consultant/Advisory Board, $20,001-$100,000 USD; Education/Research, $20,001-$100,000 USD Abeer Khurram, Saluda Medical, Employee, > $100,000 USD Ian Gould, Saluda Medical, Employee, > $100,000 USD Dean Karantonis, Saluda Medical, Employee, > $100,000 USD

Disclosure: Administrative support to authors funded by Saluda Medical.

O085

Oral Presentations
NEUROSTIMULATION FOR PAIN - CLINICAL UPDATE 03: CLOSED LOOP SCS
14-05-2024 16:30 - 18:20

REAL-WORLD TREATMENT OUTCOMES WITH ECAP-CONTROLLED CLOSED-LOOP SPINAL CORD STIMULATION: THE DUTCH TRIANGLE PAIN CLINIC EXPERIENCE

Lars Elzinga, MD[1], Hans Aukes, MD[2], Johan Van De Minkelis, MD[3]
[1]Triangle Pain Clinic, Location Bravis Hospital, Roosendaal, Netherlands, [2]Triangle Pain Clinic, Location Albert Schweitzer Hospital, Zwijndrecht, Netherlands, [3]Triangle Pain Clinic, Location Elisabeth-tweesteden Hospital, Tilburg, Netherlands

Introduction: Evoked Compound Action Potential (ECAP)-controlled closed-loop spinal cord stimulation (SCS) measures and controls neural activation in real-time. Consistent and accurate neural activation resulted in superior pain relief in closed-loop compared to traditional, open-loop SCS patients [1],[2]. Here, real-world interim results from 3 Dutch clinics (Triangle Pain Clinics) are presented (Netherlands Trial Register, ID: NL7889; NL9392).

Materials / Methods: This ongoing '3-center study' collects real-world patient reported outcomes for pain relief (NRS), satisfaction and stimulation sensation quality (often referred to as paresthesia). In addition, electrophysiological data (ECAPs) and patient therapy utilization data were collected during standard-of-care visits for patients treated with an ECAP-controlled closed-loop SCS system. Here, interim data for 1-, 3-, 6-,12- and 24-months are presented.

Results: A total of 75 patients underwent a permanent implantation starting from November 2020. Baseline characteristics and demographics are presented in Table1. Most frequent pain etiologies were PSPS type 2 with primary pain in the leg. There were 38 females and 37 males permanently implanted.

Table 1: Patient demographics and baseline characteristics

Baseline characteristics	
Gender [Female/Male]	38/37
Mean pain duration [months] (±SD)	78.34 (±75.41)
Mean BMI [kg/cm2] (±SD)	28.64 (±3.49)
Indication PSPS type 2 leg/back PSPS typ 2 neck Polyneuropathies Others	 61 7 5 2

In this real-world, post-approval experience the NRS score is decreasing over time from 8.25 (± 0.08) at baseline to 2.60 (0.81) at 24-months (Fig. 1 A). At all follow-up visits 92% - 100% of the patients were very satisfied or satisfied with the ECAP-controlled closed-loop therapy (Fig.1 B). Additionally, the majority of the patients experience either pleasant sensation or were agnostic to stimulation sensation quality (neither pleasant nor unpleasant stimulation sensation; Fig.1

B).

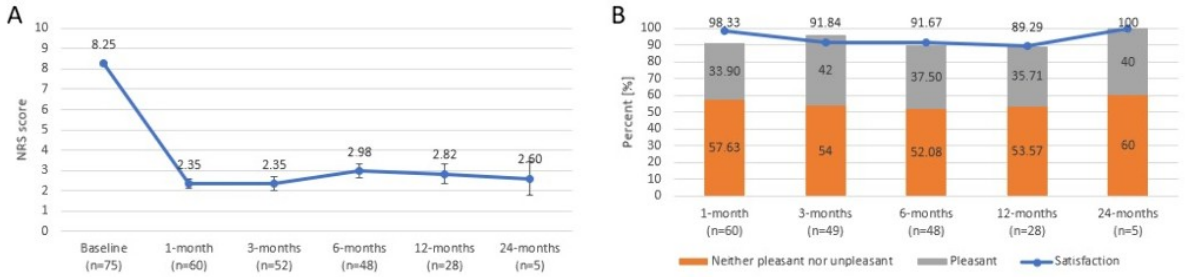


Figure 1: Patient reported outcome. (A) Mean NRS score. Mean NRS (±SEM) at baseline, 1-, 3-, 6-, 12-, and 24-months after permanent implant of a closed-loop spinal cord stimulation device. **(B) Satisfaction and stimulation quality.** Percent of satisfied subjects and patient reported stimulation quality at 1-, 3-, 6-, 12-, and 24-months after permanent implant.

Discussion: ECAP-controlled closed-loop SCS lead to a high degree of pain relief and patient satisfaction at 24-months post-implant. Stimulation sensation quality assessments indicated that the majority of patients felt that ECAP-controlled closed-loop SCS sensation quality was pleasant or were agnostic to it.

Conclusions: The interim results of this data collection suggest that closed-loop SCS results in a stable pain relief over time. However, more long-term data are needed to support these outcomes.

Supplemental Data:

References: [1] N. Mekhail *et al.*, “Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial,” *Lancet Neurol.*, p. S1474442219304144, Dec. 2019, doi: 10.1016/S1474-4422(19)30414-4. [2] N. Mekhail *et al.*, “Durability of Clinical and Quality-of-Life Outcomes of Closed-Loop Spinal Cord Stimulation for Chronic Back and Leg Pain: A Secondary Analysis of the Evoke Randomized Clinical Trial,” *JAMA Neurol.*, Jan. 2022, doi: 10.1001/jamaneurol.2021.4998. [3] M. Russo *et al.*, “Sustained Long-Term Outcomes With Closed-Loop Spinal Cord Stimulation: 12-Month Results of the Prospective, Multicenter, Open-Label Avalon Study,” *Neurosurgery*, Feb. 2020, doi: 10.1093/neuros/nyaa003.

Acknowledgements:

Learning Objectives: To demonstrate ECAP-controlled closed-loop SCS results in stable pain relief over time in real world patients. To show that ECAP-controlled closed-loop SCS leads to an increase in patient satisfaction over 24-months. To demonstrate the patient’s awareness to stimulation sensation in ECAP-controlled closed-loop SCS therapy.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O086

Oral Presentations
NEUROSTIMULATION FOR PAIN - CLINICAL UPDATE 03: CLOSED LOOP SCS
14-05-2024 16:30 - 18:20

SALVAGING OPEN-LOOP SCS LOSS OF EFFICACY WITH ECAP-CONTROLLED CLOSED-LOOP SCS: INTERIM RESULTS

Harold Nijhuis, MD[1], Willem-Jan Hofsté, MD[2], Ralph Aarsman, MD[2]
[1]St. Antonius Hospital, Anesthesiology, Nieuwegein, Netherlands, [2]St. Antonius Hospital, Nieuwegein, Netherlands

Introduction: Spinal cord stimulation (SCS) is an established treatment for patients suffering from chronic pain. Loss or lack of efficacy is the most frequent reason for an SCS explant[1] and is responsible for the 20-25% explant rate over a 5-year period reported in the literature[1–4]. A recent advance has been the development of evoked compound action potential (ECAP)-controlled closed-loop SCS, which uses real-time measurement of dorsal column activation to maintain SCS therapy[5]. Here, we present interim results from a case series of 22 patients who previously had unsuccessful SCS therapy (Burst, High-Frequency, Conventional or DRG stimulation system) due to loss of efficacy and were implanted with an ECAP-controlled closed-loop SCS system.

Materials / Methods: This monocentric case series presents patient reported outcomes for pain relief (NRS) and satisfaction (ranging from “Very satisfied” to “Very unsatisfied”). Additionally, electrophysiological data (ECAPs) and device data (stimulation parameters, patient usage) were collected during standard-of-care visits for patients treated with ECAP-controlled closed-loop SCS system in a real-world setting. All patients had a diagnosis of chronic intractable pain of the trunk and/or limbs (details in Figure 1). Twenty-two patients underwent permanent implantation of the ECAP-controlled closed-loop system at the St. Antonius Hospital in Nieuwegein,

Netherlands.

Sex (F/M/D)	Previous Neuromodulation	Aetiology	Bmi (kg/m^2)
Female	DRG Stimulation	Persistent Spinal Pain Syndrome Type 2	21.8
Female	Burst Stimulation, Conventional SCS High Density Stimulation	Persistent Spinal Pain Syndrome Type 2	26.23
Female	High Frequency	Persistent Spinal Pain Syndrome Type 2	26.4
Female	Burst Stimulation	Persistent Spinal Pain Syndrome Type 2	24.09
Male	Burst Stimulation	Polyneuropathy	27.17
Female	Burst Stimulation, Conventional SCS	Polyneuropathy	26.81
Male	DRG Stimulation	Persistent Spinal Pain Syndrome Type 2	30.59
Female	DRG Stimulation	Complex Regional Pain SyndromeType1	29
Female	DRG Stimulation	Persistent Spinal Pain Syndrome Type 2	25.56
Male	Conventional SCS	Diabetic Polyneuropathy	38.58
Male	Conventional SCS, DRG Stimulation	Persistent Spinal Pain Syndrome Type 2	29.39
Female	Conventional SCS	Persistent Spinal Pain Syndrome Type 2	28.12
Female	Conventional SCS	Persistent Spinal Pain Syndrome Type 2	25.69
Male	Conventional SCS	Persistent Spinal Pain Syndrome Type 2	25.25
Female	DRG Stimulation	Persistent Spinal Pain Syndrome Type 2	35.08
Male	Conventional SCS, DRG Stimulation	Persistent Spinal Pain Syndrome Type 2	21.19
Female	DRG Stimulation	Raynaud's Phenomenon	25.16
Female	DRG Stimulation	Complex Regional Pain SyndromeType1	20.45
Female	Conventional SCS	Complex Regional Pain SyndromeType1	20.18
Male	DRG Stimulation	Polyneuropathy	24.65
Female	DRG Stimulation	Complex Regional Pain SyndromeType1	31.89
Female	Conventional SCS, DRG Stimulation	Persistent Spinal Pain Syndrome Type 2	24.45

Figure 1: Patient Characteristics and Demographics. DRG = Dorsal Root Ganglion; SCS = Spinal Cord Stimulation

Results: Mean (±SEM) baseline (n=22) numerical rating scores (NRS) were 8.2±0.2 (Figure 2A). At 1-month (n=19) average NRS scores decreased to 4.3±0.4, at 3-months (n=19) to 4.4±0.4, and at 6-months (n=22) to 4.2±0.5 (Figure 2A). During standard of care follow-up visits, patient satisfaction was collected (Figure 2B). At the 1-month visits, 95% (n=18 out of 19) of the patients reported being very satisfied, satisfied with their therapy. At 3-months 100% (n=18 out of 18) and at 6-months 95% (n=21 out of 22) of the patients were very satisfied, satisfied or quite satisfied with the ECAP-controlled closed-loop therapy (Figure

2B).

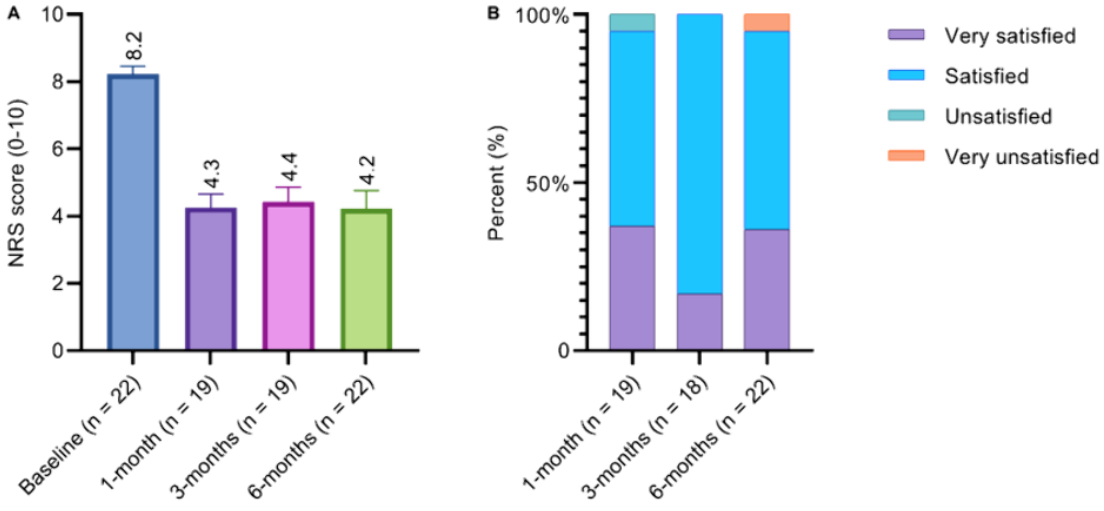


Figure 2: Patient reported outcome NRS scores (A) Mean NRS score (±SEM) and Patient Satisfaction (B) at 1-, 3-, and 6-months follow up visit. Data collection is ongoing and interim results are presented.

Discussion: ECAP-controlled closed-loop SCS results in robust pain relief and satisfaction in patients who previously experienced loss of efficacy.

Conclusions: Preliminary data suggests that ECAP-controlled closed-loop can potentially recapture pain relief and patient satisfaction in chronic pain patients who underwent explants due to loss of efficacy with an open-loop neurostimulation system (SCS or DRG). However, additional research and follow-up is required to validate these preliminary findings.

Supplemental Data:

References: 1. Pope, J.E., Deer, T.R., Falowski, S., Provenzano, D., Hanes, M., Hayek, S.M., Amrani, J., Carlson, J., Skaribas, I., Parchuri, K., et al. (2017). Multicenter Retrospective Study of Neurostimulation With Exit of Therapy by Explant. Neuromodulation Technol. Neural Interface *20*, 543–552. 10.1111/ner.12634. 2. Van Buyten, J.-P., Wille, F., Smet, I., Wensing, C., Breel, J., Karst, E., Devos, M., Pöggel-Krämer, K., and Vesper, J. (2017). Therapy-Related Explants After Spinal Cord Stimulation: Results of an International Retrospective Chart Review Study. Neuromodulation Technol. Neural Interface *20*, 642–649. 10.1111/ner.12642. 3. Al-Kaisy, A., Royds, J., Al-Kaisy, O., Palmisani, S., Pang, D., Smith, T., Padfield, N., Harris, S., Wesley, S., Yearwood, T.L., et al. (2020). Explant rates of electrical neuromodulation devices in 1177 patients in a single center over an 11-year period. Reg. Anesth. Pain Med. *45*, 883–890. 10.1136/rapm-2020-101681. 4. Wang, V.C., Bounkousohn, V., Fields, K., Bernstein, C., Paicius, R.M., and Gilligan, C. (2020). Explantation Rates of High Frequency Spinal Cord Stimulation in Two Outpatient Clinics. Neuromodulation Technol. Neural Interface, ner.13280. 10.1111/ner.13280. 5. Mekhail, N., Levy, R.M., Deer, T.R., Kapural, L., Li, S., Amirdelfan, K., Hunter, C.W., Rosen, S.M., Costandi, S.J., Falowski, S.M., et al. (2022). Durability of Clinical and Quality-of-Life Outcomes of Closed-Loop Spinal Cord Stimulation for Chronic Back and Leg Pain: A Secondary Analysis of the Evoke Randomized Clinical Trial. JAMA Neurol. *79*, 251–260. 10.1001/jamaneurol.2021.4998.

Acknowledgements: Trial sponsored by Saluda Medical.

Learning Objectives: 1. To learn that ECAP-controlled closed-loop SCS results in robust pain relief in patients who previously experienced loss of efficacy. 2. To understand that ECAP-controlled closed-loop SCS results in robust satisfaction in patients who previously experienced loss of efficacy. 3. To learn that ECAP-controlled closed-loop can potentially recapture pain relief and patient

satisfaction in chronic pain patients who underwent explants due to loss of efficacy with an open loop neurostimulation system (SCS or DRG).

Financial Disclosures: Harold Nijhuis, Saluda Medical, Consultant/Advisory Board, 18,000 Willem-Jan Hofsté, Saluda Medical, Consultant/Advisory Board, 800 Ralph Aarsman, Saluda Medical, Consultant/Advisory Board, 800

Disclosure: Administrative support to authors funded by Saluda Medical.

O087

Oral Presentations
NEUROSTIMULATION FOR PAIN - CLINICAL UPDATE 03: CLOSED LOOP SCS
14-05-2024 16:30 - 18:20

VALIDATION OF A HOLISTIC COMPOSITE OUTCOME FOR THE EVALUATION OF CHRONIC PAIN INTERVENTIONS

Rod Taylor, PhD[1], Daniel Clauw, PhD[2], Sam Eldabe, FRCA[3], Jan Willem Kallewaard, MD[4,5], Peter Staats, MD[6]
[1]University of Glasgow, Population Health Research, Glasgow, United Kingdom, [2]University of Michigan, Ann Arbor, United States of America, [3]James Cook Hospital, Pain Department, Middlesbrough, United Kingdom, [4]Rijnstate Hospital, Arnhem, Netherlands, [5]Amsterdam University Medical Centre, Amsterdam, Netherlands, [6]National Spine & Pain Centers, Pemier Pain Centers, Shrewsbury, United States of America

Introduction: Chronic pain is a personal experience influenced to varying degrees by biopsychosocial factors.[1] However, the assessment of response to chronic pain interventions remains primarily focused on treatment effects on pain intensity which may not adequately capture the chronic pain experience. Composite outcomes provide a more comprehensive evaluation of treatment response to a complex condition. A holistic composite outcome for chronic pain has been developed that uses recommended and validated patient reported outcome measures (PROMs), to evaluate treatment response based on changes that are meaningful to patients based on their level of pre-treatment impairment.[2] This study describes the validation of this novel holistic composite outcome.

Materials / Methods: The holistic composite measure consists of five outcome domains: pain intensity, sleep quality, health-related quality of life (HRQoL), physical and emotional function. Validated PROMs were used to assess treatment response in each of the domains with the use of published minimal clinically important differences (MCIDs). The composite score is summarized as the Holistic MCID, obtained via the sum of each of the MCID domain scores, adjusted for each patients' number of impaired domains at baseline. Validation was based on data from both treatment arms of the EVOKE trial for chronic back and leg pain with 111 patients reporting complete outcomes from 1 to 24-months post-implant.[3,4] Internal consistency of the Holistic MCID was assessed using Cronbach's alpha statistic and dimensional exploration using Principal Component Analysis (PCA). Three approaches were used to assess external validity by using the Patients' Global Impression of Change (PGIC), EQ-VAS and 'leave-one-out' validation method.

Results: Meaningful patient improvement following SCS implantation, quantified by ≥1 MCID following SCS, was seen at all timepoints for each of the individual outcome domains. A Cronbach's alpha of >0.7 was observed at each follow-up, demonstrating strong internal consistency. PCA showed one overarching holistic dimension to be present in the composite measure. External validity was demonstrated by an increase in the Holistic MCID score being associated with both increased PGIC, EQ-VAS score and by each of the outcome domains in the 'leave-one-out' analysis (all $p<0.001$).

Discussion: By capturing treatment responses across five different outcome domains in a single measure, the Holistic MCID provides a more comprehensive and representative measure of the chronic pain experience for chronic pain patients and healthcare providers than pain response alone.

Conclusions: The Holistic MCID provides a valid measure of the biopsychosocial assessment of response for patients following a chronic pain intervention.

Supplemental Data:

References: 1. Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. Pain 2020;161(9):1976-1982. 2. Levy R, Mekhail N, Abd-Elsayed A, et al. Holistic treatment response: an international expert panel

definition and criteria for a new paradigm in the assessment of clinical outcomes of spinal cord stimulation. Neuromodulation 2023;26(5):1015-1022. 3. Mekhail N, Levy RM, Deer TR, et al. Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial. Lancet Neurology 2020;19(2):123-134. 4. Mekhail N, Levy RM, Deer TR, et al. Durability of clinical and quality-of-life outcomes of closed-loop spinal cord stimulation for chronic back and leg pain: A secondary analysis of the evoke randomized clinical trial. JAMA Neurology 2022;3(79):251-260.

Acknowledgements:

Learning Objectives: 1. The pain intensity outcome alone is insufficient to capture the complexity of the chronic pain experience and treatment response 2. A holistic composite outcome that includes five biopsychosocial components has been developed to provide a more comprehensive evaluation of treatment response to chronic pain interventions 3. The Holistic MCID provides a valid measure for evaluation of the comprehensive biopsychosocial response to treatments for chronic pain patients

Financial Disclosures: Rod Taylor (Saluda Medical, consultant, $501 - $5,000 USD) Daniel Clauw (No significant relationships) Sam Eldabe (Saluda Medical, consultant, $501 - $5,000 USD) Jan Willem Kallewaard (Saluda Medical, consultant, $501 - $5,000 USD) Peter Staats (Saluda Medical, consultant, $5,001 - $20,000 USD; Education / Research, $20,001 - $100,000 USD; Stock options, $20,001 - $100,000 USD)

Disclosure: No significant relationships.

O088

Oral Presentations
NEUROSTIMULATION FOR PAIN - CLINICAL UPDATE 03: CLOSED LOOP SCS
14-05-2024 16:30 - 18:20

EVALUATING LONG-TERM CHRONIC PAIN EXPERIENCE USING HOLISTIC OUTCOMES: 3-YEAR RESULTS WITH ECAP-CONTROLLED CLOSED LOOP SCS

Corey Hunter, MD[1], Leonardo Kapural, MD[2], Sean Li, MD[3], Kasra Amirdelfan, MD[4], Nagy Mekhail, MD[5]
[1]Ainsworth Institute of Pain Management, New York, United States of America, [2]Carolinas Pain Institute and Wake Forest University School of Medicine, Winston-Salem, United States of America, [3]Premier Pain Centers, Shrewsbury, United States of America, [4]IPM Medical Group, Walnut Creek, United States of America, [5]Cleveland Clinic, Evidence-based Pain Management Research, Cleveland, United States of America

Introduction: Chronic pain patients may experience impairments in multiple health-related domains. The design and interpretation of clinical trials of chronic pain interventions, however, remains primarily focused on treatment effects on pain intensity. A holistic composite outcome for chronic pain has been developed that uses IMMPACT recommended and validated patient reported outcome measures (PROMs) to evaluate treatment response based on changes that are meaningful to patients' every-day life based on their level of pre-treatment impairment.[1] Herein, we report a novel, multidimensional holistic treatment response and the neurophysiologic measurements observed for the cohort of the EVOKE RCT (NCT02924129),[2-4] that were assigned to and remained in ECAP-controlled closed-loop SCS (CL-SCS) for the 36-month study period.

Materials / Methods: The holistic composite measure consists of five outcome domains: pain intensity, sleep quality, health-related quality of life, physical and emotional function.[4] Validated PROMs were used to assess treatment response in each of the domains with the use of published minimal clinically important differences (MCIDs). The composite score is summarized as a cumulative responder score calculated to reflect total MCIDs across all impaired domains, and as the Holistic MCID, obtained via the sum of each of the MCID domain scores, adjusted for each patients' number of impaired domains at baseline. Objective physiologic measurements of therapy delivery were also collected.

Results: Forty-one patients randomized to CL-SCS remained in their treatment allocation and were followed-up through 36-months. At all timepoints, all patients obtained an MCID in ≥1 domain impaired at baseline. The cumulative responder score was >11 MCIDs at all timepoints. The Holistic MCID was ≥2.5 at all timepoints. No significant differences were observed in the number of MCIDs achieved in the individual holistic domains, cumulative responder score and Holistic MCID between the 3- and 36-month timepoints ($p>0.05$ for all). Patients' stimulation was supra-ECAP threshold >95% of the time with no differences between 3- and 36-month assessments.

Discussion: All patients obtained a clinically meaningful change in ≥1 outcome domain at all timepoints. Responders in multiple domains were observed as early as 3-months following SCS implantation and treatment response was sustained through 36-months.

Conclusions: The results of this study suggest that ECAP-controlled CL-SCS, delivering consistent neural activation, can result in true improvement of the complex, multifactorial chronic pain experience.

Supplemental Data:

References: 1. Levy RM, et al. Holistic Treatment Response: An International Expert Panel Definition and Criteria for a New Paradigm in the Assessment of Clinical Outcomes of Spinal Cord Stimulation. Neuromodulation 2023; 26: 1015-1022. 2. Mekhail N, et al. Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised,

controlled trial. Lancet Neurol 2020*;* 19: 123-134. 3. Mekhail N, et al. Durability of Clinical and Quality-of-Life Outcomes of Closed-Loop Spinal Cord Stimulation for Chronic Back and Leg Pain: A Secondary Analysis of the Evoke Randomized Clinical Trial. JAMA Neurol 2022; 79: 251-260. 4. Mekhail NA, et al. ECAP-Controlled Closed-loop versus Open-Loop SCS for the Treatment of Chronic Pain: 36-Month Results of the EVOKE Blinded Randomized Clinical Trial. Reg Anesth Pain Med 2023; In press.

Acknowledgements: Submitted on behalf of the EVOKE Study Group. Trial sponsored by Saluda Medical.

Learning Objectives: 1. The holistic composite outcome provides a comprehensive approach to the assessment of treatment impact on chronic pain patients' overall health and well-being 2. Evaluation of a holistic treatment response is paramount in chronic pain populations given that impairment can be present in several domains other than just pain intensity 3. ECAP-controlled closed-loop SCS can provide consistent neural activation to produce a long-term holistic response

Financial Disclosures: Corey Hunter, Saluda Medical, Consultant/Advisory Board ($5,001 - $20,000 USD); Abbott - Consultant/ Advisory Board, Research ($20,001 - $100,000 USD); PainTEQ - Stock Options (> $100,000 USD); Vertos - Stock Options ($20,001 - $100,000 USD); Mainstay - Stock Options (> $100,000 USD); Nalu - Stock Options (> $100,000 USD); Vivex - Stock Options ($20,001 - $100,000 USD); Tissuegene - Research (> $100,000 USD); Spine Biopharma - Research ($5,001 - $20,000 USD); Avertitas - Research ($5,001 - $20,000 USD); FUSMobule - Research ($5,001 - $20,000 USD) Leonardo Kapural, Saluda Medical, Consultant/Advisory Board, $500-$5000 USD; Education/Research, $500-$5000 Sean Li, Consultant/Advisory Board, $20,001-$100,000 USD Kasra Amirdelfan, Consultant/Advisory Board, $500-$5000 USD Nagy Mekhail, Saluda Medical, Consultant/Advisory Board (Medical Monitor), $5,001-$20,000 USD; Mainstay, Consultant/Advisory Board (Medical Monitor), $5,001-$20,000 USD; Nevro, Consultant/Advisory Board (Medical Monitor), $0 USD; Sollis Therapeutics, Consultant/Advisory Board (Medical Monitor), $5,001-$20,000 USD; Vertos, Consultant/Advisory Board (Medical Monitor), $0 USD; Vivex Biologics, Consultant/Advisory Board (Medical Monitor), $500-$5000 USD; Mesoblast, Education/Research, $0 USD; Neuros, Education/Research, $0 USD

Disclosure: Administrative support to authors funded by Saluda Medical.

O089

Oral Presentations
NEUROSTIMULATION FOR PAIN - CLINICAL UPDATE 03: CLOSED LOOP SCS
14-05-2024 16:30 - 18:20

CLINICAL HOLISTIC RESPONDERS IN PATIENTS WITH PERSISTENT SPINAL PAIN SYNDROME TYPE II TREATED BY SUBTHRESHOLD SPINAL CORD STIMULATION COMPARED TO BEST MEDICAL TREATMENT: PRELIMINARY RESULTS OF A RCT

Lisa Goudman, PhD[1], Koen Putman, PhD[2], Maxime Billot, PhD[3], Manuel Roulaud, MSc[3], Philippe Rigoard, MD[4], Tradition Consortium, MD[5], Maarten Moens, MD[6]
[1]Laarbeeklaan 103, Stimulus Research Group, Jette, Belgium, [2]Vrije Universiteit Brussel, I-cher, Jette, Belgium, [3]CHU de Poitiers, Neurosurgery Departement/prismatics Lab, Poitiers, France, [4]Poitiers University, Spinal Neurosurgery, Neuromodulation, Poitiers, France, [5]Vrije Universiteit Brussel, Jette, Belgium, [6]Vrije Universiteit Brussel, Stimulus Research Group, Jette, Belgium

Introduction: Integrating information on bodily functions, pain intensity and quality of life into one composite measure of a holistic responder has recently been proposed as a useful method to evaluate treatment efficacy of Spinal Cord Stimulation (SCS) in patients with therapy-refractory Persistent Spinal Pain Syndrome Type II (PSPS-T2). Previous studies already demonstrated the efficacy of standard SCS over Best Medical Treatment (BMT) and the superiority of new subthreshold (i.e. paresthesia free) SCS paradigms compared to standard SCS. Nevertheless, the efficacy of subthreshold SCS compared to BMT has not yet been investigated in patients with PSPS-T2, neither with unidimensional outcomes, nor with a composite measure. The current objective is to examine whether subthreshold SCS, compared to BMT, provided to patients with PSPS-T2 results in a different proportion of clinical holistic responders (as composite measure) at 6 months.

Materials / Methods: A two-arm multicentre randomised controlled trial is conducted whereby 114 patients will be randomised (1:1) to (a) BMT or (b) paresthesia-free SCS. After a follow-up period of 6 months (primary time endpoint), patients receive the opportunity to cross over towards the other treatment group. The primary outcome is the proportion of clinical holistic responders at 6 months (i.e. a composite measure of pain intensity, medication, disability, health-related quality of life and patient satisfaction). The secondary outcomes are work status, self-management, anxiety, depression and healthcare expenditure.

Results: Preliminary results collected from patients who are already included in this study will be discussed.

Discussion: Within the TRADITION project we propose to shift the focus from a unidimensional outcome measure towards a composite measure as primary outcome measure to evaluate the efficacy of currently used subthreshold SCS paradigms.

Conclusions: The lack of methodologically rigorous trials exploring the clinical efficacy and socio-economic consequences of subthreshold SCS paradigms is pressing, especially in light of the growing burden of PSPS-T2 on society.

Supplemental Data:

References: 1) Goudman L, Putman K, Van Doorslaer L, Billot M, Roulaud M, Rigoard P; TRADITION consortium; Moens M. Proportion of clinical holistic responders in patients with persistent spinal pain syndrome type II treated by subthreshold spinal cord stimulation compared to best medical treatment: a study protocol for a multicentric randomised controlled trial (TRADITION). Trials. 2023 Feb 20;24(1):120. doi: 10.1186/s13063-023-07140-3.

Acknowledgements:

Learning Objectives: 1) To learn about the use of holistic outcome measurements as primary outcome variable in a randomized controlled trial. 2) To know preliminary data about the efficacy of subthreshold SCS versus conventional medical management for patients with Persistent Spinal Pain Syndrome Type II. 3) Being able to interpret shortcomings and strengths of currently available RCT's in the field of neuromodulation.

Financial Disclosures: This study is funded by Research Foundation Flanders (FWO), Belgium (project number 12ZF622N).

Disclosure: No significant relationships.

O090

Oral Presentations
NEUROSTIMULATION FOR PAIN - CLINICAL UPDATE 03: CLOSED LOOP SCS
14-05-2024 16:30 - 18:20

DURABILITY OF ECAP-CONTROLLED, CLOSED-LOOP SCS IN REAL-WORLD PATIENTS: DR STUDY FINAL RESULTS

Harold Nijhuis, MD[1], Jan Willem Kallewaard, MD[2,3], Johan Van De Minkelis, MD[4], Willem-Jan Hofsté, MD[5], Lars Elzinga, MD[6], Philippa Armstrong, MB ChB[7], Ismaïl Gültuna, MD[8], Emre Almac, MD[9], Ganesan Baranidharan, FRCA[10], Serge Nikolic, MD[11], Ashish Gulve, MD[12], Jan Vesper, MD[13], Frank Huygen, MD, PhD[14]
[1]St. Antonius Hospital, Anesthesiology, Nieuwegein, Netherlands, [2]Rijnstate Hospital, Velp, Netherlands, [3]Academisch Medisch Centrum, Amsterdam, Netherlands, [4]Elisabeth-Tweesteden Hospital, Tilburg, Netherlands, [5]St. Antonius Hospital, Nieuwegein, Netherlands, [6]Bravis Hospital, Roosendaal, Netherlands, [7]York and Scarborough Teaching Hospitals, York, United Kingdom, [8]Albert Schweitzer Hospital, Zwijndrecht, Netherlands, [9]Alrijne Hospital, Leiderdorp, Netherlands, [10]Leeds Teaching Hospital, Leeds, United Kingdom, [11]St Bartholomew's Hospital, London, United Kingdom, [12]James Cook University Hospital, Middlesbrough, United Kingdom, [13]University Hospital Düsseldorf, Düsseldorf, Germany, [14]Erasmus University Medical Center, Rotterdam, Netherlands

Introduction: Evoked compound action potential (ECAP)-controlled closed-loop spinal cord stimulation (SCS) provides superior pain relief compared to traditional 'open-loop' SCS due to its ability to maintain consistent and accurate activation of the spinal cord[1,2]. Results from controlled studies are sometimes hard to repeat in the real-world. Here, final real-world results of the multi-center data collection study are presented from 13 centers across Europe.

Materials / Methods: This multi-center data collection (Clinical Trials registry ID: NCT05272137) was designed to collect patient reported outcomes for pain relief, Verbal Numerical Rating Scale (NRS) and satisfaction (four options, ranging from "Very satisfied" to "Very unsatisfied"). Additionally, electrophysiological data (ECAPs) and device data (stimulation parameters, patient usage) were collected during standard-of-care visits for patients treated with ECAP-controlled closed-loop SCS system (Evoke® SmartSCS™, Saluda Medical, Australia) in a real-world setting under normal clinical use in Europe. Patients presenting with complex regional pain syndrome, persistent spinal pain syndrome type 2 and polyneuropathy, post amputation stump pain and peripheral plexopathy were enrolled (Fig.1). Post-market visit requirements followed standard of care; if a follow-up visit was not performed, or patient outcomes were not taken due to time limitations, it was not regarded as a protocol
deviation.

Etiology	Count
Persistent Spinal Pain Syndrome Type 2	121
Complex Regional Pain Syndrome	10
Others including Polyneuropathy, Mononeuropathy, Post-Amputation Pain, Peripheral Plexopathy	13
Unknown	4

Figure 1: Etiologies studied.

Results: A total of 148 patients underwent permanent implantation of the ECAP-controlled closed-loop system. Mean (±SEM) baseline (n=148) NRS scores were 8.196±0.08449. At 3-months (n=103) average NRS scores decreased to 2.553±0.2266, at 6-months (n=91) to 2.648±0.2541 and at 12-

months (n=85) to 2.624±0.2419 (Fig.2A). At 12-months there were 76% responders (≥50% pain relief), and 41% high-responders (≥80% pain relief; Fig.2B). At 12-months, 92% of the patients reported being very satisfied or satisfied with their therapy (Fig.2C; n=78 of 85 patients).

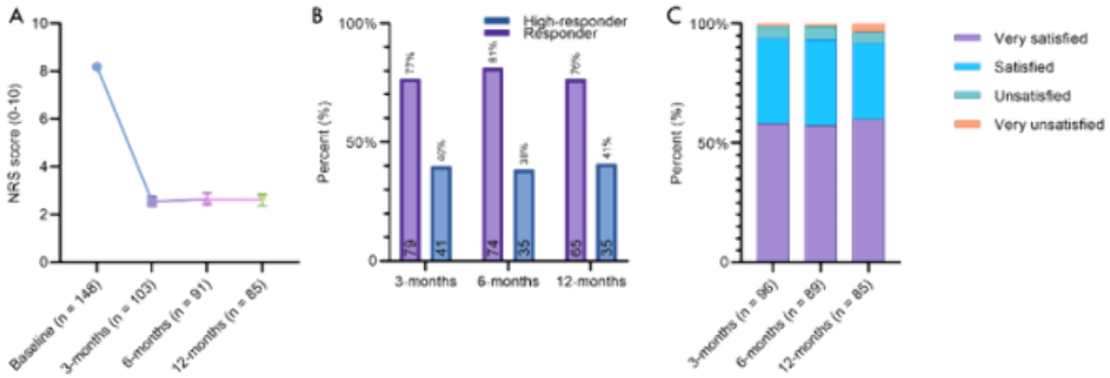


Figure 2: Patient Reported Outcomes and Electrophysiological Measurements.

A. Mean (±SEM) baseline (n=148) NRS scores were 8.196±0.08449. At 3-months (n=103) average NRS scores decreased to 2.553±0.2266, at 6-months (n=91) to 2.648±0.2541, at 12-months (n=85) to 2.624±0.2419.

B. Patients who showed exceptional pain relief were defined as high-responders (≥80%) and patients who responded with ≥50% pain relief were defined as responders. At 3-months, there were 77% responders and 40% high-responders, at 6-months, 81% responders and 38% high-responders, at 12-months 76% responders and 41% high-responders.

C. At 12-months, 92% of the patients reported being very satisfied or satisfied with their therapy (n=78 of 85 patients).

Discussion: Results strongly suggest that ECAP-controlled closed-loop SCS can lead to a high degree of pain relief and patient satisfaction 12-months post-implantation in a real-world setting.

Conclusions: Real-world results are comparable to results from the controlled AVALON multi-center-study[3] and the controlled EVOKE randomized controlled trial[1] in pain relief outcomes.

Supplemental Data:

References: 1. Mekhail, N. *et al.* Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial. *Lancet Neurol.* S1474442219304144 (2019) doi:10.1016/S1474-4422(19)30414-4. 2. Mekhail, N. *et al.* Durability of Clinical and Quality-of-Life Outcomes of Closed-Loop Spinal Cord Stimulation for Chronic Back and Leg Pain: A Secondary Analysis of the Evoke Randomized Clinical Trial. *JAMA Neurol.* **79**, 251–260 (2022). 3. Russo, M. *et al.* Sustained Long-Term Outcomes With Closed-Loop Spinal Cord Stimulation: 12-Month Results of the Prospective, Multicenter, Open-Label Avalon Study. *Neurosurgery* (2020) doi:10.1093/neuros/nyaa003.

Acknowledgements: Trial sponsored by Saluda Medical.

Learning Objectives: 1. To learn that ECAPs are used to adjust stimulation levels in real-time to maintain consistent activation of the spinal cord. 2. To learn that ECAP-controlled closed-loop SCS in the real-world can lead to a high degree of pain relief 12-months post-implantation. 3. To learn that ECAP-controlled closed-loop SCS in the real-world can lead to a high patient satisfaction 12-months post-implantation.

Financial Disclosures: Harold Nijhuis, Saluda Medical, Consultant/Advisory Board, 18,000 Jan-Willem Kallewaard, Saluda Medical, Consultant/Advisory Board, 6,000 Johan van de Minkelis has no

relevant conflicts of interest to disclose Willem-Jan Hofsté, Saluda Medical, Consultant/Advisory Board, 800 Lars Elzinga has no relevant conflicts of interest to disclose Philippa Armstrong, Saluda Medical, Consultant/Advisory Board, 700 Ismaïl Gültuna has no relevant conflicts of interest to disclose Emre Almac has no relevant conflicts of interest to disclose Ganesan Barani, Saluda Medical, Consultant/Advisory Board, 1200 Serge Nikolic, Saluda Medical, Consultant/Advisory Board, 13,000 Ashish Gulve has no relevant conflicts of interest to disclose Jan Vesper has no relevant conflicts of interest to disclose Frank Huygen has no relevant conflicts of interest to disclose

Disclosure: Administrative support to authors funded by Saluda Medical.

O091

Oral Presentations
NEUROSTIMULATION FOR PAIN - CLINICAL UPDATE 03: CLOSED LOOP SCS
14-05-2024 16:30 - 18:20

CONSISTENT NEURAL ACTIVATION USING PRECISION, DOSE-CONTROL CLOSED-LOOP SCS LEADS TO DURABLE 3-YEAR OUTCOMES

Nagy Mekhail, MD[1], Leonardo Kapural, MD[2], Steven Falowski, MD[3], Sean Li, MD[4], Timothy Deer, MD[5]
[1]Cleveland Clinic, Evidence-based Pain Management Research, Cleveland, United States of America, [2]Carolina's Pain Institute and Center for Clinical Research, Winston-Salem, United States of America, [3]Argires-Marotti Neurosurgical Associates of Lancaster, Lancaster, United States of America, [4]Premier Pain Centers, Shrewsbury, United States of America, [5]The Spine and Nerve Center of the Americas, Pain, Charleston, United States of America

Introduction: A recently introduced spinal cord stimulation (SCS) system delivers ECAP-controlled therapy to guide programming and confirm activation of the intended target; and to deliver closed-loop therapy to maintain accurate and consistent neural activation with every stimulus (CL-SCS). The EVOKE double-blind RCT evaluated the safety and efficacy of ECAP-controlled CL-SCS for chronic back and leg pain (NCT02924129).[1-3] Herein we report the results for the cohort that were assigned to and remained in CL-SCS for the 36-month study period to elucidate the durability of CL-SCS therapy and the long-term neurophysiological dose-response.

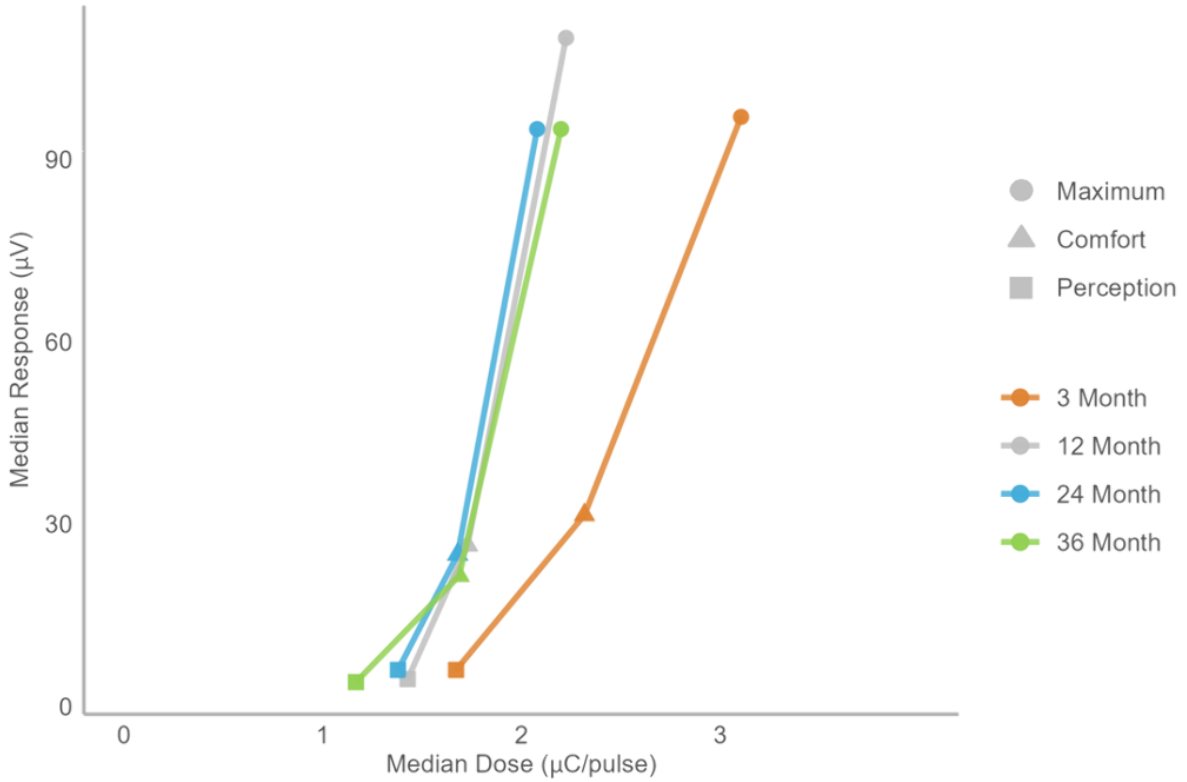
Materials / Methods: Pain relief was assessed by ≥50% and ≥80% reduction in overall back and leg pain compared to baseline (VAS). Objective neurophysiological data, including measures of spinal cord activation, were collected. Differences between 3- and 36-months timepoints for pain relief and neurophysiological data were evaluated.

Results: Forty-one patients randomized to CL-SCS that remained in CL-SCS were followed-up through 36-months. Most patients obtained ≥50% reduction (83% [34/41]) and ≥80% reduction (59% [24/41]) in pain at 36-months, with no differences in these rates between 3- and 36-months (p=0.083 and p=0.405, respectively). For patients obtaining ≥50% response at 3-months (88%), there was >90% chance of maintaining this response through 36-months. At all timepoints, in-clinic therapy accuracy was within <4μV of the target ECAP, system utilization was >80%, and stimulation was above ECAP threshold >95% of the time. The patients' ECAP dose was ≥19.3μV and the average dose ratio was >1.3. There was significantly less utilization (p<0.001) and ECAP dose (p=0.005) from 3- to 36-months. Additionally, there was a significant left-shift in the dose-response curves at perception, comfort, and maximum (discomfort) threshold from 3- to 36-months (Figure 1). The slope of the dose-response curve (μV/μC), representative of spinal cord sensitivity to stimulation, did not significantly change over time (p=0.593).

Discussion: The stability of therapeutic effect while requiring reduced ECAP dose discredits the notion previously discussed in SCS publications that consistent activation may lead patients to develop a tolerance to SCS over time and that habituation may explain loss of therapeutic effect.

Conclusions: ECAP-controlled CL-SCS resulted in sustained, durable pain relief through 36-months with no evidence of loss of therapeutic effect. The results suggest that when ECAP-controlled CL-SCS is used as intended, less therapy may be required overtime to achieve the same clinical benefit. Further, long-term neurological safety with CL-SCS was supported by no difference in spinal cord sensitivity overtime and no reported neurological deficits.

Supplemental Data: Figure 1. Dose-Response Curves for CL-SCS through 36 months



References: 1. Mekhail N, et al. Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial. Lancet Neurol 2020*;* 19: 123-134. 2. Mekhail N, et al. Durability of Clinical and Quality-of-Life Outcomes of Closed-Loop Spinal Cord Stimulation for Chronic Back and Leg Pain: A Secondary Analysis of the Evoke Randomized Clinical Trial. JAMA Neurol 2022; 79: 251-260. 3. Mekhail NA, et al. ECAP-Controlled Closed-loop versus Open-Loop SCS for the Treatment of Chronic Pain: 36-Month Results of the EVOKE Blinded Randomized Clinical Trial. Reg Anesth Pain Med 2023; In press.

Acknowledgements:

Learning Objectives: 1. ECAP-controlled CL-SCS enables monitoring of physiological adherence to the prescribed neural activation level to maximize individual patient outcomes. 2. ECAP-controlled CL-SCS provides durable improvements in chronic pain with no evidence of loss of therapeutic effect through 36-months follow-up. 3. Loss of therapeutic effect (usually described in SCS literature as tolerance or habituation) is not a failure mode for ECAP-controlled CL-SCS.

Financial Disclosures: Nagy Mekhail: - Saluda Medical, Consultant / Advisory Board (Medical Monitor), $5,001 - $20,000 - Mainstay, Consultant / Advisory Board (Medical Monitor), $5,001 - $20,000 - Nevro, Consultant / Advisory Board (Medical Monitor), $0 - Sollis Therapeutics, Consultant / Advisory Board (Medical Monitor), $501 - $5000 - Vertos, Consultant / Advisory Board (Medical Monitor), $0 - Vivex Biologics, Consultant / Advisory Board (Medical Monitor), $1 - $500 - Mesoblast, Education / Research, $0 - Neuros, Education / Research, $0 Leo Kapural: - Saluda Medical, Consultant / Advisory Board, $501-$5000 - Saluda Medical, Education / Research, $501-$5000 Steven Falowski: - Saluda Medical, Consultant / Advisory Board, $20,001 - $100,000 - Saluda Medical, Education / Research, $5,001 - $20,000 - Saluda Medical, Stock Options, >$100,000 Sean Li: - Saluda Medical, Consultant / Advisory Board, $20,001 - $100,000 Tim Deer: - Saluda Medical, Consultant / Advisory Board, $5,001 - $20,000

Disclosure: No significant relationships.

O092

Oral Presentations
NEUROSTIMULATION FOR PAIN - CLINICAL UPDATE 03: CLOSED LOOP SCS
14-05-2024 16:30 - 18:20

MEDICATION TAPERING DURING TREATMENT WITH ECAP-CONTROLLED CLOSED-LOOP SPINAL CORD STIMULATION

Tony Van Havenbergh, MD, PhD, Pieter Van Looy, RN, Raf Van Paesschen, MD
ZAS Hospitals, Neurosurgery, Antwerp, Belgium

Introduction: Little is known about the effects of medication on spinal-cord-stimulation (SCS) and patient's experiences with SCS therapy. Chronic opioid use can cause opioid-induced-hyperalgesia (OIH) due to neuroplastic changes in the central nervous system (1,2) and SCS has been shown to reduce opioid intake (3). It is unclear if the central effects of opioids in turn affect patients' experiences with SCS. This study was designed to prospectively evaluate such interactions in a clinical SCS user population.

Materials / Methods: 20 patients routinely selected for SCS with a pain condition approved for SCS in Belgium will be enrolled in this single-centre, single-arm prospective study. The Evoke closed-loop SCS system (Saluda Medical, Australia) will be utilized in this study. The Evoke system can measure evoked-compound-action-potentials (ECAPs) and assess other neurophysiological characteristics in-vivo over time. The relationship between patient sensitivity and spinal cord activation is evaluated by comparing patient reported sensation intensity to ECAP size (μV) using a fixed set of stimulation and recording settings to allow assessment over time. Neurophysiological parameters are obtained weekly during the trial (at least 3 weeks) and after permanent implant (1-,3-, and 6-months follow-up). Patients will be encouraged to reduce their medication intake during the trial procedure in line with standard practice in Belgium. Medication intake and patient reported outcomes (VAS, sleep-score, activity-score) will be collected on the Belgium-pain-platform at each visit. Herein, trial results of the first 5 patients are presented. Approximately 15 patients will be presented at the INS meeting.

Results: Daily MME intake reduced by ≥66.6 % in each patient during trial (Fig.1A). Spinal cord activation (ECAP size-μV) was determined at a maximal tolerable stimulation intensity. This ECAP at baseline (after lead implantation but prior to medication reduction) was compared to that at trial end and normalized to allow comparison across patients. In all 5 patients less activation (smaller ECAP) was required to induce a maximal sensation after medication reduction, ranging from 16% to 52% of the activation needed at baseline (Fig.1B).

Discussion: This study is designed to prospectively assess the relationship between patients' perception of SCS therapy, spinal cord activation, and pain medication. Preliminary trial data shown here demonstrated a marked increase in sensitivity during the standard trial in Belgium.

Conclusions: If this effect is consistent in this study, a better appreciation of the relationship between SCS and pain medication will assist clinicians in modifying SCS parameters to take account of such changes in sensitivity. The study is ongoing.

Supplemental Data:

References: 1. Glajchen M, et al. Chronic Pain: Treatment Barriers and Strategies for Clinical Practice. Journal of the American Board of Family Practice May 2001, 14 (3) 211-218; 2. Lee M. , Silverman S., Hansen H., Patel V., Manchikanti L. A Comprehensive Review of Opioid-Induced Hyperalgesia. Pain Physician. 2011 Mar-Apr;14(2):145-61. 3. Brooker C, Russo M, Cousins MJ, Taylor N, Holford L, Martin R, et al. ECAP-Controlled Closed-Loop Spinal Cord Stimulation Efficacy and Opioid Reduction Over 24-Months: Final Results of the Prospective, Multicenter, Open-Label Avalon Study. Pain Pract. 2021 May 2;papr.13008.

Acknowledgements:

Learning Objectives: Centrally acting pain medications alter patients' appreciation of the intensity of stimulation. Understanding that less activation, or stimulation, will be required by patients as they reduce some pain medications will assist clinical caregivers as they consider titration of both SCS parameters and medication over time in chronic pain patients.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O093

Oral Presentations
NEUROSTIMULATION FOR PAIN - CLINICAL UPDATE 03: CLOSED LOOP SCS
14-05-2024 16:30 - 18:20

ATTAINING MAXIMAL ANALGESIC EFFECT WITH OBJECTIVE NEUROPHYSIOLOGICAL MEASUREMENTS USING A NOVEL PRECISION, DOSE-CONTROL CLOSED-LOOP SPINAL CORD STIMULATION SYSTEM

Erika Petersen, MD[1], Robert Levy, PhD[2], Jason Pope, MD[3], Leonardo Kapural, MD[4], Jan Willem Kallewaard, MD[5,6], Simon Thomson, MBBS[7], Peter Staats, MD[8], Lawrence Poree, MD, PhD[9]
[1]University of Arkansas for Medical Sciences, Little Rock, United States of America, [2]Anesthesia Pain Care Consultants, Tamarac, United States of America, [3]Evolve Restorative Center, Santa Rosa, United States of America, [4]Carolinas Pain Institute and Wake Forest University School of Medicine, Winston-Salem, United States of America, [5]Amsterdam University Medical Centre, Arnhem, Netherlands, [6]Rijnstate Hospital, Arnhem, Netherlands, [7]Mid & South Essex University Hospitals, Essex, United Kingdom, [8]National Spine & Pain Centers, Shrewsbury, United States of America, [9]Univeristy of California San Francisco, San Francisco, United States of America

Introduction: Similar to medicines[1], electroceuticals require optimal dosing to attain maximal clinical effect. Spinal cord stimulation (SCS) has been challenged by the lack of neurophysiologic data to inform therapy optimization. Use of trial-and-error methods[2] has led to decreased battery life, as well as variability or loss of therapeutic effect. A novel physiologic closed-loop (CL) SCS system measures neural activation via evoked-compound action potentials (ECAPs) and delivers CL therapy to maintain accurate and consistent neural activation with every stimulus. Physiologic data from the spinal cord is now available to study optimal neural dosing with SCS. Here, we report neurophysiologic data that corresponded with the maximal analgesic effect (MAE) obtained with CL-SCS therapy from three clinical studies: EVOKE[3-5] (NCT02924129), ECAP[6] (NCT04319887) and Durability (NCT04627974).

Materials / Methods: Subjects with baseline back and leg pain ≥60mm and physical function in the severe to crippled category are included: EVOKE (patients randomized to CL-SCS, n=54), ECAP (n=99), Durability (n=12). MAE was defined at the visit with the maximum percent reduction in pain intensity (VAS) of the back and/or leg within the first three-months of CL-SCS implantation. Objective neurophysiological data that produced the MAE was analyzed.

Results: The mean MAE for EVOKE was 82.4% and for ECAP/Durability real-world studies was 77.1% (p=0.096). CL-SCS therapy accuracy (i.e., in-clinic deviation from ECAP target) was optimized at 2.4μV for EVOKE and 3.6μV for ECAP/Durability (p=0.149). On average, EVOKE patients used their system 92% of the time and ECAP/Durability patients 91% (p=0.936). Time the stimulation was above ECAP threshold was significantly greater for EVOKE (100% [IQR=96-100]) versus ECAP/Durability (97% [IQR=69-100], p<0.001). EVOKE patients received a significantly greater ECAP dose (40.4μV [IQR=18.8-83.4]) versus ECAP/Durability (25.8μV [IQR=4.7-48.1], p=0.005). Significantly greater dose ratio (estimated current at median ECAP/ECAP threshold current) was observed for EVOKE (1.5 [IQR=1.3-1.6]) versus ECAP/Durability (1.4 [IQR=1.1-1.5],

p=0.019).

Table 1. Observed Physiologic Therapy Metrics for CL-SCS Maximal Analgesic Effect (MAE) – VAS Percent Change from Baseline

	Evoke CL (n=54)	ECAP & PMCF (n=111)	Observed Physiologic Correlates of MAE Attained with CL-SCS (n=165, pooled)
Maximal Analgesic Effect (MAE) (percent change from baseline in VAS back and/or leg pain intensity) (mean (SD))	82.4% (17.4)	77.1% (19.9)	The observed MAE was 78.9% (19.2) back and/or leg pain reduction
Difference between means and 95% CI p-value (difference between means)		-5.3 (-11.6, 0.9) P=0.096	
Frequency (of use)			
System Utilization – percent time (median [IQR])	92% [73-98%]	91% [62-98%]	Observed MAE system utilization was 91% [65-98%]
p-value (difference between medians)		P=0.936	
Physiologic Dose Metrics			
Percent Time Above ECAP Threshold (out of total stimulating time) (median [IQR])	100% [96-100%]	97% [69-100%]	Observed MAE stimulation time above ECAP threshold was 99% [79-100%]
p-value (difference between medians)		P<0.001	
ECAP Dose (normalized median ECAP amplitude, µV) (median [IQR])	40.4 [18.8-83.4]	25.8 [4.7-48.1]	Observed MAE ECAP dose was 29.2µV [9.2-53.8]
p-value (difference between medians)		P=0.005	
Dose Ratio (estimated current at median ECAP/ECAP threshold current) (median [IQR])	1.5 [1.3-1.6]	1.4 [1.1-1.5]	Observed MAE dose ratio was 1.4 [1.2-1.5], that is 40% above ECAP threshold current (IQR: 20 to 50% above)
p-value (difference between medians)		P=0.019	
Loop Performance			
Dose Accuracy (in-clinic deviation from ECAP target, RMSE (µV))	2.4 [1.8-4.6]	3.6 [2.3-5.9]	Observed MAE therapy accuracy was 3.4µV [2.2-5.8]
p-value (difference between medians)		P=0.149	

Discussion: ECAP CL-SCS facilitates the development and implementation of neural dosing guidelines to attain MAE. The MAE observed in the EVOKE RCT was greater than that observed in real-world studies. While there were no differences in system utilization or loop performance, the neural activation or actual therapy received (i.e., stimulation time above ECAP threshold, ECAP dose, dose ratio) was significantly greater in the RCT.

Conclusions: ECAP CL-SCS provides profound clinical benefit to chronic pain patients in both RCT and real-world setting. An objective neural panel consisting of physiologic metrics has the potential to maximize clinical benefit and provide a transparent and reproducible guideline for neural dosing of SCS therapy.

Supplemental Data:

References: 1. Blaschke TF, Osterberg L, Vrijens B, Urquhart J. Adherence to medications: insights arising from studies on the unreliable link between prescribed and actual drug dosing histories. *Annu Rev Pharmacol Toxicol* 2012; 52: 275-301. 2. Levy RM. The need for mechanism-based medicine in neuromodulation. *Neuromodulation*. 2012;15(4): 273-279. 3. Mekhail N, et al. Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial. *Lancet Neurol* 2020*;* 19: 123-134. 4. Mekhail N, et al. Durability of Clinical and Quality-of-Life Outcomes of Closed-Loop Spinal Cord Stimulation for Chronic Back and Leg Pain: A Secondary Analysis of the Evoke Randomized Clinical Trial. *JAMA Neurol* 2022; 79: 251-260. 5. Mekhail NA, et al. ECAP-Controlled Closed-loop versus Open-Loop SCS for the Treatment of Chronic Pain: 36-Month Results of the EVOKE Blinded Randomized Clinical Trial. Reg Anesth Pain Med 2023; In press. 6. Leitner A, et al. Real World Clinical Utility of Neurophysiological Measurement Utilizing Closed-Loop Spinal Cord Stimulation in a Chronic Pain Population: The ECAP Study Protocol. J Pain Res 2023; 16: 2497-2507.

Acknowledgements: Submitted on behalf of the EVOKE and ECAP investigators. Trials sponsored by Saluda Medical.

Learning Objectives: 1. Electroceuticals as with medicines, require optimal dosing to obtain the maximum clinical effect 2. ECAP-controlled closed-loop SCS enables evaluation of spinal cord physiologic data and development of neural dosing guidelines to optimize SCS therapy 3. SCS therapy (or actual neural activation) received, informed by physiologic data, was significantly greater in the RCT study compared to the real-world population

Financial Disclosures: Erika Petersen, Saluda Medical, Consultant/Advisory Board, $20,001-$100,000 USD Robert Levy, Saluda Medical, Stock Options Jason Pope, Saluda Medical, Consultant/Advisory Board, >$100,000 USD Leonardo Kapural, Saluda Medical, Consultant/Advisory Board, $500-$5000 USD; Education/Research, $500-$5000 Jan-Willem Kallewaard, Saluda Medical, Consultant/Advisory Board, 6,000 Simon Thomson, Saluda Medical, Speaker Program, $500-$5000 USD, Consultant/Advisory Board, $500-$5000 USD, Education/Research, $500-$5000 USD Peter Staats, Saluda Medical, Consultant/Advisory Board, $5,001-$20,000 USD, Education/Research, $20,001-$100,000, Stock Options, $20,001-$100,000 Lawrence Poree, Saluda Medical, Consultant/Advisory Board

Disclosure: Administrative support to authors funded by Saluda Medical.

O094

Oral Presentations
PERIPHERAL NERVE STIMULATION – CLINICAL UPDATE
15-05-2024 16:30 - 18:20

A NEW RECOMMENDATION FOR PLACING ELECTRODES AT THE EXTERNAL OCCIPITAL PROTUBERANCE IN OCCIPITAL NERVE STIMULATION BASED ON GREATER OCCIPITAL NERVE ANATOMICAL VARIABILITY.

Wim Pollet, MD[1], Bart Billet, MD[2], Frank Huygen, MD, PhD[3], Nicolas Van Vlasselaer, MSc[4], Erik Cattrysse, PhD[4], Paul Frank, MBBS[5]
[1]Salvia Bioelectronics, Eindhoven, Netherlands, [2]AZ Delta, Roeselare, Belgium, [3]Erasmusmc, Centre Of Pain Medicine, Rotterdam, Netherlands, [4]Vrije Universiteit Brussel, Belgium, Belgium, [5]Resolve Pain, Buderim, Australia

Introduction: Occipital nerve stimulation (ONS) has been proposed as a surgical solution for patients with medically refractory neurovascular headache conditions, like migraine and cluster headache. However, treatment efficacy varies, potentially influenced by patient selection, unilateral versus bilateral electrode placement, and differences in waveforms and stimulation settings.[1,2] Lead placement, however, might also play an important role in the variability of treatment outcomes. Traditionally, ONS lead location is based on the mean exit point of the greater occipital nerve (GON) through the trapezius muscle, as can be found in the anatomy books. Historically, the craniocervical junction and C1 are used as anatomic landmarks.[3] Another suggested approach involves placing the lead 3 cm below the external occipital protuberance (EOP)[4]. Lead placement at these locations has been associated with complications, including lead migration, lead breakage, and neck muscle spasms. To date, the optimal ONS lead location remains undetermined.

Materials / Methods: We evaluated the anatomical variability in the location of the exit point of the GON and the bifurcation of its branches by dissecting 10 formaldehyde-fixed human cadaver heads in relation to the midline and the location of EOP. Variations in the GON anatomy, such as differences in trajectory, orientation, and bifurcation, were identified through detailed measurements and observed intra- and inter-individually. A CT scan was taken of each cadaver head after the dissection. Employing 3D modelling, we utilised torus rings for reference points at the Orbito-Meatal Line (OML), at EOP and 1 cm and 2 cm above the EOP (EOP+1 and EOP+2, respectively).

Results: Table 1 shows the minimum medial and maximum lateral distances where the GON intersects reference lines at OMP, EOP, EOP+1, and EOP+2.

	Left (n=10)		Right (n=10)	
	Maximum lateral distance (mm)	Minimal medial distance (mm)	Minimal medial distance (mm)	Maximum lateral distance (mm)
EOP+2	86.0	27.6	32.8	83.6
EOP+1	71.5	32.0	24.2	70.7
EOP	61.3	19.5	16.4	59.9
OML	34.0	11.5	7.4	27.2

Table 1 – Showing the minimal medial distances and maximum lateral distances if the 10 dissected cadaver heads.

Discussion: These findings indicate that electrodes above the EOP cover the occipital nerve. Leads at the OML (C1-C2) level may not stimulate GON nerves exiting the trapezius aponeurosis between the OML and EOP.

Conclusions: To account for intra- and interpatient variability in the GON exit point through the trapezius muscle, we propose placing the ONS higher (around EOP) to increase ONS therapy responders and reduce device and stimulation-related complications like lead breakage and muscle cramps.

Supplemental Data:

References: 1. Miller S, Watkins L, Matharu M. Predictors of response to occipital nerve stimulation in refractory chronic headache. *Cephalalgia*. 2018;38(7):1267-1275. doi:10.1177/0333102417728747 2. Trentman TL, Zimmerman RS, Seth N, Hentz JG, Dodick DW. Stimulation ranges, usage ranges, and paresthesia mapping during occipital nerve stimulation. *Neuromodulation*. 2008;11(1):56-61. doi:10.1111/j.1525-1403.2007.00143.x 3. Miller S, Sinclair AJ, Davies B, Matharu M. Neurostimulation in the treatment of primary headaches. *Pract Neurol*. 2016;0(May 5. 2016):[Epub ahead of print]. doi:10.1136/practneurol-2015-001298 4. Mueller O, Hagel V, Wrede K, Schlamann M, Hohn HP, Sure U, Gaul C. Stimulation of the greater occipital nerve: anatomical considerations and clinical implications. Pain Physician. 2013 May-Jun;16(3):E181-9. PMID: 23703417.

Acknowledgements:

Learning Objectives: 1. Analysis of Occipital Nerve Stimulation (ONS) Variables and Complications:
- Learners should be able to discuss the concept of Occipital Nerve Stimulation (ONS) as a treatment for headache conditions and understand the factors affecting its efficacy, such as patient selection, electrode placement, and stimulation settings. They should also be knowledgeable about the common complications associated with traditional ONS lead locations, including lead migration, breakage, and muscle spasms. 2. Evaluation of Anatomical Variability in GON:
- Learners should be able to assess the variability in the anatomical structure and exit points of the Greater Occipital Nerve (GON) based on detailed dissections and 3D modelling studies. This includes understanding the differences in GON's trajectory, orientation, and bifurcation and how these factors might influence the effectiveness of ONS treatments. 3. Application of Research Findings to Clinical Practice:
- Learners should be able to apply the research findings concerning GON anatomy to propose more effective ONS lead placement strategies. Specifically, they should understand why placing the ONS leads higher (around the EOP) could increase the number of responders to ONS therapy and decrease device and stimulation-related complications. This involves a comprehensive understanding of the relationship between GON exit points, electrode coverage, and stimulation efficacy.

Financial Disclosures: Bart Billet - Salvia Bioelectronics - Consultancy Agreement Bart Billet - Saluda - Consultancy Agreement and Contracted Research Bart Billet - Aboott - Consultancy Agreement Bart Billet - Medtronic - Consultancy Agreement Frank Huygen - Abbott - Consultancy Agreement - Teaching Frank Huygen - Grunenthal - Consultancy Agreement Wim Pollett - Salvia Bioelectronics - Chief Medical Officer Nicolas Van Vlasselaer - Nothing to disclose Erik Cattrysse - Nothing to disclose

Disclosure: I am the chief medical officer for Salvia Bioelectronics

O095

Oral Presentations
PERIPHERAL NERVE STIMULATION – CLINICAL UPDATE
15-05-2024 16:30 - 18:20

A NOVEL CRANIOFACIAL IMPLANTABLE NEUROSTIMULATOR WITH COMBINED SUPRA-ORBITAL AND OCCIPITAL NERVE STIMULATION FOR INTRACTABLE CHRONIC MIGRAINE

Bart Billet, MD[1], Karel Hanssens, MD[1], Ruben De Vos, MD[1], Paul Frank, MBBS[2], Maarten Goethals, MD[3], Mark Plazier, MD[4], Frank Huygen, MD, PhD[5]
[1]AZ Delta, Roeselare, Belgium, [2]Resolve Pain, Buderim, Australia, [3]AZ Delta, Torhout, Belgium, [4]Jessa Hospital, Neurosurgery, Hasselt, Belgium, [5]Erasmusmc, Centre Of Pain Medicine, Rotterdam, Netherlands

Introduction: Chronic migraine (CM) is a disabling neurological disorder with a complex pathophysiology—including central sensitization, cortical spreading depression, neurogenic inflammation, and dysfunctional processing of pain signals. Despite new pharmaceutical solutions able to help many patients, an important group still experiences limited efficacy and/or intolerable side effects. A novel craniofacial implantable neurostimulator system has been developed to address this medical need. The system comprises two implants, each with an ultra-thin lead connected to an integrated, battery-free stimulator; one covering both the left and right supra-orbital nerves, and the other covering both the left and right occipital nerves. The implants are placed during a short, minimally invasive, non-traumatic procedure using specially designed surgical instruments.

Materials / Methods: The primary objective of our feasibility study was to evaluate the safety and performance of this system in treating refractory CM using combined supra-orbital and occipital nerve stimulation. The inclusion criteria specified that study participants be non-responsive to at least three preventive therapies, including CGRP monoclonal antibodies or onabotulinumtoxin A.

Results: Initial results from 7 participants over three months showed an early and substantial decrease in the number of monthly migraine days (MMD), with individual reductions between 45% and 95%. Furthermore, participants reported an important increase in the number of monthly crystal-clear days. This was reflected in an increase in the EuroQol 5-Dimensional VAS score.

Discussion: Along with daily periods of stimulation for preventive treatment, the system’s on-demand feature allowed patients to activate acute therapy to suppress or moderate their migraine attacks and lessen their need for triptans and other medications.

Conclusions: These early results show the potential of this novel neurostimulator system as an effective treatment for refractory CM. A larger study is warranted to confirm these findings.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. Understanding the Pathophysiology of Chronic Migraine:
- Learners should be able to explain the complex pathophysiology behind chronic migraine, including central sensitization, cortical spreading depression, neurogenic inflammation, and dysfunctional processing of pain signals. They should also be able to discuss the limitations of current pharmaceutical treatments in addressing these aspects effectively for all patients. 2. Comprehension of the Novel Craniofacial Implantable Neurostimulator System:
- Learners should be able to describe the components and operational mechanics of the new craniofacial implantable neurostimulator, which involves combined supra-orbital and occipital nerve stimulation. This includes an understanding of the system's ultra-thin leads, integrated, battery-free stimulator, and the minimally invasive procedure required for its implantation. 3. Evaluation of the

Feasibility Study Results and Potential Implications:
- Learners should be able to analyze and interpret the initial results of the feasibility study, including the observed decrease in monthly migraine days and increase in monthly crystal-clear days among participants. They should also understand the significance of these results in terms of patient quality of life (as indicated by the EuroQol 5-Dimensional VAS score), the system's on-demand feature for acute therapy, and the potential reduction in the need for other medications. Additionally, learners should recognize the need for larger, more comprehensive studies to confirm these preliminary findings.

Financial Disclosures: Bart Billet - Salvia Bioelectronics - Consultancy Fee Bart Billet - Saluda - Consultancy Fee and Research Grant Bart Billet - Abbott - Consultancy Fee Bart Billet - Medtronic - Consultancy Fee Karel Hannseens - Nothing to disclose Ruben De Vos - Nothing to disclose Maarten Goethals - Nothing to disclose Mark Plazier - Abbott - Consultancy Agreement and Scientific Sponsor Mark Plazier - Boston Scientific - Consultancy Agreement Mark Plazier - Medtronic - Consultancy Agreement and Scientific Sponsor Mark Plazier - Salvia Bioelectronics - Consultancy Agreement Frank Huygen - Abbott - Teaching Agreement Frank Huygen - Grunenthal - Teaching Agreement

Disclosure: Salvia Bioelectronics, lead implanter as part of the first feasibility study to evaluate the safety and performance of the system

O096

Oral Presentations
PERIPHERAL NERVE STIMULATION – CLINICAL UPDATE
15-05-2024 16:30 - 18:20

CENTRAL SENSITISATION RESPONSE FOLLOWING OCCIPITAL NERVE STIMULATION: A NINE-YEAR FOLLOW-UP.

Theresa Wodehouse, PhD[1], Kavita Poply, FRCA, FCARCSI, FFPMRCA[2], Anish Bahra, MD[3], Vivek Mehta, MBBS, MD, FRCA, FFPMRCA[2]
[1]Barts NHS trust, Pain Research Center, London, United Kingdom, [2]St Bartholomew's Hospital London, Barts Health NHS Foundation Trust, Spinal Pain & Neuromodulation, London, United Kingdom, [3]Oxford University Hospital, Department Of Neurology, Oxford, United Kingdom

Introduction: Central sensitization and impaired conditioned pain modulation (CPM) response has been reported to contribute to migraine progression. Migraine patients can present with allodynia possibly attributed to increased sensitivity of peripheral ends of nociceptors with both peripheral and central sensitization. Occipital nerve stimulation (ONS) is an established neuromodulation procedure for selected patients with medically intractable chronic cluster headache and migraine with autonomic symptoms. Although clinically effective, there has been no long-term outcome data on its effect on central sensitisation. Efficacy outcomes for ONS typically employ standardised headache questionnaire measures but objective tests of endogenous pain mechanisms such as Quantitative Sensory Testing (QST) are yet to be utilised to measure efficacy of ONS. Our group has published one- year outcomes in central sensitisation following ONS (1). The aim of this study was to evaluate whether QST detects a change in pain in chronic migraine and provide more long-term outcome data in patients receiving ONS.

Materials / Methods: Six patients, 3 chronic migraine, 2 new persistent daily headache and 1 chronic cluster headache were implanted between 2014-2015 with percutaneous leads placed bilaterally parallel to the greater occipital nerve, IPG (Genesis/ Prodigy St Jude Medical, Plano, TX,USA)/Medtronic ONS). Baseline QST and questionnaires were completed, and they were monitored up to a 12-month period and then annual review for 9 years.

Results:

	Baseline			12 months			9 years		
	HIT-6	PPT kPa	CPM	HIT-6	PPT kPa	CPM kPa	HIT-6	PPT kPa	CPM
1	78	37	66	62	54	79	60	27	83
2	78	34	28	53	112	157	44	38	140
3	78	57	34	62	54	65	32	91	155
4	60	99	61	58	62	104	50	74	139
5	74	18	14	62	17	15	46	42	86
6	60	79	71	46	142	204	30	67	219

HIT-6- Headache Impact Test, Pressure pain thresholds - PPT, Conditioned pain modulation - CPM, kPa - kilopascal.

Discussion: This is first long term follow up in our knowledge investigating the effect of central sensitisation following ONS. Responders showed substantial reductions in headache-related disability and improvements in conditioned pain modulation over 9-year duration.

Conclusions: ONS has been extensively investigated as a treatment for chronic migraine; however, there remains a need for well-designed, randomised controlled studies, with adequately timed double-blind comparison to demonstrate true difference between sham and stimulated patients.

Supplemental Data:

References: 1) Changes in peripheral and central sensitization in patients undergoing occipital nerve stimulation. **Wodehouse T**, Bahra A, Mehta V.Br J Pain. 2020 Nov;14(4):250-255.

Acknowledgements:

Learning Objectives: 1 Long term effects of Occipital Nerve stimulation 2 A better understanding of migraine treatments 3 A better understanding of the pathogenesis of migraines in relation to central sensitisation

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O097

Oral Presentations
PERIPHERAL NERVE STIMULATION – CLINICAL UPDATE
15-05-2024 16:30 - 18:20

MULTIFIDUS DYSFUNCTION AND RESTORATIVE NEUROSTIMULATION

Vinny Francio, MD, MS[1], Benjamin Westerhaus, MD[2], Alexios Carayannopoulos, DO, MPH, DABPMR[3], Dawood Sayed, MD[4]
[1]University of Kansas, Dept Anesthesiology And Pain Medicine, Kansas City, United States of America, [2]Cantor Spine Center at the Paley Institute, Interventional Spine, West Palm Beach, United States of America, [3]Brown University, Neurosurgery/pm&r, Providence, United States of America, [4]University of Kansas, Anesthesiology And Pain Medicine, Kansas City, United States of America

Introduction: Chronic low back pain (CLBP) is multifactorial in nature, with recent research highlighting the role of multifidus dysfunction in a subset of nonspecific CLBP. This review aimed to provide a foundational reference that elucidates the pathophysiological cascade of multifidus dysfunction, how it contrasts with other CLBP etiologies and the role of restorative neurostimulation.

Materials / Methods: A scoping review of the literature following the PRISMA-ScR guidelines and the JBI manual for evidence synthesis for scoping reviews. The scoping review protocol was registered on the Open Science Framework.

Results: We found 671 citations through our initial search. After removal of duplicates, 420 records remained. Of these, 218 were excluded and 194 were included. Findings were presented to highlight emerging principles related to multifidus dysfunction and restorative neurostimulation.

Discussion: Multifidus dysfunction is diagnosed by a history of mechanical, axial, nociceptive CLBP with limited/without neuropathic features. Nociplatic components may be present depending on pain chronicity. Multifidus dysfunction profile differs from facet-mediated or discovertebral etiology. Phenotypic pain profile commonly manifests as a primarily movement or positional related pain, aggravated by trivial activities and small movement tasks. Pain pattern is persistent with sustained postures such as prolonged sitting, standing, walking and driving. There is usually no radicular or referral of pain distal to the knee. Physical exam manuevers such as the prone instability test, multifidus lift test, and abberant movement patterns upon range of motion exam may demonstrate functional lumbar instability, which differs from other structural etiologies. These have demonstrated sustained interrater reliability. Diagnostic images may be used to grade multifidus atrophy and assess for other structural pathologies. While various treatments exist for CLBP, restorative neurostimulation distinguishes itself from traditional neurostimulation in a way that treats a different etiology, targets a different anatomical site, and has a distinctive mechanism of action. Several high-quality clinical studies have been published reporting long-term durable improvements (up to 4-years) in pain, disability, better quality of life, with individual studies also reporting decreased opioid use and health care utilization reduction.

Conclusions: Multifidus dysfunction has been proposed to result from loss of neuromuscular control, which may manifest clinically as muscle inhibition resulting in altered movement patterns. Over time, this cycle may result in potential atrophy, degeneration and CLBP. Restorative neurostimulation, a novel implantable neurostimulator system, stimulates the efferent lumbar medial branch nerve to elicit repetitive multifidus contractions. This intervention aims to interrupt the cycle of dysfunction and normalize multifidus activity incrementally, potentially restoring neuromuscular control and functional lumbar instability.

Supplemental Data:

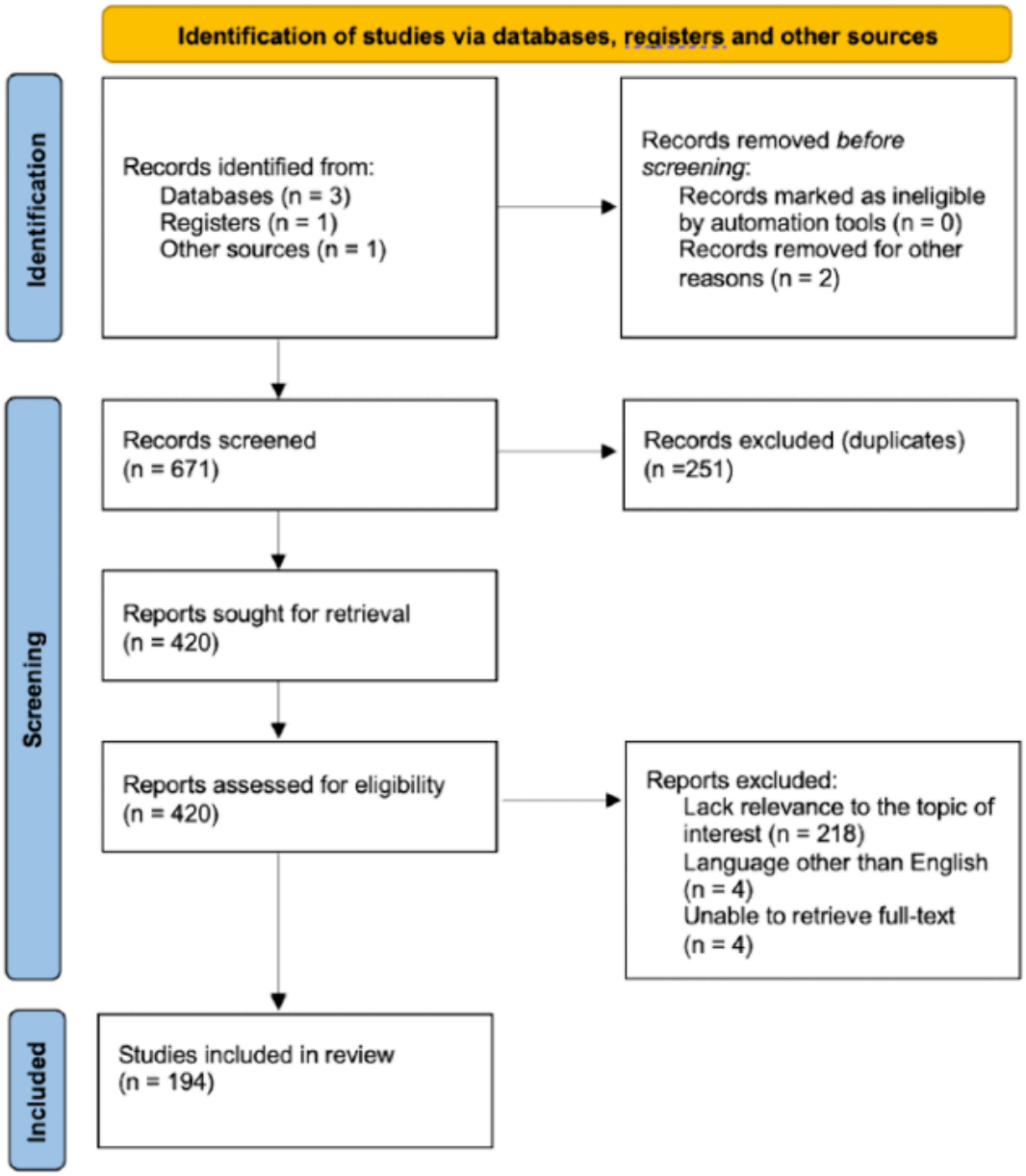


Figure 1. PRISMA-ScR diagram.

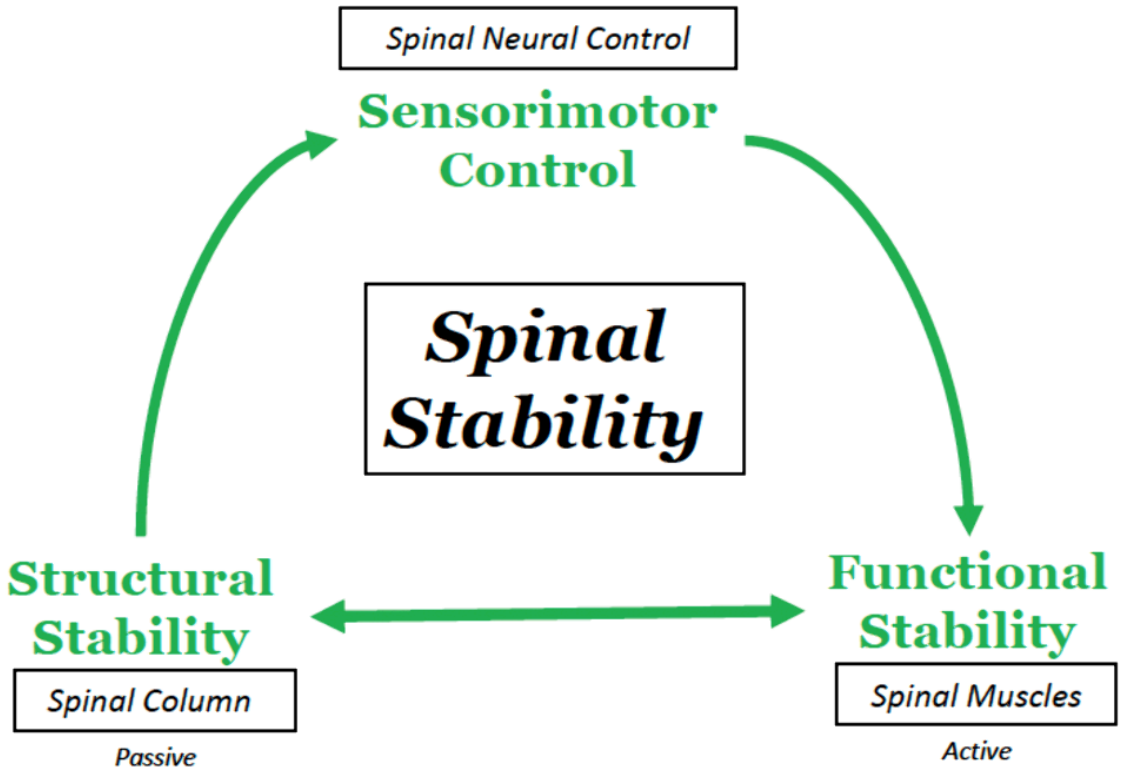


Figure 2. Updated diagram based on Panjabi's landmark and expanded models and , denoting the complex interplay among the spinal column (passive subcomponent), the spinal muscles (active subcomponent) and sensorimotor control (spinal neural control) to maintain spinal stability.

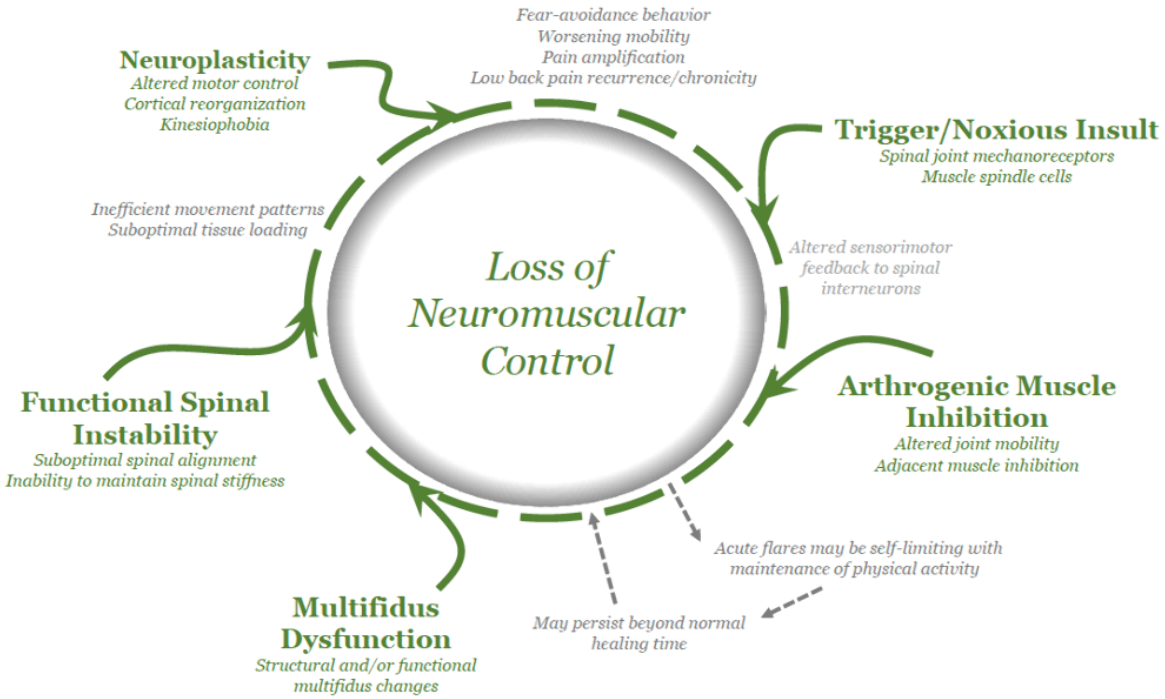


Figure 3. Diagram illustrating the complex interplay between altered sensorimotor control, arthrogenic muscle inhibition, multifidus dysfunction, functional spinal instability, and neuroplastic changes that may result in loss of neuromuscular control contributing to low back pain recurrency and chronicity.

	Palliative LMBN RFA	Palliative LMBN PNS	Restorative LMBN PNS
Candidates	Axial LBP refractory to conservative care with a prior positive response to diagnostic LMBN blocks.	Chronic axial LBP refractory to conservative care, without (Other specific requirements)	Chronic mechanical axial LBP with the presence of multifidus dysfunction evidenced on MRI and/or positive prone instability test and/or multifidus lift test; and when no other pathology seen on MRI is clearly identified as the likely cause of pain
Target	Facet joint mediated pain secondary to spondyloarthropathy	Intractable neuropathic pain Chronic axial LBP from structural changes (facet joints, discs, etc.)	Sensorimotor control Spinal instability Nociceptive pain
Procedure	Temporary joint denervation Fluoroscopic-guided facet joint rhizotomy by different ablative methods targeting is the LMBN located at the junction of the superior articular process and the transverse process	Temporary Percutaneous implant under ultrasonography (US) or fluoroscopy with coiled PNS leads targeting the L2 LMBN	Permanent implant under fluoroscopic guidance, with proprietary PNS leads targeting the most medial and inferior aspect of the L2 LMBN
Mechanism of Action	Palliative analgesia of facet-mediated pain by creating an ablative lesion of the LMBN, which provides sensory input to the facet joints, however, also innervates the multifidus muscle. Collateral effects include denervation atrophy of the multifidus and possibly other paraspinal muscles.	Palliative analgesia in an afferent fashion, by modulation of underlying central sensitization targeting afferent/sensory fibers, resulting in synaptic transmission inhibition (gate mechanism) and stimulation of efferent fibers that activate a reflex arc of proprioceptive signals. This is thought to normalize membrane hyperexcitability delivering analgesia within a short time from stimulation	Restorative neurostimulation addressing mainly motor control and compensatory nociceptive pain, in which peripherally stimulated contractions override underlying arthrogenic muscle inhibition, increasing proprioceptive signaling. In turn, this facilitates restoration of multifidus sensorimotor control, which translates to meaningful longitudinal motor control restoration, functional gains to improve spinal stability.
Typical Stimulation Settings	Test stimulation is 50 Hz for sensory and 2 Hz for motor. Thermal ablation occurs at 500 kHz. Ablative methods include conventional RFA, cooled RFA and pulsed RFA.	Frequency (12-Hz); Pulse width (15-200ms); Amplitude (5-20mA); Duration (6 hours/daily); Time (< 60 days)	Frequency (20-Hz); Pulse width (214ms); Amplitude (2.5mA); Duration (30 minutes/twice daily); Repetitive, graduated multifidus contractions by stimulating LMBN 10 seconds on, 20 seconds off).

Table 1. Comparative details of lumbar radiofrequency ablation, spinal cord stimulation, and peripheral nerve stimulation of the lumbar medial branch nerve.

References: REFERENCES Wu A, March L, Zheng X, et al. Global low back pain prevalence and years lived with disability from 1990 to 2017: estimates from the Global Burden of Disease Study 2017. *Ann Transl Med* 2020;8(6):299. doi:10.21037/atm.2020.02.175 Hartvigsen J, Hancock MJ, Kongsted A, et al. What low back pain is and why we need to pay attention. *Lancet* 2018; 391:2356-67. Bagg MK, Wand BM, Cashin AG, et al. Effect of Graded Sensorimotor Retraining on Pain Intensity in Patients With Chronic Low Back Pain: A Randomized Clinical Trial. *JAMA* 2022 Aug 2;328(5):430-439 Urits, Ivan, et al. Low back pain, a comprehensive review: pathophysiology,

diagnosis, and treatment. *Curr pain and headache rep* 2019; 23:1-10 Knezevic NN, Candido KD, Vlaeyen JWS, Van Zundert J, Cohen SP. Low back pain. *Lancet* 2021 Jul 3;398(10294):78-92. Hoy D, Brooks P, Blyth F, et al. The Epidemiology of low back pain. *Best Pract Res Clin Rheumatol* 2010; 24(6):769-81. Stevans JM, Delitto A, Khoja SS, et al. Risk factors associated with transition from acute to chronic low back pain in US patients seeking primary care. JAMA network open. 2021 Feb 1;4(2):e2037371. George, Steven Z., et al. Transforming low back pain care delivery in the United States. *Pain* 2020; 161(12): 2667. Costa N, Ferreira ML, Setchell J, et al. A Definition of "Flare" in Low Back Pain: A Multiphase Process Involving Perspectives of Individuals with Low Back Pain and Expert Consensus. *J Pain* 2019; 20(11):1267-1275. Refshauge KM, Maher CG. Low back pain investigations and prognosis: a review. *Br J Sports Med*2006;40(6):494–498. Tieppo Francio V, Westerhaus BD, Rupp A, et al. Non-Spinal Neuromodulation of the Lumbar Medial Branch Nerve for Chronic Axial Low Back Pain: A Narrative Review. *Front Pain Res (Lausanne)* 2022; 25; 3:835519. Tieppo Francio V, Gill B, Rupp A, et al. Interventional Procedures for Vertebral Diseases: Spinal Tumor Ablation, Vertebral Augmentation, and Basivertebral Nerve Ablation-A Scoping Review. *Healthcare (Basel)*2021;15;9(11):1554. Cohen SP, Vase L, Hooten WM. Chronic pain: an update on burden, best practices, and new advances. Lancet. 2021 May 29;397(10289):2082-2097. doi: 10.1016/S0140-6736(21)00393-7. PMID: 34062143. International Association for the Study of Pain (IASP). IASP terminology. 2017. Available at:https://www.iasppain.org/Education/Content.aspx?ItemNumber=1698&navItemNumber=576. Accessed June 2023. Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. *Pain* 2020 Sep 1;161(9):1976-1982 Jensen TS, Baron R, Haanpaa M, et al. A new definition of neuropathic pain. *Pain* 2011; 152:2204–5. Fitzcharles MA, Cohen SP, Clauw DJ, et al. Nociplastic pain: towards an understanding of prevalent pain conditions. *Lancet* 2021;397(10289):2098-2110. Brumagne S, Diers M, Danneels L, et al. Neuroplasticity of sensorimotor control in low back pain. . *J Ortho Sports Phys Ther* 2019; 49(6):402-414. Russo M, Deckers K, Eldabe S, et al. Muscle Control and Non-specific Chronic Low Back Pain. *Neuromodulation* 2018 Jan;21(1):1-9 Deckers K, De Smedt K, van Buyten JP, et al. Chronic low back pain: restoration of dynamic stability. *Neuromodulation* 2015; 18:478-486. Deckers K, De Smedt K, Mithcell B, et al. New therapy for refractory chronic mechanical low back pain – restorative neurostimulation to activate the lumbar multifidus: one years results of a prospective multicenter clinical trial. *Neuromodulation* 2018; 21:48-55. Hodges PW, Van Dieen JP, Cholewicki J. Time to reflect on the role of motor control in low back pain. *J Ortho Sports Phys Ther* 2019;49(6)-367-369. Hodges PW, Danneels L. Changes in Structure and Function of the Back Muscles in Low Back Pain: Different Time Points, Observations and Mechanisms. *J Ortho Sports Phys Ther* 2019; 6:464-473. Gabel CP, Mokhtarinia HR, Melloh M. The Politics of Chronic LBP: Can We Rely on a Proxy-Vote? Linking Multifidus Intra-Myo-Cellular Lipid (IMCL) Fatty Infiltration with Arthrogenic Muscle Inhibition (AMI)-induced Chronic Nonspecific Low Back Pain. *Spine* 2021;46(2):129-130. Freeman MD, Woodham MA, Woodham AW. The Role of the lumbar Multifidus In Chronic Low Back Pain: A Review. *PM R* 2010; 2:142-146. Barz T, Mellow M, Lord SJ, et al. A conceptual model of compensation/decompensation in lumbar segmental instability. Medical Hypothesis 2014; 83(3):312-316. Beazell JR, Mullins M, Grindstaff TL. Lumbar instability: an evolving and challenging concept. J Man Manip Ther. 2010 Mar;18(1):9-14. doi: 10.1179/106698110X12595770849443. PMID: 21655418; PMCID: PMC3103111. Biely SA, Smith SS, Silfies SP. Clinical instability of the lumbar spine: diagnosis and intervention. Orthpaedic Physical Therapy Practice. 2006;18:11-19. Chakravarthy K, Lee D, Tram J, et al. Restorative Neurostimulation: A Clinical Guide for Therapy Adoption. *J Pain Res* 2022 Jun 20;15:1759-1774. Gilligan C, Volschenk W, Russo M, et al. An implantable restorative-neurostimulator for refractory mechanical chronic low back pain: a randomized sham-controlled clinical trial. *Pain* 2021; 1;162(10):2486-2498. Gilligan C, Volschenk W, Russo M, et al. Long-Term Outcomes of Restorative Neurostimulation in Patients with Refractory Chronic Low Back Pain Secondary to Multifidus Dysfunction: Two-Year Results of the ReActiv8-B Pivotal Trial. *Neuromodulation* 2021; 18: S1094-7159(21)06386-8. Mitchell B, Deckers K, De Smedt K, et al. Durability of the Therapeutic Effect of Restorative Neurostimulation for Refractory Chronic Low Back Pain. *Neuromodulation* 2021; 24(6):1024-1032. Thomson S, Chawla R, Love-Jones S, et al. Restorative Neurostimulation for Chronic Mechanical Low Back Pain: Results from a Prospective Multi-center Longitudinal Cohort. *Pain Ther* 2021;10(2):1451-1465. Gilligan C, Volschenk W, Russo M, et al. Three-Year Durability of Restorative Neurostimulation Effectiveness in Patients with Chronic Low Back Pain and Multifidus Muscle Dysfunction. *Neuromodulation* 2022;26: S1094-7159(22)01254-5. Ardeshiri A, Shaffrey C, Stein KP, et al. Real-World Evidence for Restorative Neurostimulation in Chronic Low Back Pain- a Consecutive Cohort Study. *World Neurosurg* 2022;29: S1878-8750(22)01381-X. Shaffrey C, Gilligan C. Effect of Restorative Neurostimulation on Major

Drivers of Chronic Low Back Pain Economic Impact. *Neurosurgery* 2023 Feb 14;92(4):716–24. Tricco AC, Lillie E, Zarin W, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med* 2018 Oct 2;169(7):467-473 Peters MDJ, Godfrey C, McInerney P, et al. Chapter 11: Scoping Reviews (2020 version). In: Aromataris E, Munn Z (Editors). JBI Manual for Evidence Synthesis, JBI, 2020. Available from https://synthesismanual.jbi.global. Kim CW, Gottschalk LJ, Eng C, et al. The Multifidus Muscle is the Strongest Stabilizer of the Lumbar Spine. *Spine J* 2007; 7:76S. Kay AG. An Extensive Literature Review of the Lumbar Multifidus: Biomechanics. *J Manual & Manipulative Therapy* 2001. 9;17-39. MacDonald D, Moseley LG, Hodges PW. Why do some patients keep hurting their back? Evidence of ongoing back muscle dysfunction during remission from recurrent back pain. *Pain* 2009;142(3):183-188. Moseley GL, Hodges PW, Gandevia SC. Deep and superficial fibers of the lumbar multifidus muscle are differentially active during voluntary arm movements. *Spine* 2002;27(2): E29–E36. Rosatelli AL, Ravichandiran K, Agur AM. Three-dimensional study of the musculotendinous architecture of lumbar multifidus and its functional implications. *Clin Anat* 2008; 21:539–46. doi:10.1002/ca.20659. Ward SR, Kim CW, Eng CM, et al. Architectural analysis, and intraoperative measurements demonstrate the unique design of the multifidus muscle for the lumbar spine stability. *J Bone Joint Surg Am* 2009; 91:176-185. Tran J, Peng P, Loh E. Anatomical study of the medial branches of the lumbar dorsal rami: implications for image guided intervention. Reg Anesth Pain Med 2022; 47:464-474. Hansen L, de Zee M, Rasmussen J, et al. Anatomy and biomechanics of the back muscles in the lumbar spine with reference to biomechanical modeling. Spine 2006; 31:1888-1899. Dreyfuss P, Stout A, Aprill C, et al. The significance of multifidus atrophy after successful radiofrequency neurotomy for low back pain. PM R. 2009 Aug;1(8):719-22. Wu PBJ, Date ES, Kingery WS. The lumbar multifidus muscle is polysegmentally innervated. Electromyog Clin Neurophysiol 2000;40:483-485. Panjabi MM. The stabilizing system of the spine. Part I. Function, dysfunction, adaptation, and enhancement. J Spinal Disord 1992; 5:383-389. Panjabi MM. The stabilizing system of the spine. Part II. Neutral zone and instability hypothesis. *J Spinal Disord* 1992;5: 390-396. Panjabi MM. Clinical spine instability and low back pain. *J Electromyog Kinesiol* 2003; 13:371-37. Hoffman J, Gabel P. Expanding Panjabi's stability model to express movement: a theoretical model. *Med Hypotheses 2013* Jun;80(6):692-7. Brumagne S, Cordo P, Lysens R, et al. The role of paraspinal muscle spindles in lumbosacral position sense in individuals with and without low back pain. *Spine* 2000; 25(8):989-994. van Dieën JH, van Drunen P, Happee R. Sensory contributions to stabilization of trunk posture in the sagittal plane. *J Biomech* 2018; 70:219-227. Holm S, Indahl A, Solomonow M. Sensorimotor control of the spine. *J Electromyo and Kiensi* 2002; 12: 219-234. Vitterso AD, Halicka M, Buckingham G, et al. The sensorimotor theory of pathological pain revisited. *Neuroscience and Biobehvioral* Review 2022; 139:104735. Riemann BL, Lephart SM. The sensorimotor system, part I: the physiologic basis of functional joint stability. J Athl Train. 2002 Jan;37(1):71-9. PMID: 16558670; PMCID: PMC164311. Hodges PW, Barbe MF, Loggia ML, et al. Diverse Role of Biological Plasticity in Low Back Pain and Its Impact on Sensorimotor Control of the Spine. *J Orthop Sports Phys Ther* 2019 Jun;49(6):389-401. van Dieën JH, Reeves NP, Kawchuk G, et al. Motor Control Changes in Low Back Pain: Divergence in Presentations and Mechanisms. *J Orthop Sports Phys Ther* 2019 May;49(6):370-379. Sonnery-Cottet B, Saithna A, Quelard B, et al. Arthrogenic muscle inhibition after ACL reconstruction: a scoping review of the efficacy of interventions. British journal of sports medicine. 2019 Mar 1;53(5):289-98. Sonnery-Cottet B, Hopper GP, Gousopoulos L, et al. Arthrogenic Muscle Inhibition Following Knee Injury or Surgery: Pathophysiology, Classification, and Treatment. Video Journal of Sports Medicine. 2022 Apr;2(3):26350254221086295. Hopkins JT, Ingersoll CD. Arthrogenic Muscle Inhibition: A limiting Factor In Joint Rehabilitation. *J Sport Rehabil* 2000; 9:135-159. Lepley AS, Lepley LK. Mechanisms of Arthrogenic Muscle Inhibition. *J Sport Rehabil* 2021 Sep 1:1-10. Young A. Current issues in arthrogenic inhibition. *Ann Rheum Dis* 1993: 52:829-834. Stokes M, Young A. The contribution of reflex inhibition to arthrogenous muscle weakness. *Clin Sci* 1984; 67:7-14. Gabel CP, Mokhtarinia HR, Melloh M, Mateo S. Slacklining as therapy to address non-specific low back pain in the presence of multifidus arthrogenic muscle inhibition. *World J Orthop* 2021 Apr 18;12(4):178-196. Schilaty ND, McPherson AL, Nagai T, et al. Arthrogenic muscle inhibition manifests in thigh musculature motor unit characteristics after anterior cruciate ligament injury. *Eur J Sport Sci* 2022 May 2:1-11. Cervero F, Schaible HG, Schmidt RF. Tonic descending inhibition of spinal cord neurons driven by joint afferents in normal cats and in cats with inflamed knee joint. Exp Brain Res 1991; 83:675-678. Kiesel KB, Butler RJ, Duckworth A, et al. Experimentally induced pain alters the EMG activity of the lumbar multifidus in asymptomatic subjects. Man Ther 2012 Jun;17(3):236-40. Kiesel KB, Uhl T, Underwood FB, et al. Rehabilitative ultrasound measurement of select trunk muscle activation during induced pain. Man Ther 2008(2):132-8 Tucker KJ, Hodges PW. Changes in motor unit recruitment strategy during pain alters force direction. *Eur J Pain* 2010; 14:932-8. Mannion AF.

Fibre type characteristics and function of the human paraspinal muscles: normal values and changes in association with low back pain. *J Electromyogr Kinesiol 1999*;9(6):363-77. Larivière C, Gagnon D, Loisel P. The comparison of trunk muscles EMG activation between subjects with and without chronic low back pain during flexion-extension and lateral bending tasks. *J Electromyogr Kinesiol* 2000 (2):79-91. Falla D, Gizzi L, Tschapek M, et al. Reduced task-induced variations in the distribution of activity across back muscle regions in individuals with low back pain. *Pain* 2014;155(5):944-53. Dannels L, Coorevits P, Cools A et al. Differences in electromyographic activity in the multifidus muscle and iliocostalis lumborum between healthy subjects and patients with sub-acute and chronic low back pain. *Eur Spine J* 2002; 11:13-19. Clark N, Voight ML, Campbell AM, et al. The Relationship Between Segmental Rolling Ability and Lumbar Multifidus Activation Time. *Int J Sport Phys Ther* 2017; 12(6):921-930 Goubert D, De Pauw R, Meeus M, et al. Lumbar muscle structure and function in chronic versus recurrent low back pain: a cross-sectional study. *Spine J* 2017;17(9):1285-1296. He K, Head J, Mouchtouris N, et al. The Implications of Paraspinal Muscle Atrophy in Low Back Pain, Thoracolumbar Pathology and Clinical Outcomes After Spine Surgery: A review of the literature. Global Spine J 2020, 10(5)657-666. Moseley GL, Nicholas MK, Hodges PW. Does anticipation of back pain predispose to back trouble? *Brain*2004; 127:2339-2347. Hodges PW, Richardson CA. Inefficient muscular stabilization of the lumbar spine associated with low back pain. A motor control evaluation of transversus abdominis. *Spine* 1996;21(22):2640–2650. Tsao H, Galea MP, Hodges PW. Driving plasticity in the motor cortex in recurrent low back pain. *Eur J Pai*n 2010; 14:832-839. Massé-Alarie H, Beaulieu LD, Preuss R, et al. Corticomotor control of lumbar multifidus muscles is impaired in chronic low back pain: concurrent evidence from ultrasound imaging and double-pulse transcranial magnetic stimulation. *Exp Brain Res* 2016;234(4):1033-1045. Massé-Alarie H, Beaulieu LD, Preuss R, et al. Influence of paravertebral muscles training on brain plasticity and postural control in chronic low back pain. *Scand J Pain* 2016; 12:74-83. Schabrun SM, Elgueta-Cancino EL, Hodges PW. Smudging of the Motor Cortex Is Related to the Severity of Low Back Pain. *Spine* 2017;42(15):1172-1178. Hodges PW, Tucker K. Moving differently in pain: a new theory to explain the adaptation to pain. *Pain* 2011; 152: S90-98. Meier ML, Vrana A, Schweinhardt P. Low back pain: the potential contribution of supraspinal motor control and proprioception. *The Neuroscientist* 2019; 25(6):583-96. Karayannis NV, Smeets RJ, van den Hoorn W, et al. Fear of Movement Is Related to Trunk Stiffness in Low Back Pain. *PLoS One* 2013;8(6): e67779. Wesselink E, de Raaij E, Pevenage P, et al. Fear-avoidance beliefs are associated with a high fat content in the erector spinae: a 1.5 tesla magnetic resonance imaging study. *Chiropr Man Therap* 2019; 27:14. Wertli MM, Rasmussen-Barr E, Weiser S, et al. The role of fear avoidance beliefs as a prognostic factor for outcome in patients with nonspecific low back pain: A systematic review. *Spine J* 2014 14(5), 816-836. Luque-Suarez A, Martinez-Calderon J, Falla D. Role of kinesiophobia on pain, disability, and quality of life in people suffering from chronic musculoskeletal pain: a systematic review. *Br J Sports Med* 2019;53(9):554-559. Goossens N, Janssens L, Brumagne S. Changes in the Organization of the Secondary Somatosensory Cortex While Processing Lumbar Proprioception and the Relationship With Sensorimotor Control in Low Back Pain. *The Clinical Journal of Pain* 2019;35(5):394-406. Devecchi V, Rushton AB, Gallina A, Heneghan NR, Falla D. Are neuromuscular adaptations present in people with recurrent spinal pain during a period of remission? a systematic review. *PLoS One* 2021; 1;16(4):e0249220. Brumagne S, Janssens L, Janssens E, et al. Altered postural control in anticipation of postural instability in persons with recurrent low back pain. *Gait Posture* 2008;28(4):657-62. Belavy DL, Armbrecht G, Richardson CA, et al. Muscle atrophy and changes in spinal morphology: is the lumbar spine vulnerable after prolonged bed rest? *Spine* 2011;36(2):137–145. Claus AP, Hides JA, Moseley GL, et al. Different ways to balance the spine in sitting: Muscle activity in specific postures differs between individuals with and without a history of back pain in sitting. *Clin Biomech*2018; 52:25-32. Xiao W, Yang H, Wang Z, et al. Postural Control of Patients with Low Back Pain Under Dual-Task Conditions. *J Pain Res* 2023;16:71-82. Wallwork TL, Stanton WR, Freke M. The effect of chronic low back pain on size and contraction of the lumbar multifidus muscle. *Man Ther* 2009; 14:496-500. Hildebrandt M, Fankhauser G, Meichtry A, et al. Correlation between lumbar dysfunction and fat infiltration in lumbar multifidus muscle in patients with low back pain. *BMC Musculoskelet Disord* 2017; 18:12. Hodges PW, James G, Blomster L, Hall L, et al. Multifidus Muscle Changes After Back Injury Are Characterized by Structural Remodeling of Muscle, Adipose and Connective Tissue, but Not Muscle Atrophy: Molecular and Morphological Evidence. *Spine* 2015 Jul 15;40(14):1057-71. Hides JA, Stokes MJ, Saide M, et al. Evidence of lumbar multifidus muscle wasting ipsilateral to symptoms in patients with acute/subacute low back pain. *Spine* 1994 Jan 15;19(2):165-72. Goubert D, Van Oosterwicjck, Meeus M, et al. Structural Changes of lumbar muscles in non-specific low back pain: a systematic review. *Pain Physician* 2016:19: E985-1000. Hides J, Gilmore C, Stanton W, et al. Multifidus size and symmetry among chronic low back pain and healthy asymptomatic subjects. *Man*

Ther 2008;13(1):43–49. Teichtahl AJ, Urquhart DM, Wang Y, et al. Fat infiltration of paraspinal muscles is associated with low back pain, disability, and structural abnormalities in community-based adults. *Spine J* 2015;15(7):1593–1601. Wang YX, et al. Multifidus muscle atrophy is present in patients with chronic but not acute unilateral lumbar radiculopathy. *Skeletal Radiol* 2012;41(6): 709-15. Crawford RJ, et al. Differences in Multifidus Morphology between Healthy and LBP Groups: A Systematic Review with Meta-analysis. *Spine* 2017;42(15): 1158-71. Barker KL, Shamley DR, Jackson D. Changes in the cross-sectional area of multfidus and psoas in patients with unilateral back pain: The relationship to pain and disability. *Spine* 2004;29:515-519. Shafaie FS, Ebrahimi I, Kamali M, et al. Comparison of lumbar multifidus size in athletes with and without low back pain. *JOSPT* 2017, 47(6), 421-426. Lee JC, Cha JG, Kim Y. An evaluation of multifidus cross-sectional area and position in different postures in men with chronic low back pain. *Spine* 2014, 39(7), E414-E419. Kjaer P, Bendix T, Sorensen JS, et al. Are MRI-defined fat infiltrations in the multifidus muscles associated with low back pain? BMC Med 2007; 25;5:2. Cooley JR, Jensen TS, Kjaer P. et al. Spinal degeneration is associated with lumbar multifidus morphology in secondary care patients with low back or leg pain. *Sci Rep* 2022;12, 14676. Kalichman L, Carmeli E, Been E. The Association between Imaging Parameters of the Paraspinal Muscles, Spinal Degeneration, and Low Back Pain. *Biomed Res Int* 2017; 2017:2562957. Yu B, Jiang K, Li X, et al. Correlation of the Features of the Lumbar Multifidus Muscle With Facet Joint Osteoarthritis. *Orthopedics* 2017;40(5):e793-e800. Sun D, Liu P, Cheng J, et al. Correlation between intervertebral disc degeneration, paraspinal muscle atrophy, and lumbar facet joints degeneration in patients with lumbar disc herniation. *BMC Musculoskelet Disord* 2017;18(1):167. Han, G., Zou, D., Liu, Z. et al. Paraspinal muscle characteristics on MRI in degenerative lumbar spine with normal bone density, osteopenia, and osteoporosis: a case-control study. *BMC Musculoskelet Disord* 2022; 23, 73. Wang X, Jia R, Li J, et al. Research Progress on the Mechanism of Lumbar multifidus Injury and Degeneration. *Oxid Med Cell Longev* 2021; 2021:6629037. Kalichman L, Klindukhov A, Li L, et al. Indices of Paraspinal Muscles Degeneration: Reliability and Association With Facet Joint Osteoarthritis: Feasibility Study. *Clin Spine Surg* 2016;29(9):465-470. Özcan-Ekşi EE, Ekşi MŞ, Akçal MA. Severe Lumbar Intervertebral Disc Degeneration Is Associated with Modic Changes and Fatty Infiltration in the Paraspinal Muscles at all Lumbar Levels, Except for L1-L2: A Cross-Sectional Analysis of 50 Symptomatic Women and 50 Age-Matched Symptomatic Men. *World Neurosurg* 2019;122:e1069-e1077. Shi L, Yan B, Jiao Y, et al. Correlation between the fatty infiltration of paraspinal muscles and disc degeneration and the underlying mechanism. *BMC Musculoskelet Disord* 2022 May 30;23(1):509. Faur C, Patrascu JM, Haragus H, et al. Correlation between multifidus fatty atrophy and lumbar disc degeneration in low back pain. *BMC Musculoskelet Disord* 2019;20(1):414. Jun HS, Kim JH, Ahn JH, et al. The Effect of Lumbar Spinal Muscle on Spinal Sagittal Alignment: Evaluating Muscle Quantity and Quality. *Neurosurgery* 2016;79(6):847-855. Bok DH, Kim J, Kim TH. Comparison of MRI-defined back muscles volume between patients with ankylosing spondylitis and control patients with chronic back pain: age and spinopelvic alignment matched study. *Eur Spine J* 2017;26(2):528-537. Suzuki K, Hasebe Y, Yamamoto M, et al. Risk Factor Analysis for Fat Infiltration in the Lumbar Paraspinal Muscles in Patients With Lumbar Degenerative Diseases. *Geriatr Orthop Surg Rehabil* 2022; 13:21514593211070688. Huang Y, Wang L, Luo B, et al. Associations of Lumber Disc Degeneration with Paraspinal Muscles Myosteatosis in Discogenic Low Back Pain. *Front Endocrinol (Lausanne)* 2022; 13:891088. Menezes-Reis R, Bonugli GP, Salmon CEG, Mazoroski D, Herrero CFPDS, Nogueira-Barbosa MH. Relationship of spinal alignment with muscular volume and fat infiltration of lumbar trunk muscles. *PLoS One*2018;13(7):e0200198. Wang K, Deng Z, Chen X, et al. The Role of Multifidus in the Biomechanics of Lumbar Spine: A Musculoskeletal Modeling Study. *Bioengineering (Basel)* 2023;10(1):67. Shahidi B, Hubbard JC, Gibbons MC, et al. Lumbar multifidus muscle degenerates in individuals with chronic degenerative lumbar spine pathology. *J Orthop Res* 2017; 35,12:2700-2706. James G, Chen X, Diwan A, et al. Fat infiltration in the multifidus muscle is related to inflammatory cytokine expression in the muscle and epidural adipose tissue in individuals undergoing surgery for intervertebral disc herniation. *Eur Spine J* 2021;(4):837-845. James G, Millecamps M, Stone LS, et al. Dysregulation of the Inflammatory Mediators in the Multifidus Muscle After Spontaneous Intervertebral Disc Degeneration SPARC-null Mice is Ameliorated by Physical Activity. *Spine* 2018;43(20):E1184-E1194. James G, Sluka KA, Blomster L, et al. Macrophage polarization contributes to local inflammation and structural change in the multifidus muscle after intervertebral disc injury. *Eur Spine J* 2018;(8):1744-1756. De Martino E, Hides J, Elliott JM, et al. Intramuscular lipid concentration increased in localized regions of the lumbar muscles following 60-day bedrest. *Spine J* 2022(4):616-628. Seyedhoseinpoor T, Taghipour M, Dadgoo M, et al. Alteration of lumbar muscle morphology and composition in relation to low back pain: a systematic review and meta-analysis. *Spine J* 2022 (4):660-676. Yazici A, Yerlikaya T. Investigation of the

relationship between the clinical evaluation results of lumbar region muscles with cross-sectional area and fat infiltration. *J Back Musculoskelet Rehabil* 2022 May 13. Cunningham E, Wedderkopp N, Kjaer P, *et al.* The relationships between physical activity, lumbar multifidus muscle morphology, and low back pain from childhood to early adulthood: a 12-year longitudinal study. *Sci Rep* 2022;12, 8851. D'hooge R, Cagnie B, Crombez G, et al. Lumbar muscle dysfunction during remission of unilateral recurrent nonspecific low-back pain: evaluation with muscle functional MRI. *Clin J Pain* 2013 Mar;29(3):187-94. Mannion AF, Dumas GA, Cooper RG, et al. Muscle fiber size and type distribution in thoracic and lumbar regions of erector spinae in healthy subjects without low back pain: normal values and sex differences. *J Anat* 1997;190 (Pt 4)(Pt 4):505-13. Mannion AF, Käser L, Weber E, et al. Influence of age and duration of symptoms on fibre type distribution and size of the back muscles in chronic low back pain patients. *Eur Spine J* 2000;9(4):273-81. Fortin M, Lazáry À, Varga PP, et al. Association between paraspinal muscle morphology, clinical symptoms, and functional status in patients with lumbar spinal stenosis. *Eur Spine J* 2017;26(10):2543-2551. Fortin M, Macedo LG. Multifidus and paraspinal muscle group cross-sectional areas of patients with low back pain and control patients: a systematic review with a focus on blinding. *Phys Ther* 2013 Jul;93(7):873-88. Ranger TA, Cicuttini FM, Jensen TS, Peiris WL, Hussain SM, Fairley J, Urquhart DM. Are the size and composition of the paraspinal muscles associated with low back pain? A systematic review. *Spine J*2017;17(11):1729-48. Rezazadeh F, Taheri N, Okhravi SM, Hosseini SM. The relationship between cross-sectional area of multifidus muscle and disability index in patients with chronic non-specific low back pain. *Musculoskelet Sci Pract* 2019;42:1-5. Naghdi N, Mohseni-Bandpei MA, Taghipour M, Rahmani N. Lumbar Multifidus Muscle Morphology Changes in Patient with Different Degrees of Lumbar Disc Herniation: An Ultrasonographic Study. *Medicina (Kaunas)* 2021;57(7):699. Altinkaya N., Cekinmez M. Lumbar multifidus muscle changes in unilateral lumbar disc herniation using magnetic resonance imaging. *Skelet. Radiol* 2015;45:73–77. Thu KW, Maharjan S, Sornkaew K, et al. Multifidus Muscle Contractility Deficit Was Not Specific to the Painful Side in Patients with Chronic Low Back Pain During Remission: A Cross-Sectional Study. *J Pain Res* 2022;19;15:1457-1463. Crawford RJ, Volken T, Mhuiris ÁN, et al. Geography of lumbar paravertebral muscle fatty infiltration: the influence of demographics, low back pain, and disability. *Spine* 2019 Sep 15;44(18):1294-302. Fortin M, Videman T, Gibbons LE, Battie MC. Paraspinal muscle morphology and composition: a 15-yr longitudinal magnetic resonance imaging study. *Medicine and science in sports and exercise* 2014 Jan 1;46(5):893-901. Qaseem A, Wilt TJ, McLean RM, Forciea MA. Noninvasive treatments for acute, subacute, and chronic low back pain: A clinical practice guideline from the American College of Physicians. Ann Intern Med. 2017;166(7):514-530. Hides JA, Stanton WR, McMahon S, Sims K, Richardson CA. Effect of stabilization training on multifidus muscle cross-sectional area among young elite cricketers with low back pain. J Orthop Sports Phys Ther. 2008 Mar;38(3):101-8. doi: 10.2519/jospt.2008.2658. Epub 2007 Dec 7. PMID: 18349481. Danneels LA, Vanderstraeten GG, Cambier DC, et al Effects of three different training modalities on the cross-sectional area of the lumbar multifidus muscle in patients with chronic low back pain British Journal of Sports Medicine 2001;35:186-191. Kliziene I, Sipaviciene S, Klizas S, Imbrasiene D. Effects of core stability exercises on multifidus muscles in healthy women and women with chronic low-back pain. J Back Musculoskelet Rehabil. 2015;28(4):841-7. doi: 10.3233/BMR-150596. PMID: 25881694. Macedo LG, Latimer J, Maher CG, et al. Effect of motor control exercises versus graded activity in patients with chronic nonspecific low back pain: a randomized controlled trial. *Phys Ther* 2012;92: 363–77. Lindsay K, Caplan N, Weber T, et al. Effects of a six-week exercise intervention on function, pain, and lumbar multifidus muscle cross-sectional area in chronic low back pain: A proof-of-concept study. *Musculoskelet Sci Pract* 2020 Oct; 49:102190. Gorji SM, Mohammadi Nia Samakosh H, Watt P, et al. Pain Neuroscience Education and Motor Control Exercises versus Core Stability Exercises on Pain, Disability, and Balance in Women with Chronic Low Back Pain. *Int J Environ Res Public Health* 2022;19(5):2694. Galán-Martín MA, Montero-Cuadrado F, Lluch-Girbes E, et al. Pain neuroscience education and physical exercise for patients with chronic spinal pain in primary healthcare: a randomized trial protocol. *BMC Musculoskelet* Disord 2019 Nov 3;20(1):505. Ibrahim AA, Akindele MO, Ganiyu SO. Effectiveness of patient education plus motor control exercise versus patient education alone versus motor control exercise alone for rural community-dwelling adults with chronic low back pain: a randomised clinical trial. BMC Musculoskelet Disord. 2023 Feb 23;24(1):142. doi: 10.1186/s12891-022-06108-9. PMID: 36823567; PMCID: PMC9948461. Rabiei P, Sheikhi B, Letafatkar A. Comparing Pain Neuroscience Education Followed by Motor Control Exercises With Group-Based Exercises for Chronic Low Back Pain: A Randomized Controlled Trial. Pain Pract. 2021 Mar;21(3):333-342. doi: 10.1111/papr.12963. Epub 2020 Nov 21. PMID: 33135286. Saragiotto BT, Maher CG, Yamato TP, et al. Motor control exercise for chronic non-specific low-back pain. *Cochrane Database Syst Rev* 2016 Jan 8;2016(1):CD012004. Freynhagen R, Parada HA,

CalderonOspina CA, et al. Current understanding of the mixed pain concept: a brief narrative review. Curr Med Res Opin 2019; 35: 1011–18. Mok NW, Brauer SG, Hodges PW. Failure to use movement in postural strategies leads to increased spinal displacement in low back pain. *Spine* 2007 Sep 1;32(19):E537-43 Mok NW, Brauer SG, Hodges PW. Changes in lumbar movement in people with low back pain are related to compromised balance. *Spine* 2011 Jan 1;36(1). Hodges P, Holm AK, Hansson T, Holm S. Rapid atrophy of the lumbar multifidus follows experimental disc or nerve root injury. *Spine* 2006;31(25):2926-33. Claeys K, Brumagne S, Dankaerts W, et al. Decreased variability in postural control strategies in young people with non-specific low back pain is associated with altered proprioceptive reweighting. *Eur J Appl Physiol* 2011 Jan;111(1):115-23. Hemmati L, Piroozi S, Rojhani-Shirazi Z. Effect of dual tasking on anticipatory and compensatory postural adjustments in response to external perturbations in individuals with nonspecific chronic low back pain: electromyographic analysis. *J Back Musculoskelet Rehabil* 2018;31:489–497. Mohammadi M, Ghamkhar L, Alizadeh A, et al. Comparison of the reliance of the postural control system on the visual, vestibular and proprioceptive inputs in chronic low back pain patients and asymptomatic participants. *Gait Posture* 2021;85:266-272. Ito T, Sakai Y, Morita Y, et al. Proprioceptive Weighting Ratio for Balance Control in Static Standing Is Reduced in Elderly Patients With Non-Specific Low Back Pain. *Spine* 2018 Dec 15;43(24):1704-1709. Johanson E, Brumagne S, Janssens L, et al. The effect of acute back muscle fatigue on postural control strategy in people with and without recurrent low back pain. *Eur Spine J* 2011 Dec;20(12):2152-9. Shokouhyan SM, Davoudi M, Hoviattalab M, et al. Distinction of non-specific low back pain patients with proprioceptive disorders from healthy individuals by linear discriminant analysis. *Front Bioeng Biotechno*l 2022;13;10:1078805. Ferrari S, Manni T, Bonetti F, et al. A literature review of clinical tests for lumbar instability in low back pain: validity and applicability in clinical practice. *Chiropr Man Therap* 2015;23:14. Published 2015 Apr 8. Denteneer L, Stassijns G, De Hertogh, et al. Inter- and Intrarater Reliability of Clinical Tests Associated With Functional Lumbar Segmental Instability and Motor Control Impairment in Patients With Low Back Pain: A Systematic Review. *Arch Phys Med Rehabil* 2017 Jan;98(1):151-164. Hebert JJ, Koppenhaver SL, Teyhen DS, et al. The evaluation of lumbar multifidus muscle function via palpation: reliability and validity of a new clinical test. *Spine J* 2015;15(6):1196-1202. Kamath S, Venkatanarasimha N, Walsh MA, et al. MRI appearance of muscle denervation. *Skeletal Radiol* 2008; 37(5):397-404. Sayed D, Grider J, Strand N, et al. The American Society of Pain and Neuroscience (ASPN) Evidence-Based Clinical Guideline of Interventional Treatments for Low Back Pain. *J Pain Res* 2022 Dec 6;15:3729-3832. Mekhail N, Eldabe S, Templeton E, Costandi S, Rosenquist R. Pain Management Interventions for the Treatment of Chronic Low Back Pain: A Systematic Review and Meta-Analysis. Clin J Pain. 2023 Apr 24. doi: 10.1097/AJP.0000000000001116. Epub ahead of print. PMID: 37104694. Caylor J, Reddy R, Yin S, et al. Spinal cord stimulation in chronic pain: evidence and theory for mechanisms of action. *Bioelectronic Medicine* 2019; 5(12): 1-41. Tieppo Francio V, Polston KF, Murphy MT et al. Management of chronic and neuropathic pain with 10kHz spinal cord stimulation technology: summary of findings from preclinical and clinical studies. *Biomedicines* 2021; 9(644):1-15. Jensen MP, Brownstone RM. Mechanisms of spinal cord stimulation for the treatment of pain: Still in the dark after 50 years. *Eur J Pain* 2019;23(4):652-659. Lam CM, Latif U, Sack A, Govindan S, et al. Advances in Spinal Cord Stimulation. *Bioengineering (Basel)* 2023 Feb 1;10(2):185. Malinowski MN, Chopra PR, Tieppo Francio V, et al. A narrative review and future considerations of spinal cord stimulation, dorsal root ganglion stimulation and peripheral nerve stimulation. *Curr Opin Anaesthesiol* 2021;34(6):774-780. Strand N, J M, Tieppo Francio V, et al. Advances in Pain Medicine: a Review of New Technologies. *Curr Pain Headache Rep* 2022;26(8):605-616. Char S, Jin MY, Francio VT, et al. Implantable Peripheral Nerve Stimulation for Peripheral Neuropathic Pain: A Systematic Review of Prospective Studies. *Biomedicines* 2022; 10(10):2606. Helm S, Shirsat N, Calodney A, et al. Peripheral Nerve Stimulation for Chronic Pain: A Systematic Review of Effectiveness and Safety. *Pain Ther* 2021 Dec;10(2):985-1002. Strand N, D'Souza RS, Hagedorn JM, et al. Evidence-Based Clinical Guidelines from the American Society of Pain and Neuroscience for the Use of Implantable Peripheral Nerve Stimulation in the Treatment of Chronic Pain. *J Pain Res* 2022;23;15:2483-2504. Gilmore CA, Desai MJ, Hopkins TJ, et al. Treatment of chronic axial back pain with 60-day percutaneous medial branch PNS: Primary end point results from a prospective, multicenter study. *Pain Pract*2021;21(8):877-889. Deer TR, Eldabe S, Falowski SM, et al. Peripherally Induced Reconditioning of the Central Nervous System: A Proposed Mechanistic Theory for Sustained Relief of Chronic Pain with Percutaneous Peripheral Nerve Stimulation. *J Pain Res* 2021 Mar 12; 14:721-736. SPRINT Therapeutics Physician Reference Guide. Available at: https://www.sprtherapeutics.com/wp-content/uploads/2022/01/2022-SPRINT-Physician-Reference-Guide-MA-000004-03.pdf Deer TR, Gilmore CA, Desai MJ, et al. Percutaneous Peripheral Nerve Stimulation of the Medial Branch Nerves for the Treatment of Chronic Axial Back Pain in

Patients After Radiofrequency Ablation. *Pain Med*2021;22(3):548-560. Lee DW, Pritzlaff S, Jung MJ, et al. Latest Evidence-Based Application for Radiofrequency Neurotomy (LEARN): Best Practice Guidelines from the American Society of Pain and Neuroscience (ASPN). *J Pain Res*2021; 14:2807-2831. Russo MA, Santarelli DM. Development and Description of a New Multifidus-Sparing Radiofrequency Neurotomy Technique for Facet Joint Pain. *Pain Pract* 2021 Sep;21(7):747-758. Sadeghi S, Bible JE, Cortes DH. Quantifying Dysfunction of the Lumbar Multifidus Muscle After Radiofrequency Neurotomy and Fusion Surgery: A Preliminary Study. *J of Medical Diagnostics* 2020; 3(4): 04100.1 Smuck M, Crisostomo RA, Demirjian R, et al. Morphologic changes in the lumbar spine after lumbar medial branch radiofrequency neurotomy: a quantitative radiological study. *Spine J* 2015;15:1415-1421. Oswald KAC, Ekengele V, Hoppe S, et al. Radiofrequency Neurotomy does not cause fatty degeneration of the lumbar paraspinal musculature in patients with chronic lumbar pain-a retrospective 3D-computer- assisted MRI analysis using iSix software. *Pain Med* 2023;24(1):25-31. Songjaroen, S., Sungnak, P., Piriyaprasarth, P. *et al.* Combined neuromuscular electrical stimulation with motor control exercise can improve lumbar multifidus activation in individuals with recurrent low back pain. *Sci Rep* 2021; 11, 14815. Pinto SM, Boghra SB, Macedo LG, Zet al. Does Motor Control Exercise Restore Normal Morphology of Lumbar Multifidus Muscle in People with Low Back Pain? – A Systematic Review. *J Pain Re*s 2021; 14:2543-2562. Ouchi K, Watanabe M, Tomiyama C, et al. Emotional Effects on Factors Associated with Chronic Low Back Pain*. J Pain Res 2019*;12:3343-3353. Fletcher C, Bradnam L, Barr C. The relationship between knowledge of pain neurophysiology and fear avoidance in people with chronic pain: A point in time, observational study. *Physiother Theory*

Acknowledgements: N/A

Learning Objectives: This oral presentation has the following objectives: (1) To educate physicians regarding what is multifidus dysfunction and how is it different than facet arthropathy or discogenic pain emphasizing the phenotypical profile based on the current state of the art of this extensive review study with more than 180 references. (2) To discuss if multifidus atrophy is equivalent to pain and multifidus dysfunction based on diagnostic MRI and EMG findings from the numerous studies reviewed. (3) To highlight the different mechanisms of action and paradigms (ablative versus neurostimulation of the lumba rmedial branch nerve). Should we stimulate or ablate the lumbar medial branch nerve? What are the clinical implications? Is there subsequent atrophy? What are the key principles contrasting restorative neurosimulation to other types of lumbar medial branch nerve stimulaiton? We hope to answer these frequently asked questions on this proposed oral presentation at INS 2024.

Financial Disclosures: VTF reports investigator-initiated study research grant from Nevro. VTF holds unpaid leadership position with ASPN. BDW has no conflicts of interest. AGC has research fees paid to institution in his name from Aspen, DARPA, NIH and Mainstay. AGC holds leadership positions in ASPN, ASRA, RISIPP, AAPMR, AAOE, all unpaid. AGC is the CEO of Pain Spine and Rehabilitation Consulting without conflicts of interest related to this abstract. DS reports grants from Boston Scientific; personal fees from Medtronic, Nevro, Saluda, Painteq (with options), Vertos (with options), SPR (with options), Mainstay (with options), and Surgentec. DS has no conflicts of interest directly related to this abstract.

Disclosure: No significant relationships.

O098

Oral Presentations
PERIPHERAL NERVE STIMULATION – CLINICAL UPDATE
15-05-2024 16:30 - 18:20

THE FIRST LONG TERM OBJECTIVE QUANTIFICATION OF MULTIFIDUS ACTIVITY DURING RESTORATIVE STIMULATION - 18FDG-PET-CT ASSESSMENT OF MULTIFIDUS ACTIVITY AND RADIOMICS BASED HETEROGENEITY ANALYSIS

Kavita Poply, FRCA, FCARCSI, FFPMRCA[1], Athar Haroon, MBBS, PhD[2], Theresa Wodehouse, PhD[3], Balaji Ganeshan, PhD[4], Raymond Endozo, MSc[4], Ben Goss, MSc, PhD[5], Gaurav Bajaj, MBBS[6], Vivek Mehta, MBBS, MD, FRCA, FFPMRCA[1]
[1]St Bartholomew's Hospital London, Barts Health NHS Foundation Trust, Spinal Pain & Neuromodulation, London, United Kingdom, [2]St Bartholomew's Hospital London, Barts Health NHS Foundation Trust, Radiology And Nuclear Medicine, London, United Kingdom, [3]Barts NHS trust, Pain Research Centre, London, United Kingdom, [4]University College London, Institute of Nuclear Medicine, London, United Kingdom, [5]Mainstay Medical, Research, San Diego, United States of America, [6]Bart's Health NHS Trust, Pain Research Centre, London, United Kingdom

Introduction: Restorative neurostimulation for chronic mechanical low back pain relies on stimulation of the L2 medial branch of the dorsal ramus to elicit episodic tetanic contractions of the lumbar multifidus muscle. Long term clinical, 4-year data supports the improvement in pain and quality of life indices.[1,2] This is now the first quantification of metabolic activity, heterogeneity using PET uptake measurements and radiomic based texture analysis on ^{18}F FDG-PET/CT that provides a unique opportunity to visualize and quantify changes in the segmental and entire lumbo-sacral length of multifidus and paraspinal muscles in response to restorative neurostimulation therapy.

Materials / Methods: After regulatory approval (Clin Trials Gov NCT04327817 and Rec 20/LO/0740) 7 patients underwent three ^{18}F FDG-PET/CT at baseline, 6 months and 1 year following multifidus stimulator implant. ^{18}F-FDG-PET CT was acquired on GE-Discovery 710 PET system with a 128 slice CT (approx. 250 MBq i.v). Baseline scan was performed with patients at rest while the six-month and 12-month scan was obtained immediately after a 30 minute multifidus stimulation session. Metabolic activity within the brain and multifidus was quantified using maximum standardized uptake value (SUVmax). Low dose CT texture analysis (CTTA) of the multifidus muscle was performed to examine changes in heterogeneity within the multifidus muscles (using entropy as a parameter reflecting irregularity at pixel resolution).

Results: Analysis of regions of interest specific to the deep multifidus showed significantly increased PET-FDG uptake (SUVmax) ($p<0.001$) between baseline scans and post-stimulation scans at 6 and 12 months within the deep multifidus muscle from L2 to L5 level. As part of the preliminary exploratory analysis, CTTA was available in the first 4 patients (who had a pre-stimulation and 6-month post-stimulation). CTTA (entropy) was significantly different ($p=0.004$) between post- and pre-stimulation within Deep Paraspinal muscles. CTTA (entropy) within Deep Paraspinal muscles was higher (median value: 4.12, range: 3.53-4.39) in post-stimulation compared to pre-stimulation (median value 3.81, range: 3.43-4.33). The prospective correlation for the 12-month follow-up data will be provided.

Discussion: The extent of activation observed ie. L2-L5 and textural changes in the muscle are consistent with animal studies demonstrating histological structural changes (submitted for publication).

Conclusions: This is the first long term quantification of muscle function and texture that demonstrates increased metabolic activity (^{18}FDG-PET/CT uptake and texture analysis) following stimulation of the L2 medial branch of the dorsal ramus. This could potentially explain the specific aspects of the restorative mechanism consistent with the electrophysiological finding.[3]

Supplemental Data: SUVmax at 6 months and 1 year Compared to Baseline in Superficial and Deep Mutlifidus Muscles from Levels L1-

L5

References: 1. Gilligan, C. *et al.* Three-Year Durability of Restorative Neurostimulation Effectiveness in Patients With Chronic Low Back Pain and Multifidus Muscle Dysfunction. *Neuromodulation* **26**, 98–108 (2023). 2. Gilligan, C. ID: 208698 four-year durability of restorative neurostimulation effectiveness

in patients with refractory chronic low back pain. *Neuromodulation* **26**, S148 (2023). 3. Kang, Y. M., Choi, W. S. & Pickar, J. G. Electrophysiologic evidence for an intersegmental reflex pathway between lumbar paraspinal tissues. *Spine* **27**, 56–63 (2002).

Acknowledgements:

Learning Objectives: 1. This is the first ever assessment of multifidus activity and radiomics based heterogeneity analysis data. 2. Increased metabolic activity and heterogeneity below the stimulated spinal level, suggests that there is extensive muscle activation in the lumbar region. 3. ^{18}FDG-PET/CT uptake and texture analysis could potentially be a useful tool for clinically validating the mechanism of action for restorative neurostimulation.

Financial Disclosures: Dr Ben Goss, Mainstay Medical, Company Employee, >$100,000 compensation

Disclosure: No significant relationships.

O099

Oral Presentations
PERIPHERAL NERVE STIMULATION – CLINICAL UPDATE
15-05-2024 16:30 - 18:20

RESTORATIVE NEUROSTIMULATION FOR CHRONIC MECHANICAL LOW BACK PAIN – LONG TERM RESULTS FROM THE UNITED KINGDOM POST MARKET CLINICAL FOLLOW-UP REGISTRY

Simon Thomson, MBBS
Mid & South Essex University Hospitals NHSFT, Pain And Neuromodulation Centre, Basildon, United Kingdom

Introduction: Chronic low back pain pathophysiology is complex and often a result of multiple overlapping mechanisms including modifications to motor control, reflex inhibition, and inflammatory mechanisms. Clinical evidence for the role of restorative neurostimulation in treating chronic low back pain has emerged from both prospective follow-up and randomised clinical trials, demonstrating substantial improvements in clinical outcomes such as pain, disability, and health-related quality of life.[1–3] Three year results are included here, but longer term four- and five-year outcomes will be presented.

Materials / Methods: Consented patients participated in an open label five-year prospective follow-up for treatment of chronic mechanical (nociceptive origin) chronic low back pain with a restorative neurostimulation system (ReActiv8®, Mainstay Medical, Dublin, Ireland) between September 2017 and September 2018. Data was collected at five UK sites (ClinicalTrials.gov Identifier: NCT01985230). Pain, disability, and health-related quality of life outcomes were collected at baseline, 45, 90, and 180 days, and 1-5 years after the activation visit. Patients were eligible if they met the instructions for use associated with the CE mark with the intention of reflecting real-world clinical practice.

Results: Forty-two patients were implanted with the system, and 33 (79%) were available at the three-year appointment. This cohort presented with severe chronic low back pain (numeric pain rating scale (NRS)=7.0 ± 0.2) and severe disability (Oswestry Disability Index (ODI)=46.6 ± 12.0). The health-related quality of life was also severely impacted at baseline (EQ-5D=0.426 ± 0.061). Changes in pain, disability, and quality of life at three-year follow-up demonstrated a statistically significant improvement between baseline and one, two and three years. After three years of therapy, average NRS scores had reduced to 2.7± 0.3 and mean ODI scores to 26.0 ± 3.1 while EQ-5D-5L indices improved to 0.707 ± 0.036. Missing data imputation increased these values marginally, but improvements remained both clinically substantial and statistically significant. Longitudinal analysis showed that the improvements between one and three years were statistically significant, consistent with the restorative mechanism of action. Five-year data will be presented.

Discussion: Longitudinal analysis showed that the improvements between one and three years were statistically significant, consistent with the restorative mechanism of action. Five-year data will be presented.

Conclusions: This post market cohort continues to demonstrate that restorative neurostimulation provides a statistically significant, clinically meaningful, and durable response across multiple outcome measures for patients suffering chronic mechanical low back pain drawn from a real-world population that has been refractory to conventional management.

Supplemental Data: N/A

References: 1. Gilligan, C. *et al.* An implantable restorative-neurostimulator for refractory mechanical chronic low back pain: a randomized sham-controlled clinical trial. *Pain* **162**, 2486–2498 (2021). 2. Gilligan, C. *et al.* Long-Term Outcomes of Restorative Neurostimulation in Patients With Refractory Chronic Low Back Pain Secondary to Multifidus Dysfunction: Two-Year Results of the ReActiv8-B

Pivotal Trial. *Neuromodulation* **26**, 87–97 (2023). 3. Gilligan, C. *et al.* Three-Year Durability of Restorative Neurostimulation Effectiveness in Patients With Chronic Low Back Pain and Multifidus Muscle Dysfunction. *Neuromodulation* **26**, 98–108 (2023).

Acknowledgements: The support of Mainstay Medical, Inc. for this project is gratefully acknowledged.

Learning Objectives: 1. By the end of this presentation, the audience will be able to evaluate the long term efficacy of restorative neurostimulation in mechanical chronic low back pain. 2. By the end of this presentation, the audience will be able to recognize the real-world evidence of restorative neurostimulation in patients with mechanical chronic low back pain 3. By the end of this presentation, the audience to analyze a new alternative for multifidus dysfunction in patients with chronic low back pain.

Financial Disclosures: Simon Thomson: a) Mainstay Medical; b) Consultant; c) $5,001 - $20,000 US a)Galvani Bioelectronics; b) Consultant; c) $501-$5,000 US a)Boston Scientific; b)Consultant; c) $5,001 - $20,000 US a)Saluda Medical; b)Consultant; c) $5,001 - $20,000 US Research grants all paid to institution - < $20,000 US each

Disclosure: No significant relationships.

O100

Oral Presentations
PERIPHERAL NERVE STIMULATION – CLINICAL UPDATE
15-05-2024 16:30 - 18:20

MULTI-CENTER PROSPECTIVE COHORT OF INTRACTABLE CHRONIC LOW BACK PAIN PATIENTS TREATED WITH RESTORATIVE NEUROSTIMULATION – OUTCOMES FROM 5-YEAR DATA

Christopher Gilligan, MD
Brigham and Women's Hospital Harvard Medical School, Division Of Pain Medicine, Boston, United States of America

Introduction: Mechanical chronic low back pain (CLBP), concomitant with dysfunctional neuromotor control, is often caused by underlying multifidus muscle dysfunction.[1] Restorative neurostimulation has demonstrated efficacy, safety, and durability for intractable mechanical CLBP. Direct stimulation of the dorsal rami medial branch nerves elicits multifidi muscle contractions to restore motor control, dynamic intervertebral stability, improve pain and disability by a mechanism that accrues with continued use of the implanted device.[2,3] This 5-year follow-up data evaluation from a pivotal restorative neurostimulation sham-controlled randomized clinical trial (RCT) (Clinicaltrials.gov Identifier: NCT02577354) aims to demonstrate meaningful durable improvements for this challenging population.

Materials / Methods: The RCT open label phase prospectively followed participants implanted with the system (ReActiv8®, Mainstay Medical, Inc., Dublin, Ireland) through five years. The study was conducted in the United States (US), Australia, and Europe and complied with US Food and Drug Administration regulations, ISO 14155, International Conference on Harmonization, and Declaration of Helsinki. Consented participants (N=204, age=47±9yrs; F110; BMI=28±4kg/m^2; pain duration=14.2±10.6yrs) were implanted over 21 months and randomized. Prespecified outcome measures included visual analog scale (VAS), Oswestry Disability Index (ODI), and quality of life (EQ-5D-5L) documented at intervals out to five years. Completer analysis and mixed-effects models for repeated measures for missing data imputations were conducted.

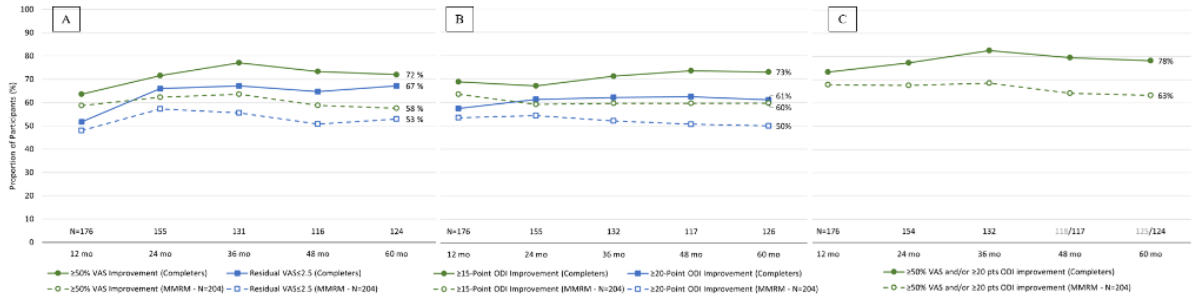
Results: A cohort with complete 5-year post-implantation records (N=126) was identified. Cohort changes from baseline for mean(±SE) VAS, ODI, and EQ-5D-5L were -4.9(±0.2) cm, -22.7(±1.4), and 0.231(±0.018), respectively (all $p<0.0001$). Of this cohort, 71.8% experienced ≥50% pain reduction, and 78.2% experienced either a ≥50% pain reduction and/or a ≥20-point ODI reduction (Fig.1). No lead migrations were observed.

Discussion: Restorative neurostimulation 5-year data from this multi-center RCT revealed significant reductions in mechanical CLBP symptoms and function with increased quality of life.

Conclusions: This is the first prospective study of chronic low back pain neurostimulation treatment with 5-year durability data. Lumbar multifidus restorative neurostimulation is safe, effective, and a durable rehabilitative treatment for patients with refractory, disabling, mechanical chronic low back pain associated with multifidus muscle dysfunction. After five years, this patient population, typically with few effective treatment options, had accrued durable and clinically substantial benefits in all predefined outcome measures including pain, disability, and healthcare-related quality of life.

Supplemental Data: Figure 1. Primary outcomes measure time points with responder percentages. A) Visual analog scale (VAS), B) Oswestry Disability Index (ODI), and C) composite scores of VAS and/or

ODI.



References: 1. Goubert, D., Van Oosterwijck, J., Meeus, M. & Danneels, L. Structural Changes of Lumbar Muscles in Non-specific Low Back Pain: A Systematic Review. *Pain Physician* **19**, E985–E1000 (2016). 2. Gilligan, C. *et al.* An implantable restorative-neurostimulator for refractory mechanical chronic low back pain: a randomized sham-controlled clinical trial. *Pain* **162**, 2486–2498 (2021). 3. Russo, M. *et al.* Muscle Control and Non-specific Chronic Low Back Pain. *Neuromodulation* **21**, 1–9 (2018).

Acknowledgements: The support of Mainstay Medical, Inc. for this project is gratefully acknowledged.

Learning Objectives: 1. By the end of this presentation, the audience will be able to evaluate the 5-year durability of restorative neurostimulation in mechanical chronic low back pain and restate its significant effectiveness in improving quality of life. 2. By the end of this presentation, the audience will be able to interpret and discuss the 5-year clinical trial evidence of restorative neurostimulation in patients with mechanical chronic low back pain. 3. By the end of this presentation, the audience will be able to summarize the overall 5- year trajectory of recovery of patients implanted with restorative neurostimulation systems and how/when they will respond to treatment.

Financial Disclosures: Christopher Gilligan, MD a) Mainstay Medical, Inc., b) Consultant/Advisory Board; c) $20,001 - $100,000 USD a) Mainstay Medical, Inc., b) Stock Options; c) $5,001 - $20,000 USD a) Pain Practice journal, b) Consultant/Advisory Board- Editor in Chief; c) not compensated a) North American Neuromodulation Society, b) Consultant/Advisory Board- finance committee member; c) not compensated a) International Neuromodulation Society; b) Consultant/Advisory Board - Board of Directors member; c) not compensated

Disclosure: No significant relationships.

O101

Oral Presentations
PERIPHERAL NERVE STIMULATION – CLINICAL UPDATE
15-05-2024 16:30 - 18:20

LOW FREQUENCY DORSAL ROOT STIMULATION IS EFFECTIVE FOR VARIOUS PAIN ETIOLOGIES AND PAIN LOCATIONS.

Pedram Tabatabaei, MD, PhD, Josef Salomonsson, RN, Pavlina Kakas, RN, Linda Bredemo, RN
University Hospital of Northern Sweden, Neurosurgery, Umeå, Sweden

Introduction: Dorsal root ganglion stimulation (DRG-S) is a novel therapy for treating various chronic neuropathic pain etiologies and locations by targeting different dorsal root ganglions (DRG)(1). However, the only data available for low frequency DRG-S is for low back pain(2, 3). One question that arises is whether low frequency stimulation, similar to 20 Hz stimulation, is also effective for other pain etiologies and pain locations. In this study, we will present real life data for low frequency DRG-S for various pain etiologies and locations.

Materials / Methods: Twenty-three patients with intractable chronic neuropathic pain, previously undergone successful DRG-S treatment, participated in a 13-day trial to compare the effectiveness of 4 Hz stimulation with traditional 20 Hz. This trial involved three phases: three days of 20 Hz stimulation, followed by a three-day washout period, and then seven days of 4 Hz stimulation. During the trial, patients were required to complete digital questionnaires three times a day. In the mornings, rating their pain levels using the Numeric Rating Scale (NRS) and reported on their sleep quality compared to the previous night. In the afternoons, rating their pain using the NRS score. Each evening, rating their pain (NRS score), as well as their activity level, mood, and social activities for the day, compared to the previous day's status. Following the trial, patients were asked to select their preferred stimulation setting for future therapy, rate their satisfaction (numeric scale 0-10), and evaluate the effectiveness of 4 Hz stimulation using the Patient Global Impression of Change self-assessment form (PGIC).

Results: 19 of 23 patients favored 4 Hz stimulation, two used both settings, and only two returned to the original 20 Hz stimulation. The average satisfaction rate for 4 Hz stimulation was 7.74 (range 4-10). Notably, 20 patients rated 4 Hz stimulation as superior to 20 Hz (PGIC score 4-5), one considered it equivalent (PGIC score 3), and two preferred 20 Hz (PGIC score 2). An alpha value of less than 0.001 indicated a significant reduction in average NRS scores when comparing the two stimulation frequencies.

Discussion: Low-frequency DRG-S appears to be a compelling option for treating intractable chronic neuropathic pain . Nonetheless, further research involving larger cohorts and longer follow-up periods is essential to thoroughly validate our findings.

Conclusions: Low-frequency DRG-S appears to be, at a minimum, as effective as 20 Hz stimulation for various pain etiologies and locations, and there appears to be a patient preference for 4 Hz stimulation.

Supplemental Data:

References: 1. Huygen F, Kallewaard JW, Nijhuis H, Liem L, Vesper J, Fahey ME, et al. Effectiveness and Safety of Dorsal Root Ganglion Stimulation for the Treatment of Chronic Pain: A Pooled Analysis. Neuromodulation. 2020;23(2):213-21. 2. Chapman KB, Yousef TA, Vissers KC, van Helmond N, M DS-H. Very Low Frequencies Maintain Pain Relief From Dorsal Root Ganglion Stimulation: An Evaluation of Dorsal Root Ganglion Neurostimulation Frequency Tapering. Neuromodulation. 2021;24(4):746-52. 3. Tabatabaei P, Salomonsson J, Kakas P, Eriksson M. Bilateral T12 Dorsal Root Ganglion Stimulation for the Treatment of Low Back Pain With 20-Hz and 4-Hz Stimulation, a Retrospective Study. Neuromodulation. 2023.

Acknowledgements:

Learning Objectives: 1. Low frequency DRG-S is effective for various pain etiologies and locations. 2. Low-frequency DRG-S appears to be, at a minimum, as effective as 20 Hz stimulation. 2. There seems to be a patient preference for 4 Hz stimulation when comparing to 20 Hz.

Financial Disclosures: Pedram Tabatabaei MD. PhD, Abbott laboratories, Speaker / Consultant / Advisory Board, $5,001 - $20,000 USD

Disclosure: No significant relationships.

O102

Oral Presentations
PERIPHERAL NERVE STIMULATION – CLINICAL UPDATE
15-05-2024 16:30 - 18:20

ENDOSCOPIC LATERAL APPROACH FOR DORSAL ROOT GANGLION BURST STIMULATION: RESULTS OF A PROSPECTIVE SINGLE-CENTER COHORT STUDY

Gregor Bara, MD[1], Jarek Maciaczyk, MD, PhD[1], Dirk De Ridder, MD[2], Jost Thissen, MD[3]
[1]University Hospital Bonn, Stereotactic And Functional Neurosurgery, Bonn, Germany, [2]University of Otago, Dunedin, New Zealand, [3]Schoen Clinic, Spine Center, Düsseldorf, Germany

Introduction: Recently, we have explored the feasibility of percutaneous transforaminal lead placement through a lateral endoscopic technique for burst-mode dorsal root ganglion (DRG) stimulation. This innovative approach aims to address the challenges DRG lead placement in patients who previous underwent prior spinal surgery with epidural scar formation and to improve the outcomes of DRG stimulation. Here we present the results of a prospective single-center cohort study examining BurstDR DRG stimulation via endoscopic transforaminal lead placement. Further we elaborate on the technique of programming.

Materials / Methods: 15 patients suffering from persistent spinal pain syndrome with predominant radicular pain who previously underwent a trial for spinal cord stimulation without significant pain reduction were enrolled. Leads were placed transforaminally via a lateral endoscopic technique and burst-mode dorsal root ganglion (DRG) stimulation was applied. Data collection included pain intensity measured in cm on VAS, Oswestry disability index (ODI), and health related quality of life (EQ5D). Data was collected prior to surgery, 2 days after surgery, 6 weeks after surgery and 12 weeks after surgery.

Results: This study shows the feasibility of endoscopic DRG lead placement and BurstDR stimulation. Significant improvements regarding pain intensity during rest and motion, disability as well as health related quality of life could be observed. The effects improved further during the postoperative course.

Discussion: This single center, prospective cohort study shows that burst stimulation on the dorsal root ganglion is feasible and can produce sufficient pain reduction, improvement of mobility and quality of life in cases of persistent spinal pain syndrome type 2. In particular, DRG burst stimulation showed to be more potent in a subset of patients who failed prior spinal cord stimulation.

Conclusions: BurstDR DRG stimulation applied via percutaneous lateral endoscopic transforaminal lead placement is feasible in a wider patient cohort and significantly eases disease burden in a subset of patients who previously failed spinal cord stimulation and underwent prior spine surgery making conventional DRG lead placement impossible due to epidural scar formation.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1) spinal cord stimulation 2) dorsal root ganglion stimulation 3) endoscopic placement of DRG leads

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O103

Oral Presentations
PERIPHERAL NERVE STIMULATION – CLINICAL UPDATE
15-05-2024 16:30 - 18:20

EXPLORING THE INFLUENCE OF DORSAL ROOT GANGLION STIMULATION ON SLEEP BEHAVIOR IN CHRONIC PAIN PATIENTS

Tariq Yousef, MD[1], Kenneth Chapman, MD[2,3,4], Julia Montag, BSc (Hons)[1], Sueda Sarica, BSc (Hons)[5], Noud Van Helmond, MD, PhD[1]
[1]THE SPINE AND PAIN INSTITUTE OF NEW YORK, New York, United States of America, [2]NYU Langone Medical Center, Anesthesiology/pain Medicine, New York, United States of America, [3]Zucker School of Medicine at Hofstra Northwell, Department Of Anesthesiology, Manhassat, United States of America, [4]Spine and Pain Institute of New York, New York, United States of America, [5]Radboud University Medical Center, Anesthesiology, Pain, And Palliative Medicine, Nijmegen, Netherlands

Introduction: Chronic pain has profound consequences on sleep quality and overall quality of life. Studies of chronic pain show sleep disturbances to be a prevalent symptom in 50–88% of patients. Insomnia scores improve with spinal cord stimulation (SCS) at six-month follow-up and correlate with improvements in pain. Dorsal Root Ganglion stimulation (DRG-S) has emerged as a promising therapeutic approach for managing chronic pain. However, its impact on sleep behavior remains underexplored. This study aims to investigate the effects of DRG stimulation on sleep patterns and quality in chronic pain patients.

Materials / Methods: We conducted a prospective observational study involving consecutive chronic pain patients who underwent DRG stimulation therapy at our institute over the past 4 years. Sleep behavior was assessed using the Insomnia Severity Index (ISI) standardized questionnaire before and after the initiation of DRG stimulation. Pain intensity (VAS), quality of life (EQ-5D), and opioid analgesic medication usage (MME) were also monitored throughout the study period. Mean scores at baseline and post implant intervals of 1, 3, 6, 12, 24, 36, and 48 months were compared for each reported outcome. Spearman's rank order correlations were run to examine relationships between change in VAS and ISI scores from baseline at 12 and 24 months.

Results: Post implant ISI scores decreased from an average baseline of moderately severe clinical insomnia (range 15-21) to no clinically significant insomnia (range 0-7). Average quality of life (EQ-5D) scores more than doubled post implant through 48 months. Pain intensity scores decreased by approximately 60% through all timepoints. Average morphine milligram equivalents (MME) decreased from 41 to 8 at 24 months. There were positive and significant correlations between change in VAS and ISI scores at 12 months (r_s=0.61, n=30, p<0.001) and 24 months (r_s=0.47, n=31, p<0.001).

Discussion: Our findings indicate DRG-S has a positive impact on sleep behavior in chronic pain patients. This novel approach not only alleviates pain but also promotes better sleep quality, ultimately enhancing the patients' overall well-being. These results highlight the potential of DRG stimulation as an effective therapeutic option for addressing the complex interplay between chronic pain and sleep disturbances. Further research is warranted to explore the underlying mechanisms and optimize treatment strategies for better sleep outcomes in this patient population.

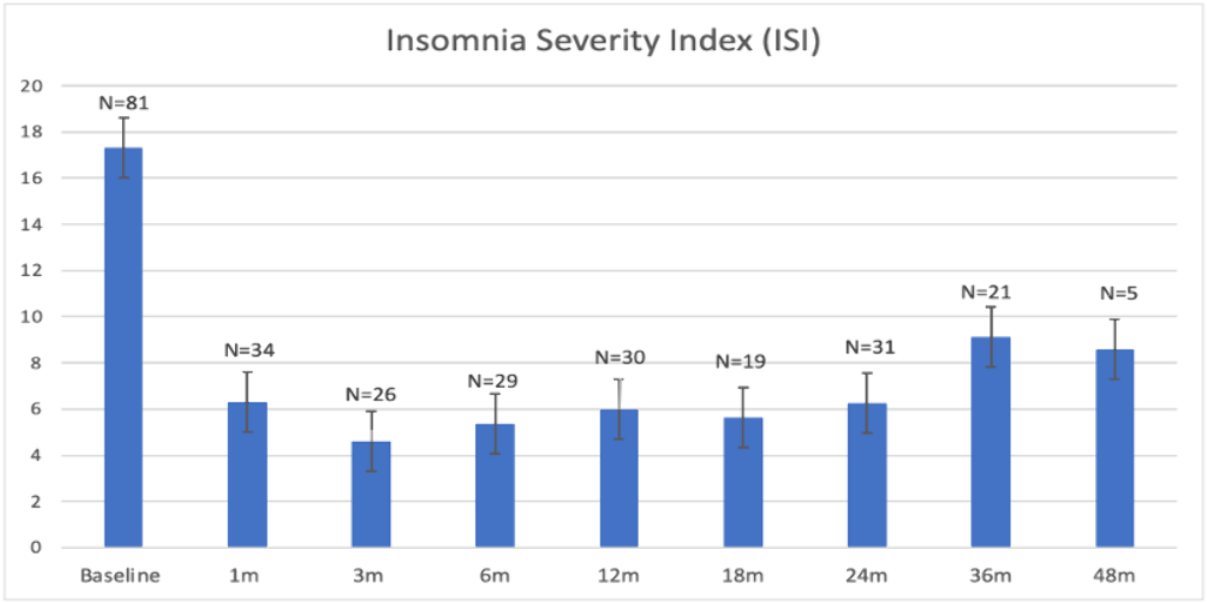
Conclusions: DRG-S improves patient reported sleep outcome measures. A follow-up study investigating objective sleep measures using Oura ring sleep monitoring devices to correlate with subjective reported outcomes is under progress.

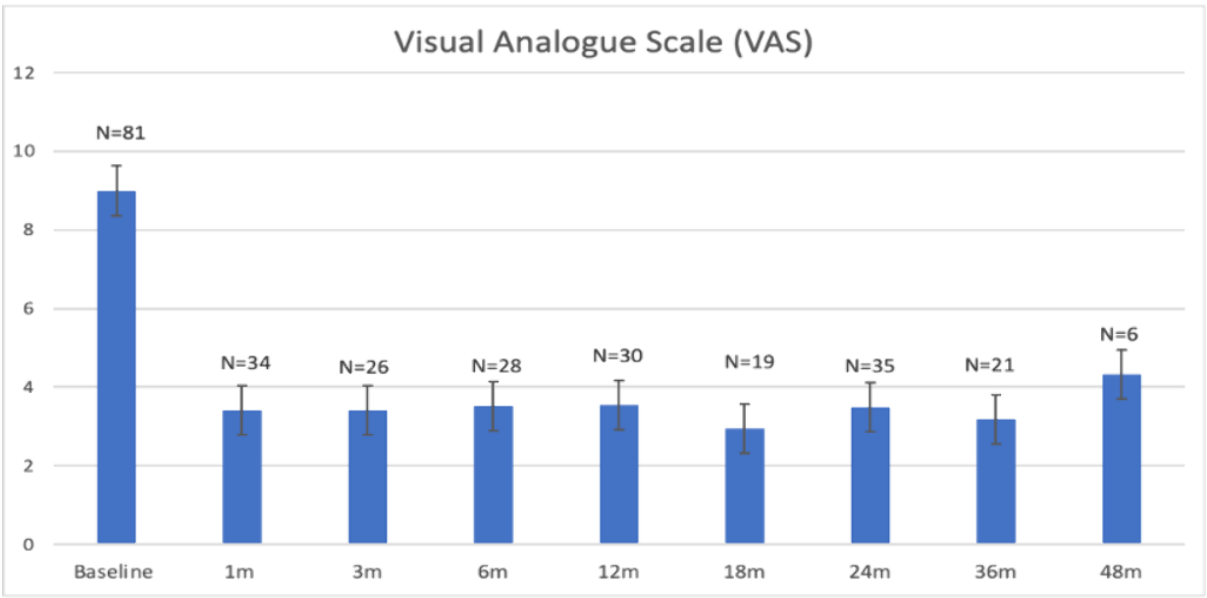
Supplemental Data: Table 1 –

Table 1. Demographic and Clinical Characteristics of Patients Who Had a DRG-S Implant.

Demographic and Clinical characteristics	Patients, *N = 81*
Demographics	
Sex, women/men	38/43
Age, y, mean ± SD	65 ± 16
Age at implant, y, mean ± SD	62 ± 16
Clinical characteristics	
Primary diagnosis, *n*	
Post Surgical Pain	37
Non-Surgical Pain	17
Neuropathic Pain	2
Radiculopathy	6
CRPS Type 1	9
Joint Pain	6
Miscellaneous	4
Medications	
Opioid use at baseline in MME, mean ± SD	41 ± 64
DRG-S treatment characteristics	
DRG-S lead location, *n*	
C7	2
C8	0
T1	2
T8	2
T11	2
T12	128
L1	7
L2	3
L3	6
L4	6
L5	7
S1	109
S2	2
S3	2
S4	2

Demographics Figure 1 – Mean patient reported outcome measures including sleep (ISI), pain (VAS), quality of life (EQ-5D) comparing baseline to post-implant timepoints (N=number of patients with survey response at each timepoint with data
available)





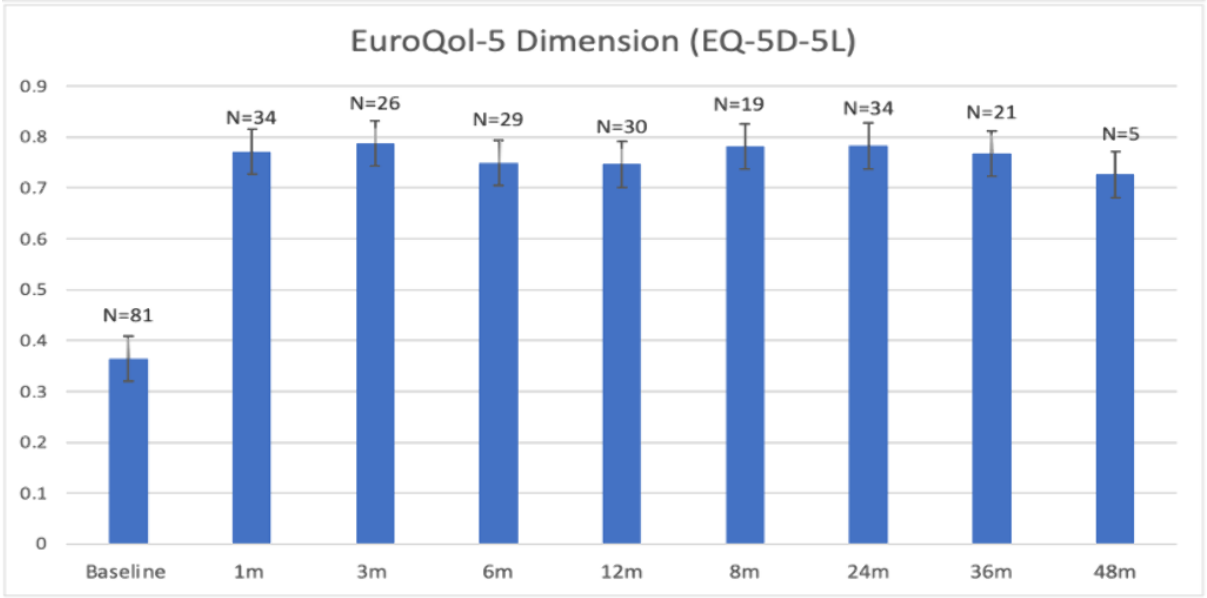
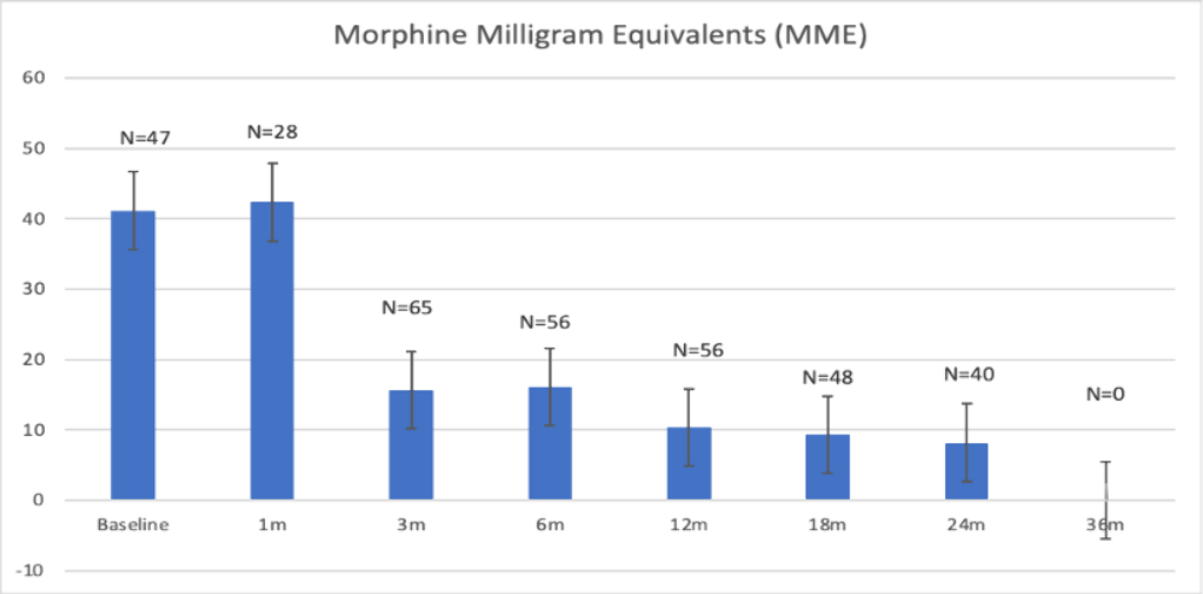


Figure 2. Mean daily opioid morphine milligram equivalent (MME) doseages at baseline and post-

implant
timepoints.



References: 1. Ramineni, T.; Prusik, J.; Patel, S.; Lange, S.; Haller, J.; Fama, C.; Argoff, C.; Pilitsis, J. The Impact of Spinal Cord Stimulation on Sleep Patterns. *Neuromodulation: Technology at the Neural Interface* **2016**, *19*, 477–481, doi:10.1111/NER.12382. 2. Haack, M.; Simpson, N.; Sethna, N.; Kaur, S.; Mullington, J. Sleep Deficiency and Chronic Pain: Potential Underlying Mechanisms and Clinical Implications. *Neuropsychopharmacology* 2020, *45*. 3. Haddadan, K.; Krames, E.S. The Effect of Spinal Cord Stimulation, Overall, and the Effect of Differing Spinal Cord Stimulation Technologies on Pain, Reduction in Pain Medication, Sleep, and Function. *Neuromodulation* 2007, *10*. 4. Lamkova, I.A.; Parfenov, V.A. Insomnia in Chronic Non-Specific Low Back Pain. *Nevrologiya, Neiropsikhiatriya, Psikhosomatika* **2021**, *13*, doi:10.14412/2074-2711-2021-5-62-67.

Acknowledgements:

Learning Objectives: 1. Analyze effects of chronic pain conditions on sleep behaviour. 2. Compare level of pain relief with improvement in sleep disturbances. 3. Analyze effects of DRG stimulation therapy specifically on sleep disturbances.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O104

Oral Presentations
PERIPHERAL NERVE STIMULATION – CLINICAL UPDATE
15-05-2024 16:30 - 18:20

LONG TERM RESULTS IN PERIPHERAL NERVE STIMULATION OF THE UPPER EXTREMITY

Alessandro Dario, MD[1], Claudio Reverberi, MD[2], Amedeo Bini, MD[3]
[1]ASST Settelaghi-Insubria University, Neurosurgical Clinic, varese, Italy, [2]Oglio Po Hospital, Pain Unit, Cremona, Italy, [3]villa Aprica Hospital, Hand Clinic, Como, Italy

Introduction: the evolution of peripheral nerve stimulation from the early ages to the current status has been facilitated by dedicated device. With these new neurostimulators the limitations found in the literature due to material designed for spinal cord stimulation have been overcome.

Materials / Methods: we studied 28 patients suffering from drug-resistant neuropathic pain of the upper limb due to only one nerve or at maximum two: 23 patients had a pathology about the median nerve, 8 the ulnar and 1 the radial. the patients were assessed before the intervention and at follow-up with the numeric rate scale (NRS) for pain and with the patient global impression of improvement (PGI-I). We reported also the surgical complications.

Results: The NRS score before implant was 8.5 at last follow-up (mean 2.7 years) was 2.7; the mean score of PGI-I was at last follow-up 1.8. One patient required replacement of the elecrocatheter for dislodgement (3.6%).

Discussion: the long-term results of this technique are satisfactory and not inferior to spinal cord stimulation; furthermore, DRG stimulation is not very applicable in patients with upper limb pain; complications are reduced and acceptable.

Conclusions: The peripheral nerve stimulation for neuropathic pain in upper extremities is a effective tool

Supplemental Data:

References:

Acknowledgements: none

Learning Objectives: 1. evaluate the effectiveness of PNS in the treatment of chronic upper limb pain 2. evaluate the complications of PNS 3. Compare SCS and PNS

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O105

Oral Presentations
NEUROMODULATION FOR GU, GI AND OTHER DISORDERS
15-05-2024 16:30 - 18:20

COMBINED SPINAL CORD AND SACRA NERVE STIMULATION FOR THERAPY OF PAIN-INCONTINENCE SYNDROME WITH MULTIPLE WAVEFORMS

Gregor Bara, MD, Jarek Maciaczyk, MD, PhD
University Hospital Bonn, Stereotactic And Functional Neurosurgery, Bonn, Germany

Introduction: Therapy resistant lower back and pelvic pain resulting from previous surgery, represents one of the most common indication for the chronic epidural spinal cord stimulation. Occasionally, as a consequence of preoperative or concomitant surgery-related injury, the patient may additionally suffer from voiding dysfunction also amenable to neurostimulation treatment. We present a combined spinal cord stimulation (SCS) and sacral nerve stimulation (SNS) in small cohort of patients suffering from voiding dysfunction accompanied by neuropathic back/leg/pelvic pain.

Materials / Methods: Patients who failed the conservative treatment were referred through an interdisciplinary pelvic floor center. The implantation was performed in 4 patients suffering from low back/leg/ pelvic floor pain combined with void dysfunction. To target both of these symptoms, an epidural SCS lead and two S3 SNS leads were placed percutaneously for the trial period and connected to external stimulator in order to assess the efficacy of the stimulation. The trial lasted between 6 and 14 days, incorporated testing of various waveforms (tonic, microburst, FAST, Contour) and was followed by the implantation of a neurostimulator upon successful trial. Neurostimulator was able to deliver distinct waveforms to each lead. Follow-up ranged from 1 to 3 months including pain intensity score and urodynamic examination.

Results: All 4 patients had a successful trial and were subsequently implanted with a neurostimulator. Under tonic stimulation, all of them reported over 90% reduction neuropathic pain (median VAS 8/10 preoperatively and 1.5/10 postoperatively). Two of these patients suffered previously from neurogenic bladder with the necessity of self-catheterization. SNS restored normal bladder function with no need of further self-catheterization. 2 patients suffered from stress-incontinence which completely disappeared. The urodynamic exams showed no residual urine. To note, patients preferred paresthesia-free stimulation for lower back/leg pain and tonic stimulation for void dysfunction.

Discussion: In this group of patients, we observed a significant response of pain-incontinence syndrome to the combined SCS/SNS therapy delivered by a single-IPG neurostimulation system with very significant pain reduction and restoration of bladder function.

Conclusions: The application of multiple waveforms broadens the therapeutic spectrum of complex pain-void dysfunction syndromes. The examination of lager cohort of patients is warranted.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1) sacral nerve stimulation for void dysfunction 2) spinal cord stimulation for chronic pain 3) concomitant usage of multiple waveforms

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O106

Oral Presentations
NEUROMODULATION FOR GU, GI AND OTHER DISORDERS
15-05-2024 16:30 - 18:20

FUNCTIONAL RECOVERY OF BLADDER AND BOWEL CONTROL IN PARAPLEGIC PATIENTS WITH USE OF SPINAL CORD STIMULATION

Dimitrios Peios, MD[1], Georgios Matis, MD[2], Sokratis Sgoutzakos, MD[3], Christina Ble, MD[1], Ioannis Moralis, MD[4], Nikolaos Psarras, MD[4], Konstantinos Kontogiannis, MD[4], Ilias Kopatzidis, MD[1], Ioannis Koutsogiannis, MD[5], Ioannis Vasilakakis, MD[5], Aikaterini Kyriakidou, MD[1], Athanasios Koulousakis, MD[6]
[1]St Luce's Hospital, Panorama Thessaloniki, Functional Neurosurgery, Thessaloniki, Greece, [2]University Hospital Cologne, Neurosurgery, Cologne, Germany, [3]Evexia Rehabilitation Center, Rehabilitation Medicine, N. Kallikrateia, Greece, [4]St Luce's Hospital, Neurosurgery, Thessaloniki, Greece, [5]St Luce's Hospital, Urology, Thessaloniki, Greece, [6]Kunibertsklinik, Cologne, Germany

Introduction: Spinal cord injury (SCI) is a life changing condition due to its neurological manifestations. One of the problems that patients with paraplegia encounter is the dysfunction of bladder and bowel control. Permanent urinary catheterisation, wearing incontinence diapers, following specific dietary instructions and of course medication can improve these conditions, but not reverse it. We describe our experience with 3 patients with complete paraplegia due to SCI who were implanted with a spinal cord stimulation (SCS) system and the effects of SCS on neurogenic bladder and bowel dysfunction.

Materials / Methods: We implanted an SCS system in 3 patients with SCI. All 3 were young males and were operated at least 18 months after the incident that caused paraplegia. All patients presented with complete motor and complete or incomplete sensory paralysis with neurogenic bladder and bowel. The lead was implanted at T11-T12 with laminectomy of L1 or T12, depending on the level of conus medullaris. A 16 electrodes (5-6-5) surgical lead was used in all cases. The lower lead contacts were activated and stimulation was tested at 20, 40 and 200 Hz (best results at 20 Hz), pulse width at 300ms and an intensity that varied according to the perception threshold or if pain, local spasticity or tremor would appear.

Results: Patient A performed 8 intermittent self catheterisations (ISC). After one year of treatment the patient is independent, occasionally performing one or rarely two self catheterisations and has recovered bowel control.
Patient B had a constant urinary catheter. After 7 months of treatment the patient occasionally performs one or two self catheterisations and bowel control has improved by 70%.
Patient C after 6 months developed bladder contractions previously absent and started self catheterisations, while bowel function remains unchanged.

Discussion: Bladder and bowel control is a crucial element in the life of paraplegic patients, because it affects their ability to go out, travel, work and generally socialize. Medication and physiotherapeutic treatments may improve the condition in long period of time and with much effort. Our observations in 3 patients with SCS with specific parameters suggest that this therapy can lead to recovery of such dysfunctions after a few months of treatment.

Conclusions: Functional recovery of neurogenic bladder and bowel improves quality of life in patients with chronic paraplegia. The positive effect of specific SCS programs should be tested in larger studies to establish their efficacy and verify the reproducibility of such results in bigger patient cohorts.

Supplemental Data:

References: Savic, G., Frankel, H.L., Jamous, M.A. *et al.* Long-term bladder and bowel management after spinal cord injury: a 20-year longitudinal study. *Spinal Cord* 2018; 56: 575–581 Goyal V, Paracka DJ, Gaur R, Shukla A. Bowel Management in Patients With Chronic Spinal Cord Injury: A Cross-Sectional Survey. Cureus. 2022 Jun 13;14(6):e25893 Hubscher CH, Herrity AN, Williams CS, Montgomery LR, Willhite AM, Angeli CA, Harkema SJ. Improvements in bladder, bowel and sexual outcomes following task-specific locomotor training in human spinal cord injury. PLoS One. 2018;13(1):e0190998

Acknowledgements:

Learning Objectives: 1. Share observations 2. Get remarks-suggestions 3. suggest reproduction to further study the results

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O107

Oral Presentations
NEUROMODULATION FOR GU, GI AND OTHER DISORDERS
15-05-2024 16:30 - 18:20

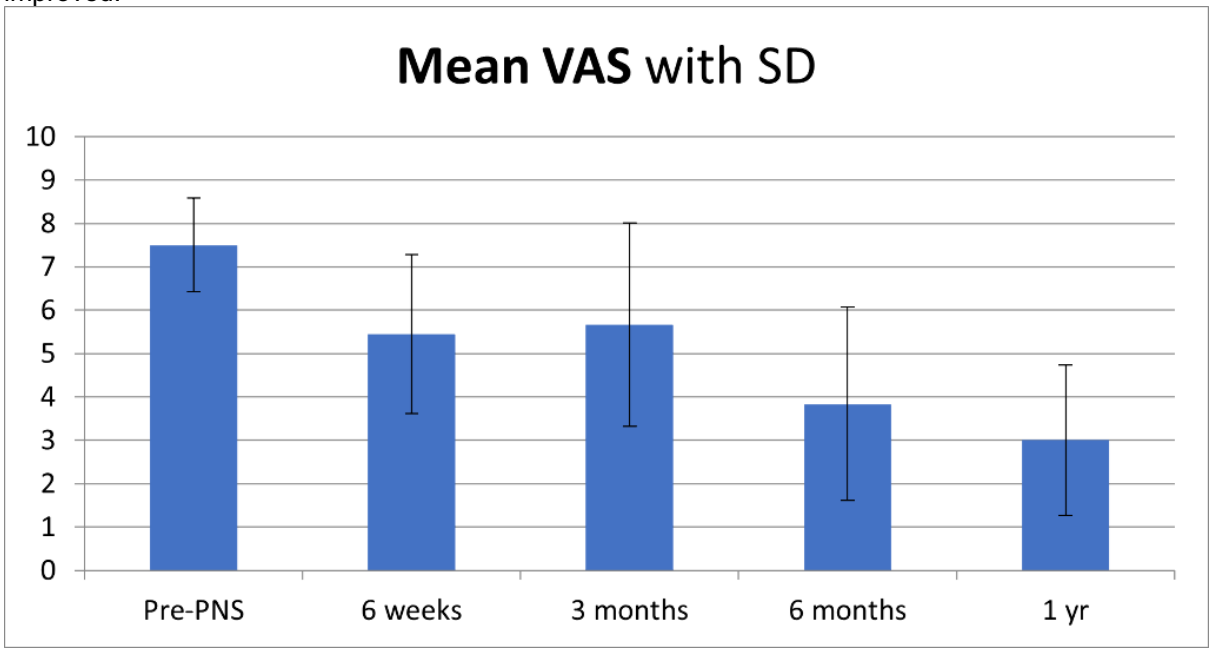
POSTERIOR TIBIAL NERVE STIMULATION FOR MANAGEMENT OF CHRONIC PELVIC PAIN

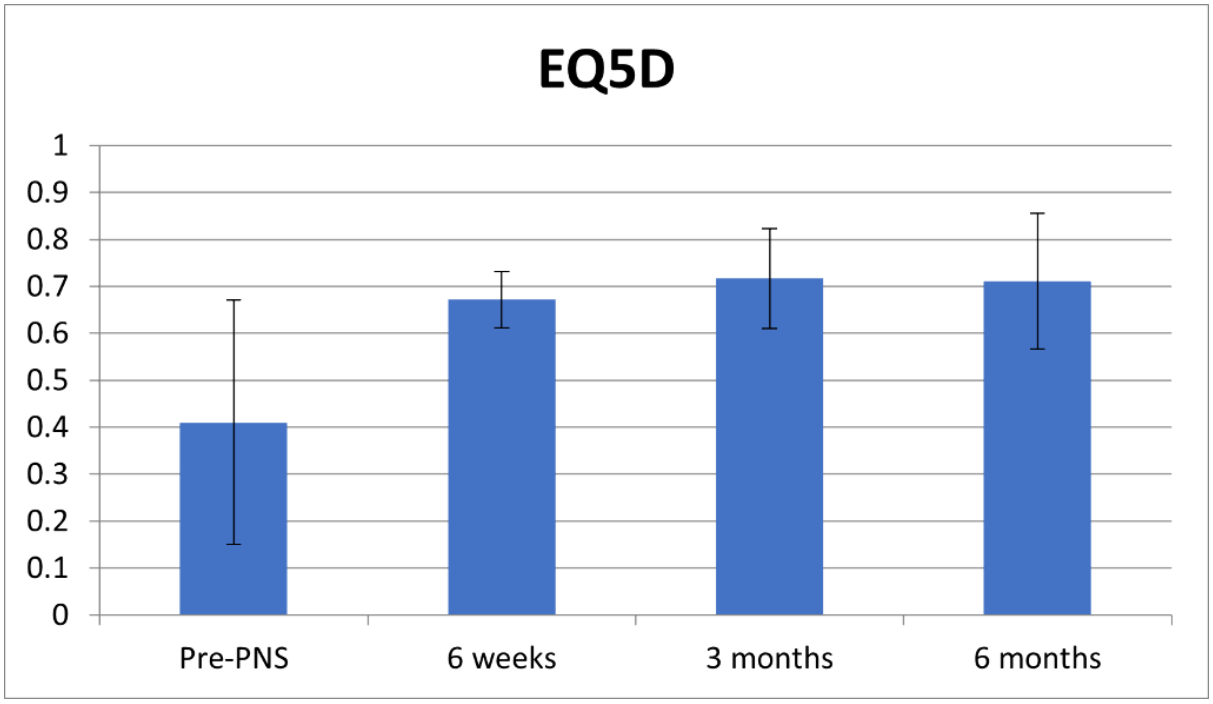
Sheila Black, MB ChB[1,2], Beatrice Bretherton, BSc (Hons), PhD[2], Karen Robertson, RN[3]
[1]Leeds teaching hospitals NHS trust, Pain Management, Leeds, United Kingdom, [2]Leeds Teaching Hospitals NHS Trust, Pain Management Department, Leeds, United Kingdom, [3]Leeds teaching hospitals NHS trust, Pain Management, EX, United Kingdom

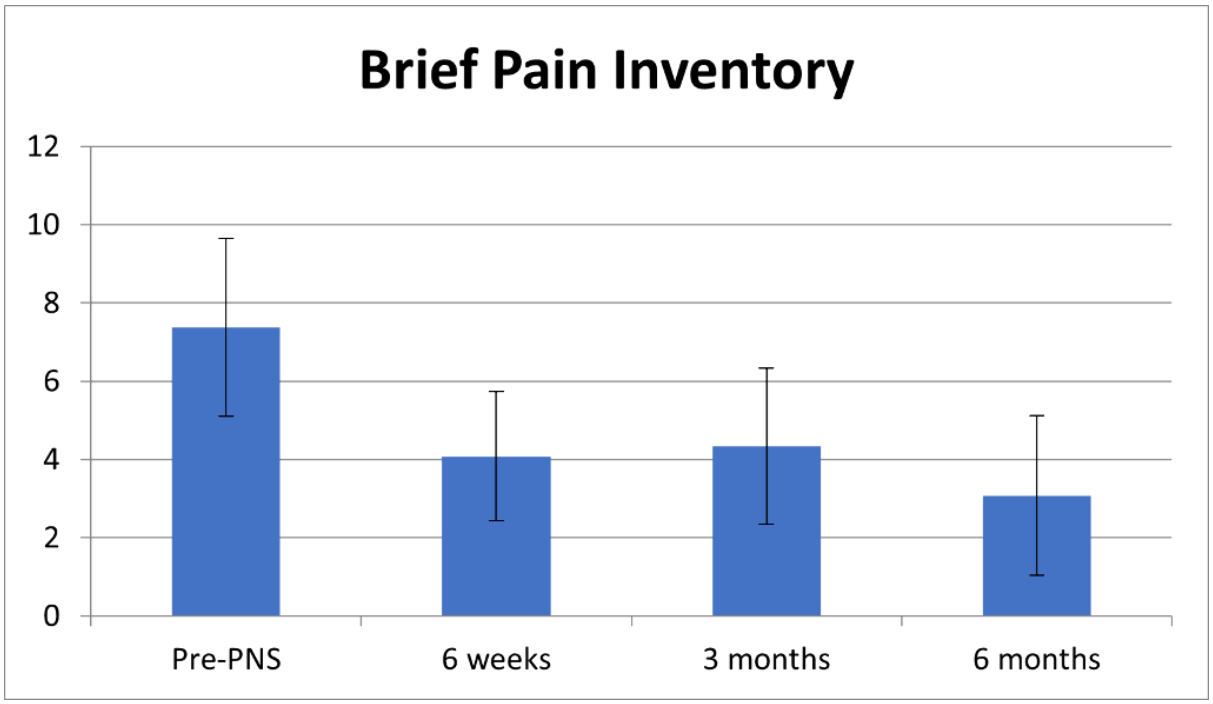
Introduction: Peripheral nerve stimulation (PNS) is an established treatment for chronic pain of peripheral nerve origin [1–4]. Posterior tibial nerve stimulation (PTNS) is effective in the treatment of overactive bladder [4–6]. Preliminary research is showing that PTNS can be used to treat chronic pelvic pain [7–9], where 9 of 15 patients reported >50% pain relief [10] and quality of life improved in 12 women who reported decreased pain intensity and more comfortable performance in daily activities [11] As this is an emerging research area, we undertook to evaluate the pain relief obtained from chronic pelvic pain with PTNS therapy.

Materials / Methods: We conducted a 10 patient case series of PTNS therapy for various pelvic pain conditions.

Results: 10 patients (8 female) were implanted with PTNS for chronic pelvic pain. Indications included: Bladder pain syndrome (5), pudendal neuralgia (2) adenomyosis (1) endometriosis (1) and non-specific pelvic/perineal pain (1). Mean age 47years (range 25-80years). 6 out of 9 patients reported ≥50% pain relief measured by VAS (post-implant results unavailable at this point for 1 patient), of which 3 patients reported over 75% pain relief, regarded as remission of pain. EQ5D was improved by mean 0.3, with 3 patients improving by ≥0.5 on EQ5D score. Mean reduction in Brief pain inventory was 4.826 points. Patient global impression of change was reported as considerably improved or very much improved in 8 patients, and 1 slightly improved.







Discussion: Further information will be available at the time of conference for the final patient in the case series. As we implanted 2 different PNS modalities, dependent on market availability, we found programming parameters differed between the 2 devices. Some patients responded to high frequency stimulation at 1500Hz, whilst others found best relief with low frequencies as low as 20Hz. Some patients used the therapy for short period once or twice daily, whilst some used the therapy for up to 4 hours at a time. Further study is required to establish optimum program parameters for PTNS stimulation, as the mode of action may differ to that required for pain of peripheral nerve origin.

Conclusions: PTNS has been shown here to provide effective pain relief from chronic pelvic pain of various origins, resulting in 6 of 9 patients reporting ≥50% pain relief measured by VAS, with improvements in quality of life and interference with daily activities. Further study is required to establish optimum program parameters.

Supplemental Data:

References: 1. Deer T, Pope J, Benyamin R, et al. Prospective, Multicenter, Randomized, Double-Blinded, Partial Crossover Study to Assess the Safety and Efficacy of the Novel Neuromodulation System in the Treatment of Patients With Chronic Pain of Peripheral Nerve Origin. Neuromodulation Technol Neural Interface. 2016;19(1):91-100. doi:10.1111/ner.12381 2. Oswald J, Shahi V, Chakravarthy K V. Prospective case series on the use of peripheral nerve stimulation for focal mononeuropathy treatment. Pain Manag. 2019;9(6):551-558. doi:10.2217/pmt-2019-0028 3. Lin T, Gargya A, Singh H, Sivanesan E, Gulati A. Mechanism of Peripheral Nerve Stimulation in Chronic Pain. Pain Med. 2020;21(Supplement_1):S6-S12. doi:10.1093/pm/pnaa164 4. Finazzi-Agrò E, Rocchi C, Pachatz C, et al. Percutaneous tibial nerve stimulation produces effects on brain activity: Study on the modifications of the long latency somatosensory evoked potentials. Neurourol Urodyn. 2009;28(4):320-324. doi:10.1002/nau.20651 5. Gaziev G, Topazio L, Iacovelli V, et al. Percutaneous tibial nerve stimulation (PTNS) efficacy in the treatment of lower urinary tract dysfunctions: a systematic review. BMC Urol. 2013;13(61). doi:10.1186/1471-2490-13-61 6. Heesakkers JPFA, Digesu GA, van Breda J, Van Kerrebroeck P, Elneil S. A novel leadless, miniature implantable Tibial Nerve Neuromodulation System for the management of overactive bladder complaints. Neurourol Urodyn. 2018;37(3):1060-1067. doi:10.1002/nau.23401 7. Gaj F, Andreuccetti J, Speziali F, Trecca A, Crispino P. [Chronic pelvic pain treatment with posterior tibial nerve stimulation]. Clin Ter. 2011;162(4). 8. van Balken MR, Vandoninck V, Messelink BJ, et al. Percutaneous Tibial Nerve Stimulation as Neuromodulative Treatment of Chronic Pelvic Pain. Eur Urol. 2003;43(2):158-163. doi:10.1016/S0302-2838(02)00552-3 9. Tirlapur SA, Vlismas A, Ball E, Khan KS. Nerve stimulation for chronic pelvic pain and bladder pain syndrome: a systematic review. Acta Obstet Gynecol Scand. 2013;92(8):881-887. doi:10.1111/aogs.12184 10. Kim SW, Paick J-S, Ku JH. Percutaneous Posterior Tibial Nerve Stimulation in Patients with Chronic Pelvic Pain: A Preliminary Study. Urol Int. 2007;78(1):58-62. doi:10.1159/000096936 11. Gokyildiz S, Kizilkaya Beji N, Yalcin O, Istek A. Effects of Percutaneous Tibial Nerve Stimulation Therapy on Chronic Pelvic Pain. Gynecol Obstet Invest. 2012;73(2):99-105. doi:10.1159/000328447

Acknowledgements:

Learning Objectives: 1. Explore use of peripheral neuromodulation devices to manage chronic pelvic pain conditions. 2. Demonstrate real-world outcomes of use in a variety of genitourinary pelvic pain conditions. 3. Analyse different program parameters to optimise the therapy.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O108

Oral Presentations
NEUROMODULATION FOR GU, GI AND OTHER DISORDERS
15-05-2024 16:30 - 18:20

DORSAL ROOT GANGLION STIMULATION FOR CHRONIC PELVIC PAIN SECONDARY TO ENDOMETRIOSIS: A CASE SERIES IN A 12 MONTH FOLLOW UP STUDY

Tiago Freitas, MD, PhD, Antônio Jorge Oliveira, MD
INDOR- Instituto da dor de Brasilia, Functional Neurosurgery, Brasília, Brazil

Introduction: Chronic pelvic pain(CPP) is a complex pain condition that generally evolves with difficulty in clinical control, presenting a difficult pathophysiology and encompasses different sources of CPP ,with endometriosis being one of the main causes (1,2,3,4,5).A multimodal treatment is the correct approach. Neuromodulation is used in difficult cases and most of attempting to utilize conventional spinal cord stimulation (SCS), with high explant rates(6). Hunter and Yang first described a case series off Dorsal Root Ganglion stimulation(DRGS) for chronic pelvic pain with good results and targeting in L1 and S2(8). We present a case series of nine patients with intractable CPP secondary to endometriosis, resistant to conventional treatment methods, treated with DRGS.

Materials / Methods: Between 2022 and 2023 10 patients with CPP secondary to endometriosis, who failed to multimodal treatments were recruited to this study. 10 patients initially submitted the trial, 9 had permanent DRG implant leads placed over the bilateral L1 and S2 DRG's. Pain scores were measured before and 12 months after permanent implant using the visual analogic scale for pain and SF -12 scale for quality of life.

Results: At 12-month follow-up, 8 of the 9 patients who underwent permanent device showed a pain reduction more than 70% or greater, and 1 patient showed a 40% reduction in pain. We observed reduction in opioid consumption. No explants occurred.

Discussion: The pelvic region involves a complex innervation with a diffuse somatic and sympathetic system and is also a sympathetically driven condition. Endometriosis is an important and serious CPP condition. Multimodal treatment and other interventional procedures have limitations. Regarding the use of invasive neuromodulation, there are some studies using spinal cord stimulation for the treatment of chronic pelvic pain syndromes in general, as well as with stimulation of sacral roots, however there is a high rate of explant due to loss of long-term efficacy. Hunter and Yang described in their article the basis for using DRG stimulation at the L1 and S2 levels. Our case series showed good response in patients with chronic pelvic pain secondary to endometriosis, with a 12-month follow-up and improvement in pain and quality of life scales. More studies with later follow-up are necessary to confirm the benefits

Conclusions: CPP secondary to endometriosis is a difficult pain syndrome, usually unresponsive to conservative treatments and other interventional procedures. Neuromodulation using DRG-stimulation in L1 and S2 sites in our case series showed good results with good sustainability in a 12-month follow-up.

Supplemental
Data:

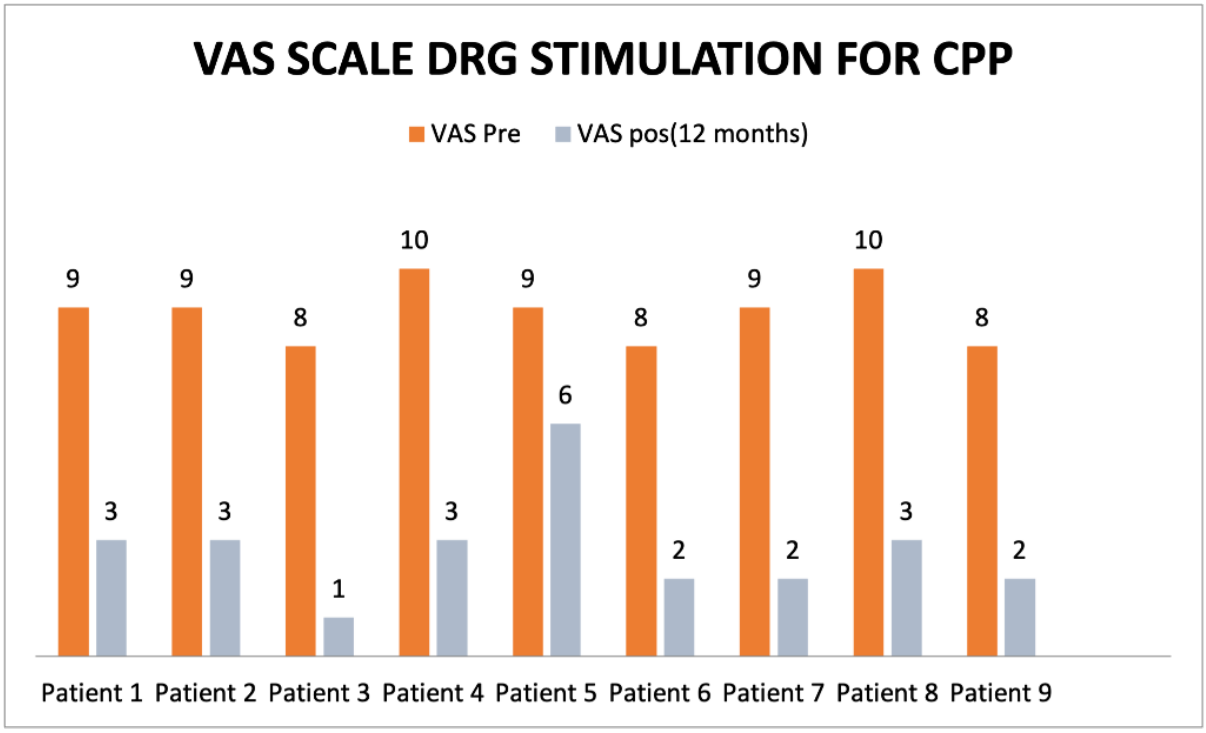
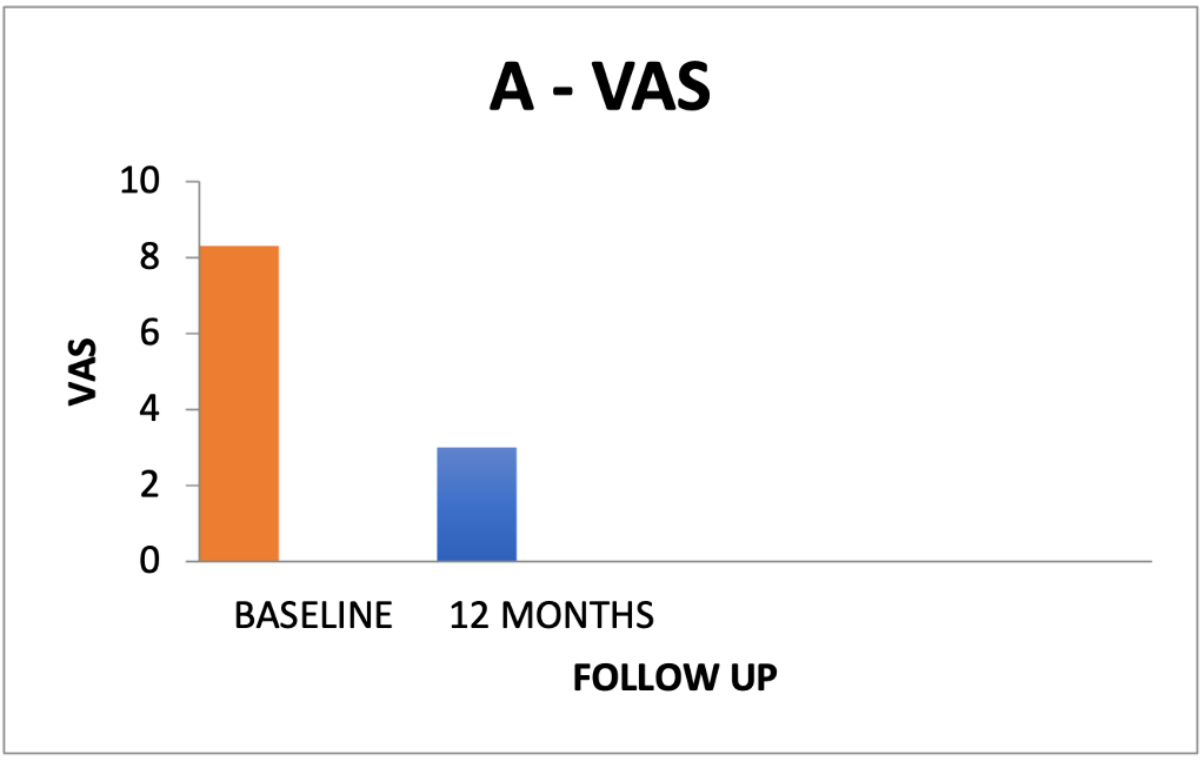
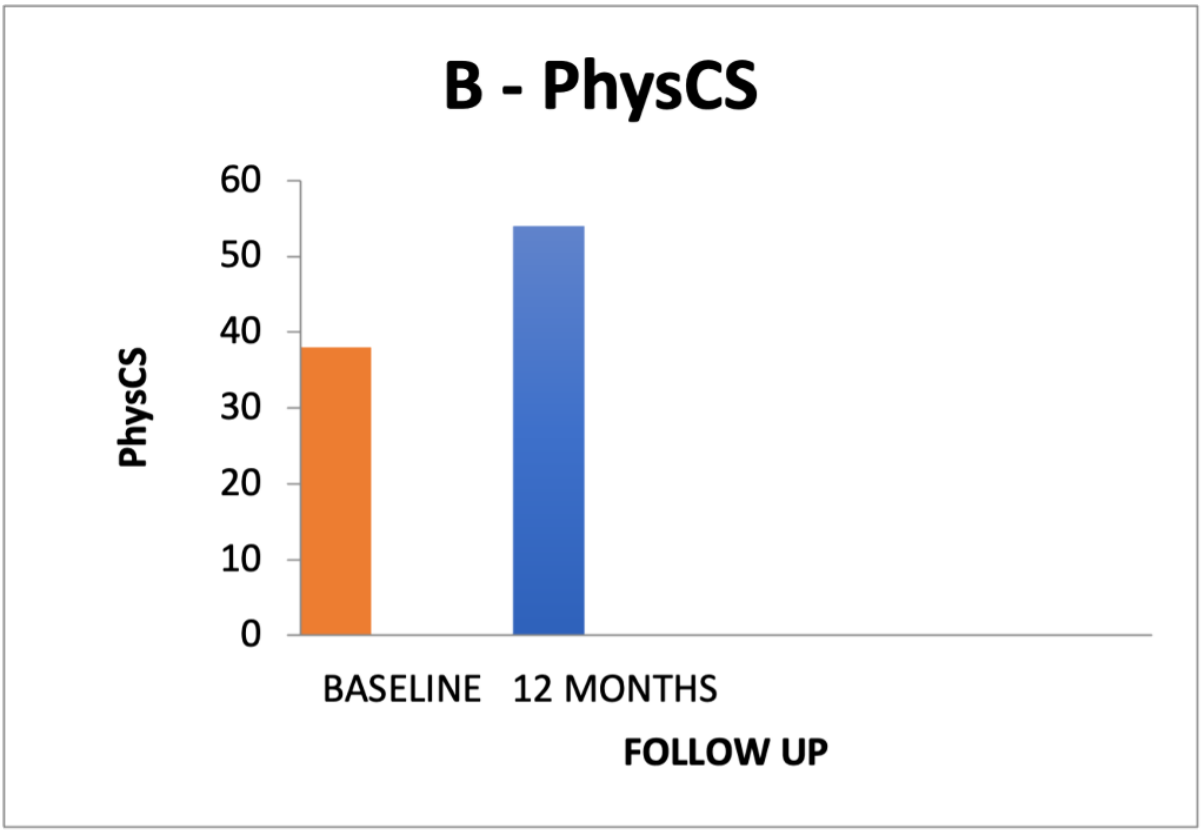


Figure 1. Changes in VAS scale after 12 months follow from 9 patients submitted to DRG-S for CPP caused by Endometriosis





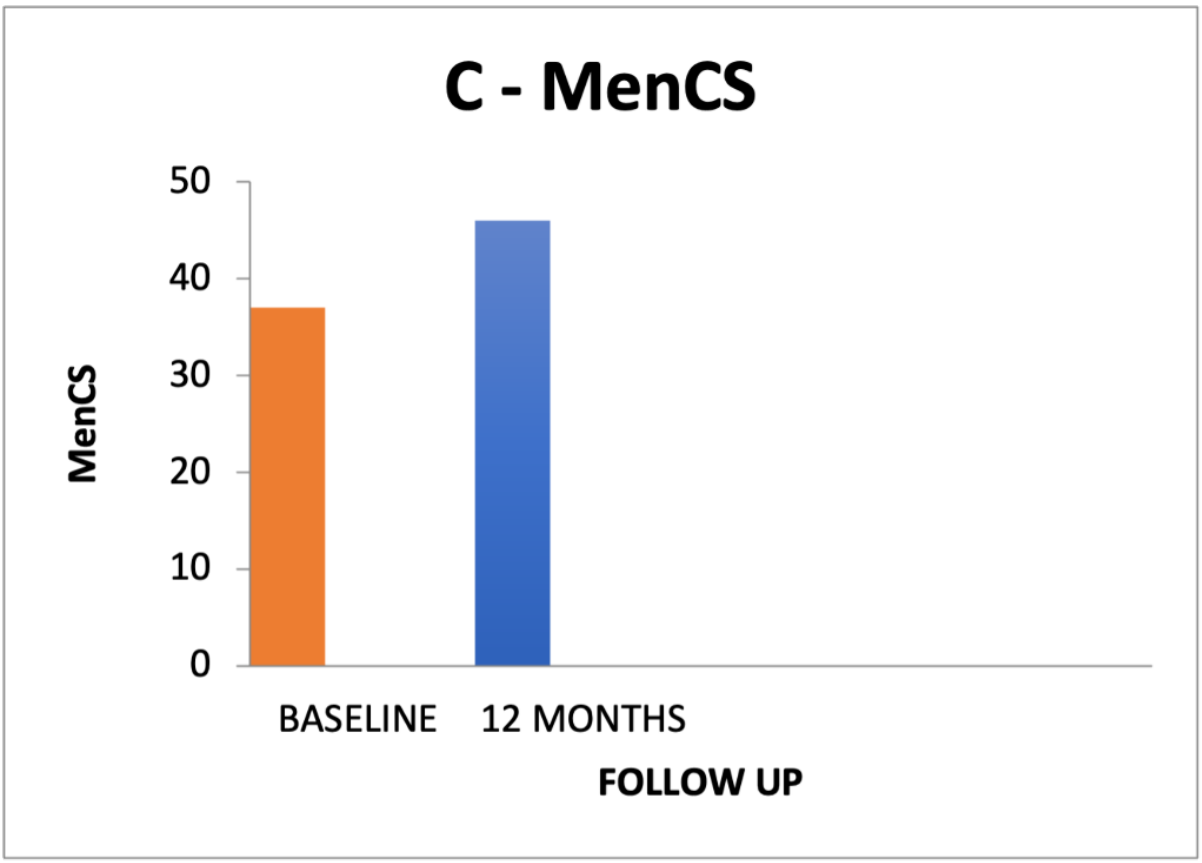
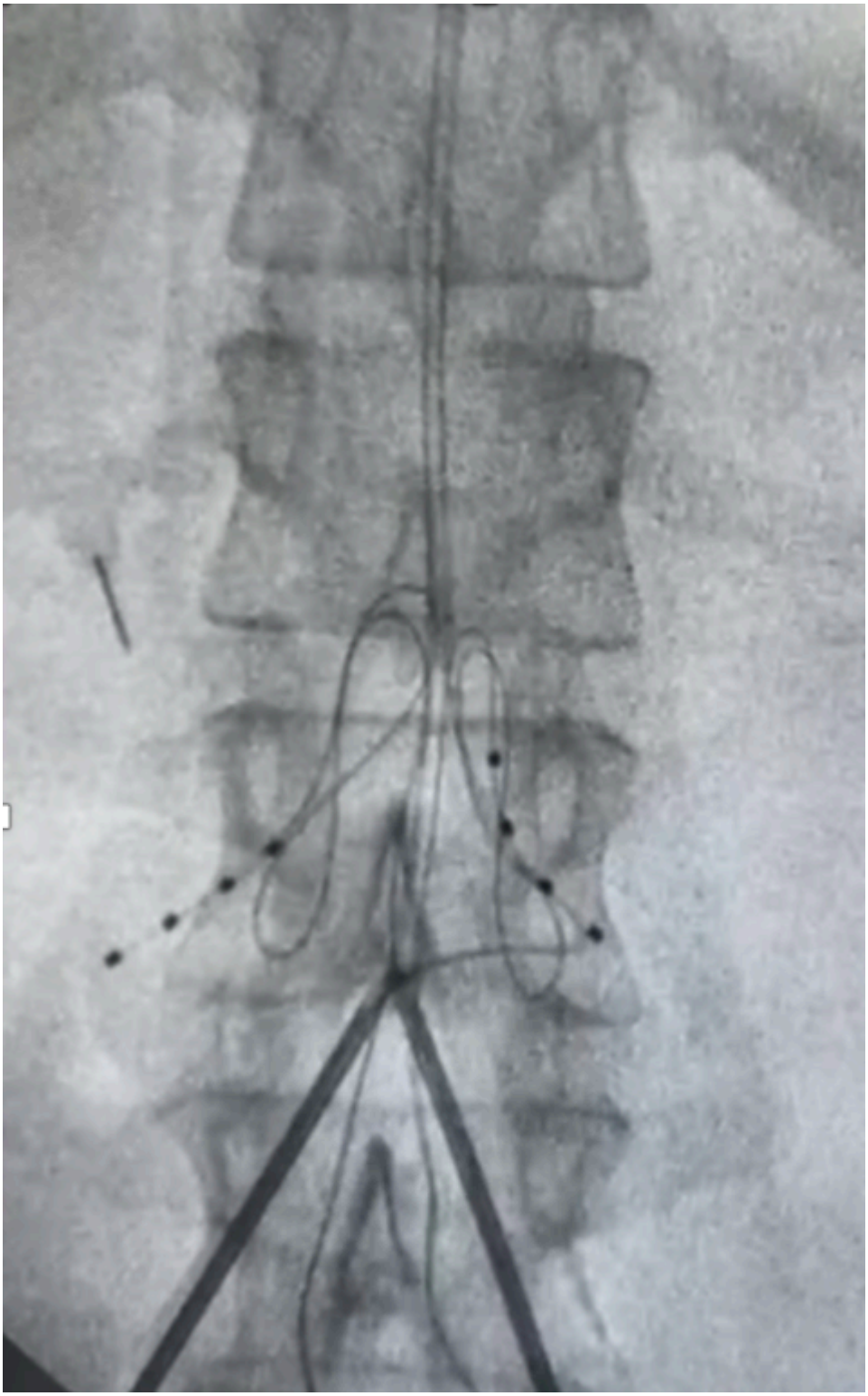


FIGURE 2. Pain and quality-of-life improvement following DRG-S. A, Twelve months after DRG-S treatment, patients reported a significant reduction in VAS scores compared to preoperative baseline. B and C, Similarly, physical (PhysCS) and mental (MenCS) components of the SF-12 assay were significantly ameliorated following BPS. Values represent average +/- standard error. Statistically significant at P <

.05.  Figure 3. Example of bilateral L1 DRG electrodes in AP view

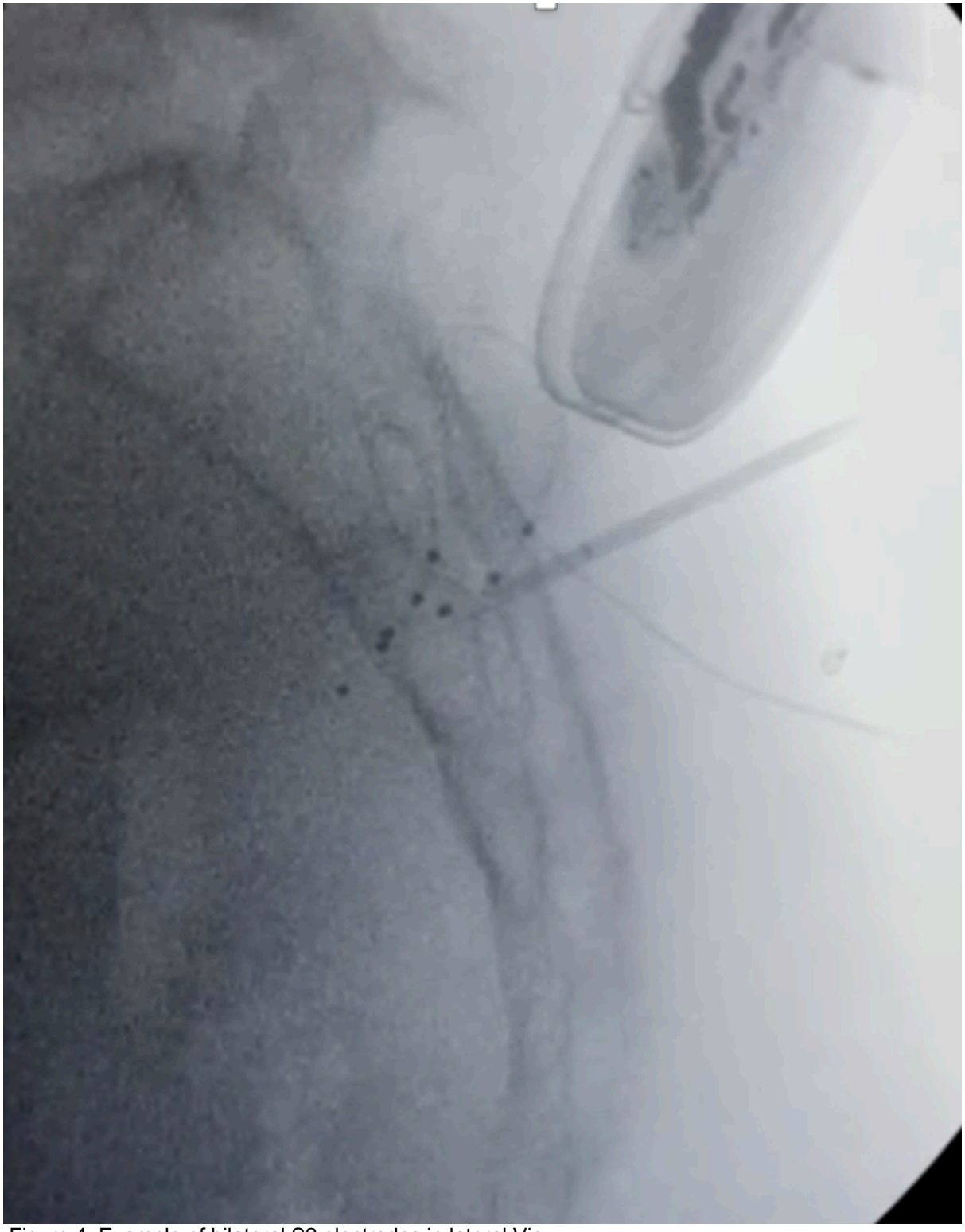


Figure 4. Example of bilateral S2 electrodes in lateral View

References: Ahangari A. Prevalence of chronic pelvic pain among women: an updated review. Pain Physician. 2014;17(2): E141eE147. Janicki TI. Chronic pelvic pain as a form of complex regional pain syndrome. Clin Obstet Gynecol 2003;46:797–803. Chronic pelvic pain: ACOG practice bulletin, number218. Obstet Gynecol. 2020;135(3):e98ee109. Nnoaham KE, Hummelshoj L, Webster P, et al. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. Fertil Steril. 2011; 96(2):366e373. e8. Simoens S, Dunselman G, Dirksen C, et al. The burden of endometriosis: costs and quality of life of women with endometriosis and treated in referral centres. Hum Reprod. 2012;27(5):1292e1299. Hayek SM,Veizi E,Hanes M. Treatment-limiting

complications of percutaneous spinal cord stimulator implants: a review of eight years of experience from an academic center database. Neuromodulation 2015;18:603–608.
GaoX,YehYC,OutleyJ,SimonJ,BottemanM,SpaldingJ. Health-related quality of life burden of women with endometriosis: a literature review. Curr Med Res Opin. 2006; 22(9):1787e1797. Hunter CW, Yang A. Dorsal root ganglion stimulation for chronic pelvic pain: a case series and technical report on a novel lead configuration. Neuromodulation. 2019;22(1): 87e95.

Acknowledgements:

Learning Objectives: 1. Offer and present a different neuromodulation approach for chronic pelvic pain in endometriosis 2.Use a previous site of DRG -S for neuromodulation and confirm good results 3.Reproduce DRG techniques for chronic pelvic pain

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O109

Oral Presentations
NEUROMODULATION FOR GU, GI AND OTHER DISORDERS
15-05-2024 16:30 - 18:20

DORSAL ROOT GANGLION STIMULATION FOR PERSISTENT PELVIC PAIN

Kiran Patel, MD[1], Aditi Malhotra, BS[2]
[1]Lenox Hill Hospital, Anesthesiology, New York, United States of America, [2]Columbia University, Neuroscience, New York, United States of America

Introduction: Persistent Pelvic Pain (PPP) is a complex neuropathic condition characterized by pain in the pelvic region, low back, abdominal wall, and/or buttocks, lasting for a minimum of 6 months [1]. Affecting 15% of women, PPP is caused by pathologies such as endometriosis, adhesions, pudendal neuralgia, and irritable bowel syndrome [2]. When conservative approaches fail, spinal cord stimulation (SCS) is typically employed for PPP treatment [3-6]. Nevertheless, SCS often results in unwanted paresthesias and declining therapeutic efficacy [7]. Dorsal Root Ganglion stimulation (DRG-S) may emerge as a potentially superior option for treating PPP, surpassing other neuromodulatory methods. DRG-S involves placing narrow leads near spinal foramen DRGs, where cerebrospinal fluid is minimal [8]. DRG's anatomical position allows for high dermatomal specificity and focal neuropathic pain relief, without relying on paresthesias [9].

Materials / Methods: This study presents a single-center prospective case series evaluating DRG-S efficacy for PPP treatment. Patients underwent a 7 days trial with bilateral leads placed at the L1 and S2 levels. If the trial was successful (greater than 50% pain relief from baseline), patients received permanent DRG-S implants. Pain and functional assessments were conducted using a 0-10 numeric rating scale (NRS) and a modified Oswestry Disability Index (ODI) at baseline (pre-implant), 3, 6, and 6-month intervals post-implantation.

Results: The case series comprised of 15 patients (14 female) with an average of 12 years of PPP. All DRG-S trials succeeded, leading to permanent implants. The post-implant follow-up ranged from 3 to 24 months. NRS scores dropped by 70%-90% from baseline and were sustained throughout follow-up. NRS scores decreased by 85.6% at 12 months and 85.4% at 24 months. The modified ODI scores decreased from baseline by 83.3% at 12 months and 82.1% at 24 months. At the 24-month follow-up, 93.3% of patients ceased opioid medications.

Discussion: DRG-S normalizes overactive primary sensory neurons by amplifying their natural filtering function at T-junctions. The optimal DRG-S target is L1 and S2 which maximizes pelvic nerve coverage, supported by the results.

Conclusions: This study demonstrates that DRG-S at L1 and S2 is effective in reducing pain and disability associated with PPP. The outcomes were sustained for up to 24 months post-implantation, even in patients with diverse pathologies and unresponsiveness to conservative treatments [10]. The findings underscore that DRG-S is a viable modality for treating PPP. A larger comprehensive prospective clinical study examining its benefits in a larger population is warranted.

Supplemental Data:

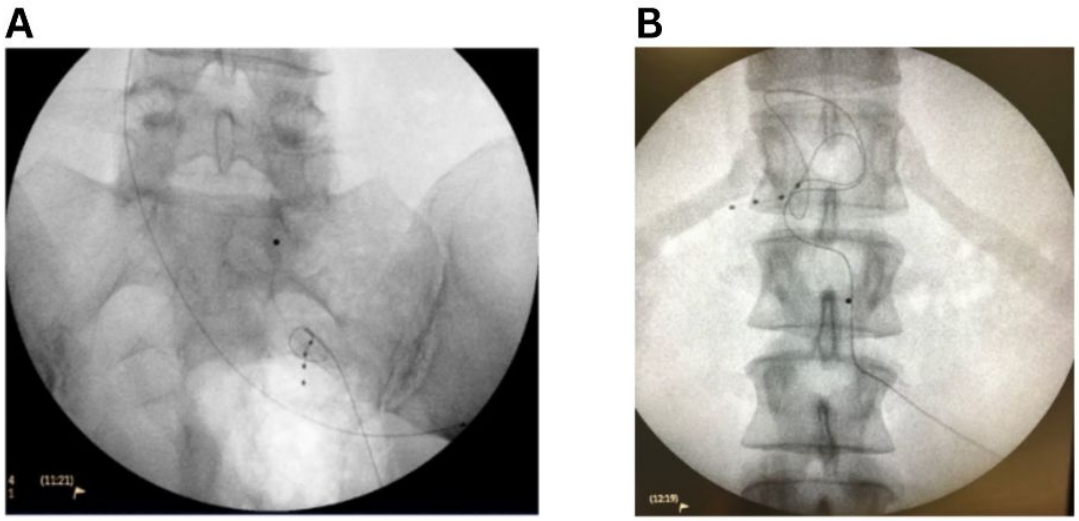


Figure 1. Fluoroscopic images of DRG lead placement at L1 and S2.

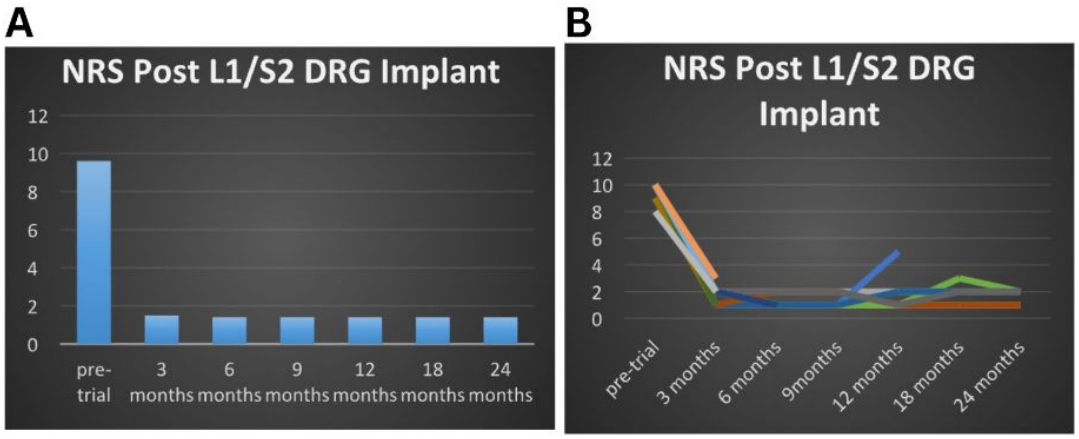


Figure 2. Pain relief by DRG implant at L1/S2, measured by NRS, from pre-implant to 24 months follow-up.

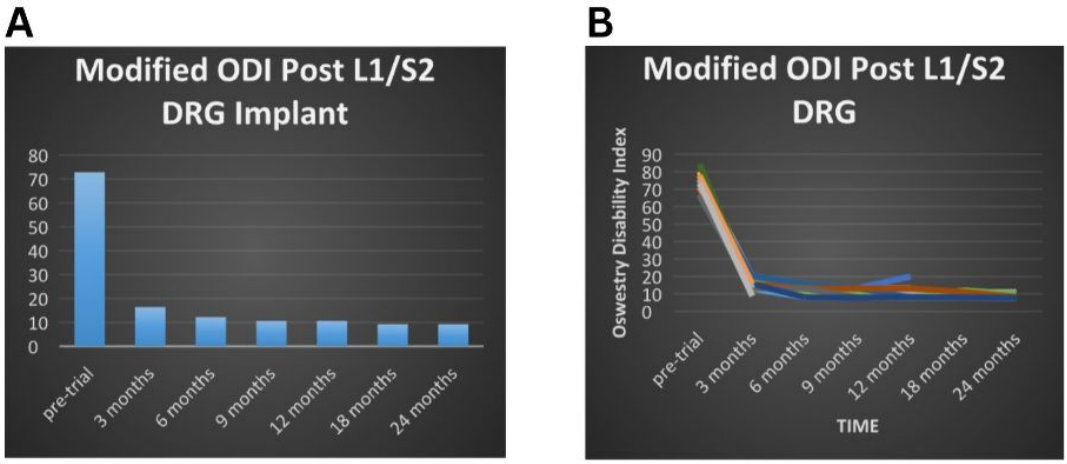


Figure 3. Functional improvement by DRG implant at L1/S2, measured by ODI, from pre-implant to 24 months follow-up.

References: [1] Chronic Pelvic Pain: ACOG Practice Bulletin, Number 218. Obstetrics & Gynecology. 2020 Mar;135(3):e98. [2] Cheong Y, William Stones R. Chronic pelvic pain: aetiology and therapy. Best Pract Res Clin Obstet Gynaecol. 2006 Oct;20(5):695–711. [3] Hunter C, Davé N, Diwan S, Deer T. Neuromodulation of pelvic visceral pain: review of the literature and case series of potential novel targets for treatment. Pain Practice. 2013;13(1):3–17. [4] Hao D, Yurter A, Chu R, Salisu-Orhurhu M, Onyeaka H, Hagedorn J, et al. Neuromodulation for Management of Chronic Pelvic Pain: A Comprehensive Review. Pain Ther. 2022 Dec;11(4):1137–77. [5] Patel CB, Patel AA, Diwan S. The Role of Neuromodulation in Chronic Pelvic Pain: A Review Article. Pain Physician. 2022 Jul;25(4):E531–42. Gish. Neuromodulation for the Management of Chronic Pelvic Pain Syndromes: A Systematic Review. Placeholder for submitted paper. [6] Gish. Neuromodulation for the Management of Chronic Pelvic Pain Syndromes: A Systematic Review. Placeholder for submitted paper. [7] Feirabend HKP, Choufoer H, Ploeger S, Holsheimer J, van Gool JD. Morphometry of human superficial dorsal and dorsolateral column fibres: significance to spinal cord stimulation. Brain. 2002 May;125(Pt 5):1137–49. [8] Kramer J, Liem L, Russo M, Smet I, Van Buyten JP, Huygen F. Lack of Body Positional Effects on Paresthesias When Stimulating the Dorsal Root Ganglion (DRG) in the Treatment of Chronic Pain. Neuromodulation. 2014 Sep 1;18(1):50–7. [9] Deer TR, Levy RM, Kramer J, Poree L, Amirdelfan K, Grigsby E, et al. Dorsal root ganglion stimulation yielded higher treatment success rate for complex regional pain syndrome and causalgia at 3 and 12 months: a randomized comparative trial. Pain. 2017 Apr;158(4):669–81. [10] Hunter CW, Yang A. Dorsal Root Ganglion Stimulation for Chronic Pelvic Pain: A Case Series and Technical Report on a Novel Lead Configuration. Neuromodulation. 2019;22(1):87–95.

Acknowledgements:

Learning Objectives: 1. Recognize Dorsal Root Ganglion stimulation (DRG-S) as a potential superior treatment for PPP by understanding its benefits over traditional spinal cord stimulation (SCS). 2. Interpret the outcomes of a case series on DRG-S efficacy for PPP treatment, emphasizing pain and disability reduction over 24 months post-implantation. 3. Advocate for a larger prospective study to assess DRG-S benefits for diverse pathologies of PPP cases that were unresponsive to conservative treatment.

Financial Disclosures: Kiran V. Patel a. Abbott b. Consultant / Advisory Board c. $5,001 - $20,000 USD

Disclosure: No significant relationships.

O110

Oral Presentations
NEUROMODULATION FOR GU, GI AND OTHER DISORDERS
15-05-2024 16:30 - 18:20

EFFECT OF NON-INVASIVE STIMULATION AND SUBSEQUENT FUNCTIONAL DYSPHAGIA THERAPY ON ASPIRATION IN POSTACUTE DYSPHAGIA

Christian Ledl, MA[1], Karolina Simmet, MSc[1], Carmen Krewer, PhD[2], Klaus Jahn, MD[3], Friedemann Mueller, MD[1]
[1]Schoen Clinik Bad Aibling, Neurology - Dysphagia, Bad Aibling, Germany, [2]Technical University of Munich, Faculty Of Sport And Health Science, Munich, Germany, [3]Ludwig-maximilians-Universität Muenchen, German Center For Vertigo And Balance Disorders (dszg), Munich, Germany

Introduction: Pharyngeal electrical stimulation (PES) and transcranial direct current stimulation (TDCS) are potential adjuncts to functional dysphagia therapy (DT). However, clinical study findings are inconsistent and seem to depend on etiology, phase of disease, severity of dysphagia, presence of a tracheostomy and study procedure. Also, low stimulation intensities in PES were associated with poorer outcome. In TDCS and PES, highest cortical excitability is reached 60 to 90 minutes post stimulation. Yet, a therapeutic paradigm combining non-invasive stimulation with functional therapy has not been tested. Hence, one of the main goals of this randomized controlled trial (RCT) is to investigate effects of electrical stimulation combined with swallowing therapy on improvement of dysphagia.

Materials / Methods: A total of 82 postacute stroke patients (58 days post unilateral lesion; 31 tracheotomized) were randomly assigned to a TDCS group (n=27), a PES group (n=27) and a sham stimulation group (n=28: sham TDCS=14, sham PES=14). Inclusion criteria were amongst others persistent dysphagia after a 2-week period of DT and aspiration during instrumental endoscopic control (FEES). Participants received 5 times 10 minutes of real or sham stimulation and DT one hour afterwards. Anodal TDCS was delivered over the non-affected hemisphere. Patients and raters were blinded to group adherence. Primary outcome was change in Penetration/ Aspiration scale (PAS) for saliva, fluids and puree. FEES was done at baseline and one week post stimulation (FU).

Results: PA-values of all tested consistencies improved significantly from baseline to FU by 1.0 point (*p*=.000) for all participants (TDCS 0.67; PES .91; sham 1.4) but showed no significant effect of stimulation group (*p*=.326). Subanalysis of tracheotomized and non-tracheotomized patients showed significant improvements (*p*=.028; *p*=.000) but again no significant group effects (*p*=.588*; p*=.531). Stimulation intensity in PES did not vary significantly across sessions and was not related to treatment success.

Discussion: This RCT shows no influence of electrical stimulation on Penetration/ Aspiration in tracheotomized or non-tracheotomized stroke patients. Treatment success did not depend on stimulation intensities nor could a benefit of PES be shown with regard to decannulation rate. However, improvements of dysphagia in the study population were relevant and are probably linked to the applied therapeutic paradigm. It seems that electrical or non-electrical stimulation worked as a prestimulation enhancing arousal and increasing the effectiveness of subsequent functional therapy.

Conclusions: Electrical stimulation in dysphagic patients could not be shown to be superior to sham stimulation. Innovative combinations of stimulation and subsequent functional therapy should be tested systematically.

Supplemental Data:

References: none

Acknowledgements: The support of Schoen Clinic Bad Aibling and its dysphagia departement for this project is gratefully acknowledged.

Learning Objectives: 1. Learn about effects and mechanisms of induced changes in cortical excitability by non-invasive stimulation in dysphagic patients 2. In tracheotomized and non-tracheotomized stroke patients, electrical stimulation is not superior to sham stimulation 3. The key to improve dysphagia outcome might be a combination of prestimulation and functional therapy

Financial Disclosures: Christian Ledl: no significant relationships Karolina Simmet: no significant relationships Carmen Krewer: no significant relationships Klaus Jahn: no significant relationships Friedemann Mueller: no significant relationships

Disclosure: No significant relationships.

O111

Oral Presentations
NEUROMODULATION FOR GU, GI AND OTHER DISORDERS
15-05-2024 16:30 - 18:20

NON-INVASIVE VAGUS NERVE STIMULATION (NVNS) FOR THE PROPHYLAXIS AND TREATMENT OF ACUTE RESPIRATORY DISTRESS SYNDROME IN COVID-19 PATIENTSL

Peter Staats, MD[1,2,3], Boyle Cheng, PhD[4], Praveer Vyas, MSc[4]
[1]NSPC, Premier Pain Centers, Atlantic Beach, United States of America, [2]National Spine & Pain Centers, Premier Pain Centers, Shrewsbury, United States of America, [3]National Spine, Chief Medical Officer, Atlantic Beach, United States of America, [4]Allergheny Health Network, Biomedical Engineering, Pittsburgh, United States of America

Introduction: Electrical stimulation of the vagus nerve, referred to as vagus nerve stimulation (VNS), is hypothesized to alleviate ARDS resulting from COVID-19 and other causes. Proposed mechanisms include direct modulation of bronchoconstriction and modulation of the inflammatory immune response.

Materials / Methods: A two-arm randomized controlled trial was conducted to compare nVNS in conjunction with standard of care (SoC) to SoC alone in patients hospitalized with COVID-19. Patients in the treatment arm received nVNS three times per day during hospitalization until discharge. Study outcomes included incidence of clinical events, mortality, levels of the pro-inflammatory cytokines TNF-α, IL-1β and IL-6 in the blood, measured by ELISA.

Results: There were 11 patients randomized to SoC and 10 patients randomized to both nVNS and SoC. There were no significant differences in age, sex, race/ethnicity and BMI. Average length of stay did not differ between groups (11.9 ± 10.2 days in the control group and 10.6 ± 7.7 days in the nVNS group). One patient in each group required mechanical ventilation, and one patient (in the control group) died within 30 days. Levels of TNF-α, IL-6 and IL-1β did not significantly differ between groups by day of hospitalization. However, a significantly larger percentage of subjects in the nVNS group had normal levels of IL-6 at discharge (<5 pg/mL; P = 0.0124). There were no differences in clinical markers for inflammation and cardiopulmonary outcomes and no differences in markers of lymphocyte and neutrophil activation. A significant difference in average PaO2/FiO2 ratio between nVNS (N = 4; 205 ± 54.83 mmHg) and control (N = 3; 74.7 ± 14.24 mmHg) patients was observed (t = -3.94; 95% CI 27.1 to 106.5; P = 0.0109).

Discussion: This study suggests improvement in oxygenation as well as the cytokine IL 6.

Conclusions: While incidence of clinical events and mortality was similar between groups, patients who received nVNS experienced comparably reduced severity of ARDS as determined based on the P/F ratio. Despite no differences between groups in cytokine levels by day, patients who were treated with nVNS were more likely to have normal IL-6 levels at discharge. IL-6 is considered an important prognostic marker for COVID-19 severity as well as an early target for reducing hyperinflammation resulting from the host response to this virus. Further research is warranted to determine whether nVNS reduces the hyperinflammatory state associated with COVID-19 in patients with ARDS.

Supplemental Data:

References:

Learning Objectives: Know which cytokines and biomarkers are relevant to understanding the pathology of, and developing treatments for, ARDS in COVID-19 patients. Describe the two mechanisms through which nVNS has the potential to reduce the severity of ARDS in COVID-19 patients. Discuss the benefits of a safe and non-invasive treatment that is effective for the prophylaxis and treatment of ARDS in COVID-19 in military healthcare settings.

Financial Disclosures: Peter S Staats Patent holder Vagus nerve Stimulation in COVID 19 employee at the time of the study electroCore

Disclosure: No significant relationships.

O112

Oral Presentations
NEUROMODULATION FOR GU, GI AND OTHER DISORDERS
15-05-2024 16:30 - 18:20

AURICULAR ALLODYNIA IS ASSOCIATED WITH WORSE OUTCOMES IN CHILDREN AND ADOLESCENTS WITH DISORDERS OF GUT-BRAIN INTERACTION UNDERGOING PERCUTANEOUS ELECTRICAL NERVE FIELD STIMULATION

Neha Santucci, MD[1,2], Umber Waheed, MD[1], Khalil El-Chammas, MD[1,2], Jesse Li, BS[2], Sherief Mansi, MD[1,2], Kahleb Graham, MD[1,2], Jennifer Hardy, MSc[2], Megan Miller, PhD[3], Rashmi Sahay, MD[4]
[1]University of Cincinnati College of Medicine, Pediatrics, Cincinnati, United States of America, [2]Cincinnati Children's Hospital Medical Center, Gastroenterology, Cincinnati, United States of America, [3]Cincinnati Children's Hospital Medical Center, Behavioral Medicine And Clinical Psychology, Cincinnati, United States of America, [4]Cincinnati Children's Hospital Medical Center, Biostatistics, Cincinnati, United States of America

Introduction: Disorders of gut-brain interaction (DGBI), are common and associated with functional disability and school absenteeism (1). Percutaneous Electrical Nerve Field Stimulation (PENFS) is a non-pharmacologic treatment for children with DGBI (2,3). PENFS has shown to have minimal adverse effects (dermatitis and bleeding, 4). Allodynia is pain from a stimulus not usually provoking pain (5). Auricular allodynia, although present, has not been characterized in patients undergoing PENFS. We aimed to examine auricular allodynia during PENFS and associate with outcomes.

Materials / Methods: We reviewed charts of patients ages 7-23y who underwent PENFS for DGBI. Patients with organic GI disorders were excluded. We included demographic data and validated questionnaire responses, collected as part of routine clinical care: abdominal pain (API), nausea (NSS), pain catastrophizing (PCS-C), functioning (FDI), insomnia (PISI), anxiety (SCARED and PROMIS), and depression (PHQ-9). Allodynia was defined if patient endorsed localized pain, soreness, or tenderness during PENFS. Baseline clinical scores and changes with treatment were compared between those with and without allodynia**.**

Results: Of 235 patients (mean age 16.2 ± 2.7y), 77% were female and 88% were Caucasian (Table 1) and most common DGBI was irritable bowel syndrome (Table 2). Twenty-eight % of patients experienced allodynia. Of the 102 total visits with allodynia, 65% of the visits had patients complain of allodynia once, 24% twice, 8% thrice, and 4% four times. The most common actions for allodynia included switching ears for device placement (29%), extra time between lead placements (28%) and placing lesser than the 4 usual leads (20%, Table 3).
Patients with allodynia had lower baseline SCARED scores than those without ($p=0.03$). They had significantly greater API, PCS-C, NSS, FDI, and PISI scores at treatment completion compared to those without allodynia ($p<0.05$, Fig 1). Comorbid headaches (66%) and joint pain (43%) were seen with allodynia. Patients with muscle pain had a trend for greater allodynia vs those without (19 % vs 13%, $p=0.08$). Comorbidities such as temporomandibular joint dysfunction, fibromyalgia, complex regional pain syndrome and amplified musculoskeletal pain syndrome as well as ear lateraloty did not affect allodynia ($p>0.05$).

Discussion: Excitation thresholds of rapidly conducting Aβ fibers in the ear are lower than nociceptive slowly conducting Aδ and C fibers. The nociceptive threshold varies from the detection threshold (Fig 2).

Conclusions: Allodynia is common with PENFS and associates with worse clinical outcomes. These patients may require adjustment of stimulation during PENFS to target the appropriate nerve fibers and improve outcomes.

Supplemental
Data:

Table 1. Demographics (n=235)

Age [Mean (y) ± SD]		16.2 ± 2.7
Sex [n (%)]	Female	181 (77.0)
	Male	54 (23.0)
Race [n (%)]	White	216 (91.9)
	Black	12 (5.1)
	Asian or Middle Eastern	6 (2.6)
	Mixed	1 (0.4)

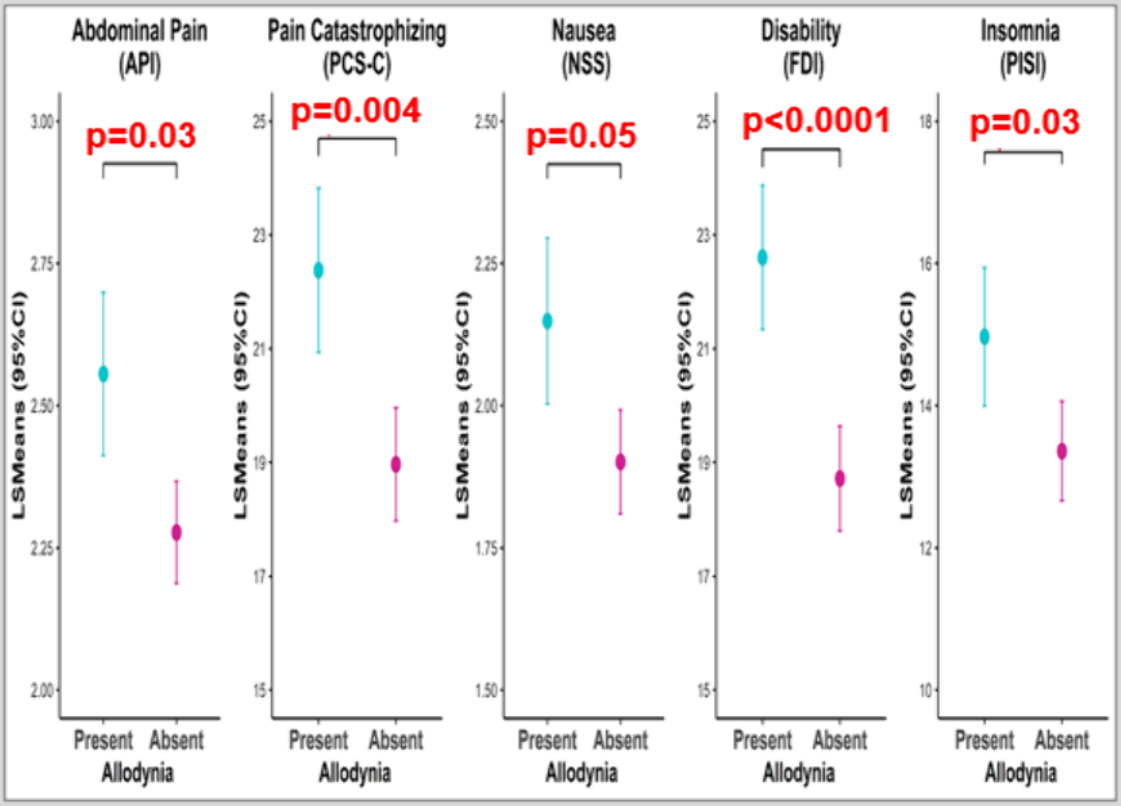
Table 2. Types of DGBI

Diagnosis	N (%)
Irritable Bowel Syndrome (IBS)	126 (53.6)
Functional Dyspepsia (FD)	116 (49.4)
Functional Abdominal Pain – Not Otherwise Specified (FAP-NOS)	47 (20.0)
Functional Nausea/Vomiting	27 (11.5)
Rumination	12 (5.1)
Cyclic Vomiting Syndrome (CVS)	6 (2.6)
Abdominal Migraine	5 (2.1)
Functional Constipation	3 (1.3)

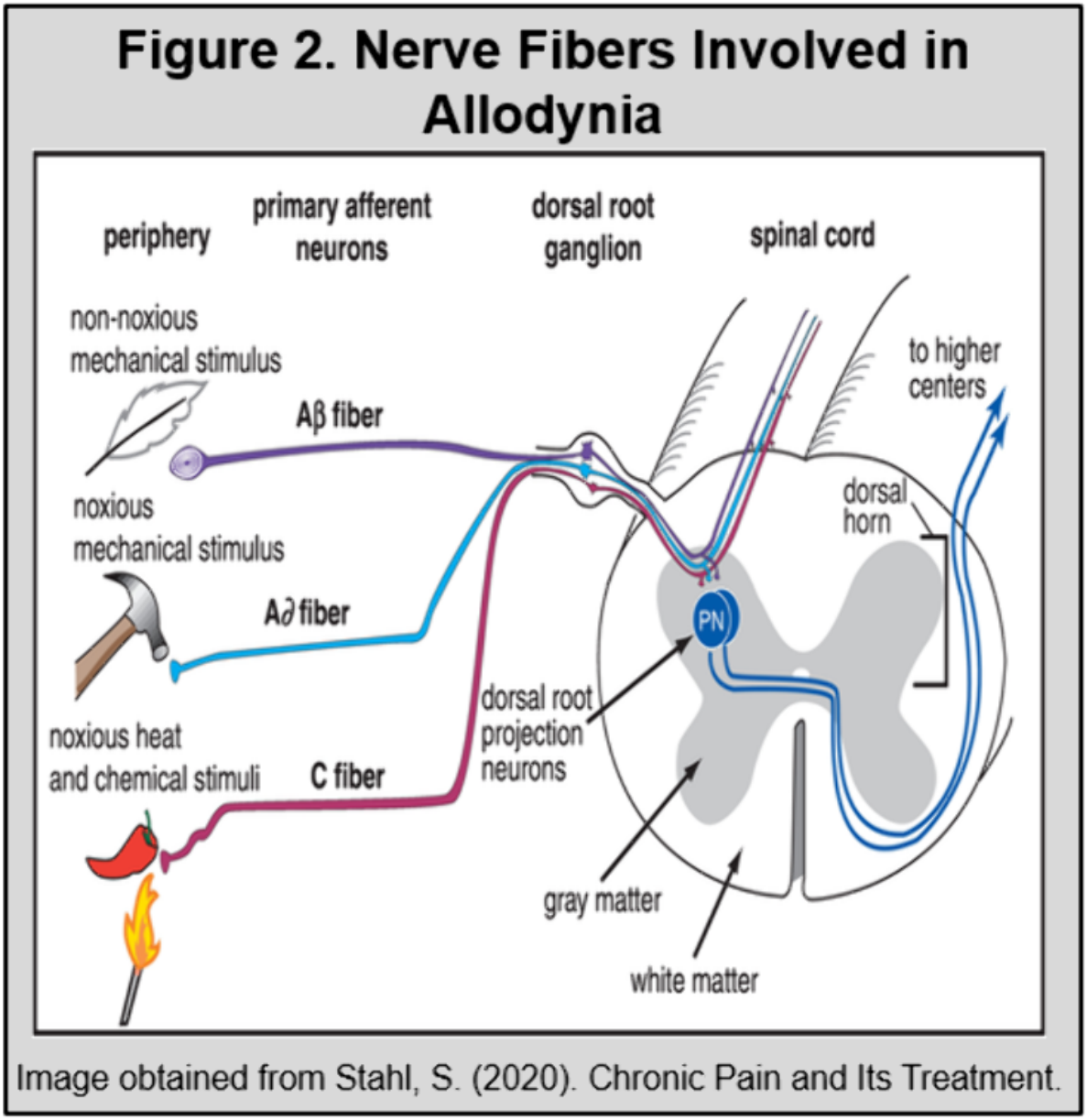
Table 3. Actions Taken for Patients with Allodynia During PENFS (n=102 visits)

Action taken (during placement)	% of Visits	Action taken (after placement)	% of Visits
Less than 4 leads placed	29	Analgesic use	9
Extra time between lead placements	28	Early device removal before 5 days	7
Psychological intervention	20		
Room darkening	4		
Switch placement ear	2		
Aborted treatment	2		

Figure 1. Treatment Outcomes Between Patients With and Without Allodynia



*API: Abdominal Pain Index, PCS-C: Pain Catastrophizing Scale for Children, NSS: Nausea Severity Scale, FDI: Functional Disability Inventory, PISI: Pediatric Insomnia Severity Index



References: 1.Hyams JS, Di Lorenzo C, Saps M, Shulman RJ, Staiano A, van Tilburg M. Functional Disorders: Children and Adolescents [published online ahead of print, 2016 Feb 15]. *Gastroenterology*. 2016;S0016-5085(16)00181-5. 2. Kovacic K, Hainsworth K, Sood M, et al. Neurostimulation for abdominal pain-related functional gastrointestinal disorders in adolescents: a randomised, double-blind, sham-controlled trial. *Lancet Gastroenterol Hepatol*. 2017;2(10):727-737. 3. Santucci NR, King C, El-Chammas KI, et al. Effect of percutaneous electrical nerve field stimulation on mechanosensitivity, sleep, and psychological comorbidities in adolescents with functional abdominal pain disorders. *Neurogastroenterol Motil*. 2022;34(8):e14358. 4. Roberts A, Sithole A, Sedghi M, Walker CA, Quinn TM. Minimal adverse effects profile following implantation of periauricular percutaneous electrical nerve field stimulators: a retrospective cohort study. *Med Devices (Auckl)*. 2016;9:389-393. Published 2016 Nov 3. 5. Stahl, S. (2022). Chronic Pain and Its Treatment. In *Stahl's Essential Psychopharmacology: Neuroscientific Basis and Practical Applications* (pp. 379-400). Cambridge: Cambridge University Press.

Acknowledgements:

Learning Objectives: 1. Familiarize with auricular percutaneous electrical nerve field stimulation (PENFS) for pediatric disorders of gut-brain interaction. 2. Describe allodynia with use of auricular

PENFS. 3. Compare outcomes in patients with and without allodynia and determine predictors of outcome.

Financial Disclosures: Dr. KEC is a consultant for Neuraxis

Disclosure: No significant relationships.

O113

Oral Presentations
NEUROMODULATION FOR GU, GI AND OTHER DISORDERS
15-05-2024 16:30 - 18:20

A REPORT ON INTERIM LONG-TERM PAIN OUTCOMES FROM THE COMFORT PERIPHERAL NERVE STIMULATION RANDOMIZED CONTROL TRIAL

John Hatheway, MD[1], Alexander Hersel, MD[2], Jonathon Song, MD[3], Mitchell Engle, MD[4], Genaro Gutierrez, MD[5], Vishal Khemlani, MD[6], Leonardo Kapural, MD[7], Gregory Moore, MD[8], Reginald Ajakwe, MD[9], Drew Trainor, MD[10], Jennifer Hah, MD[11], Mehul Desai, MD[12]
[1]Northwest Pain Care, Pain Management, Spokane, United States of America, [2]Pain Relief & Injury Management, Thousand Oaks, United States of America, [3]Arizona Pain Specialists, Scottsdale, United States of America, [4]Institute of Precision Pain Medicine, Corpus Christi, United States of America, [5]Pain Specialists of America, Round Rock, United States of America, [6]Columbia Pain Management, Milwaukie, United States of America, [7]Carolinas Pain Institute, Winston-Salem, United States of America, [8]Pacific Sports and Spine, Pain Management, Eugene, United States of America, [9]Comprehensive Spine & Pain Physicians, Burbank, United States of America, [10]The Denver Spine and Pain Institute, Pain Management, Denver, United States of America, [11]Stanford University, Anesthesiology, Perioperative, And Pain Medicine, Palo Alto, United States of America, [12]International Spine, Pain & Performance Center, DC, United States of America

Introduction: A battery-free, peripheral nerve stimulation (PNS) system with a micro-implantable pulse generator (micro-IPG; Nalu Medical, Inc., Carlsbad, CA) is being utilized in a post-market, randomized control trial (RCT; COMFORT study) to document the comparative effectiveness and safety of PNS plus conventional medical management (CMM; Active Arm) versus CMM alone (Control Arm) in the treatment of chronic, intractable peripheral neuropathic pain. We are reporting interim, long-term use results from this ongoing study. The COMFORT study is funded by the manufacturer and approved by an Institutional Review Board.

Materials / Methods: Eligible subjects prescribed PNS therapy to treat chronic pain in the shoulder, knee, low back, or foot, were consented and randomized in a 2:1 ratio (active to control). Subjects in the active arm, after completing a successful trial, were implanted with the permanent device and followed at 1, 3, 6, 9 and 12 months from device activation. Subjects in the control arm were followed at the same time points and eligible to cross-over at 3-months. Outcomes related to pain relief, functional outcomes and safety will be collected and reported.

Results: Eighty-nine (89) subjects (58 Active, 31 Control) were randomized in this ongoing study with subjects in various stages of follow-up. In the active arm, the Responder Rate at 6-months (≥ 50% improvement in NRS scores) was 91% (29/32), with a 71% average pain reduction from baseline. At 9-months, the responder rate was 75% (12/16) and an average of 71% pain reduction. At 12-months, the responder rate was 92% (12/13), with a 75% average change from baseline. Patient Global Impression of Change (PGIC) recorded at 6 and 12 months show 100% of subjects reporting improvement (very much, much or minimally improved). In the control arm, subjects eligible to crossover did so with only 1 subject opting to stay in the control arm. In this crossover group, 9 subjects have completed 6-months, with the remaining subjects in follow-up. At 6-months, crossover subjects showed a 78% (7/9) responder rate with a 71% improvement in pain scores from baseline. PGIC improved in 89% (8/9) subjects with 1 subject reporting “minimally worse”, even though they were a responder. No serious adverse device effects have been reported to date.

Discussion: Combined with Conclusion

Conclusions: Interim results, from the ongoing COMFORT study demonstrate that subjects receiving PNS therapy along with CMM continue to show sustained pain relief and functional improvements[1] with longer term use. Additional data from this study will be reported as available.

Supplemental Data:

References: Engle M, et al. A Report on the Interim Analysis of 3-month Outcomes from the COMFORT PNS RCT. ASPN Conference, Miami 2023.

Acknowledgements:

Learning Objectives: - Peripheral Nerve Stimulation provides efficacious pain relief compared to conventional medical management alone - Peripheral Nerve Stimulation provides substantial pain relief for patients - Peripheral Nerve Stimulation provides improvements in functional outcomes

Financial Disclosures: All authors listed are investigators in an ongoing clinical study funded by Nalu Medical, Inc.

Disclosure: Employee of Nalu Medical, Inc.

O114

Oral Presentations
NEUROMODULATION FOR GU, GI AND OTHER DISORDERS
15-05-2024 16:30 - 18:20

A PROSPECTIVE STUDY ASSESSING INITIAL SAFETY AND PERFORMANCE OF AN IMPLANTABLE NOVEL MIGRAINE THERAPY SYSTEM IN RELIEVING, INTERRUPTING, AND PREVENTING CHRONIC MIGRAINE (RELIEV-CM)

Marc Russo, MBBS[1], Matthew Green, MD[2], John Salmon, MBBS[3], James Yu, MD[4], Christopher Gilligan, MD[5], Robert Levy, PhD[6]
[1]Hunter Pain Specialists, Hunter Pain Specialists, Broadmeadow, Australia, [2]CerCare, Clinical Research Alliance, Broadmeadow, Australia, [3]PainCare Perth, Pain Medicine, Perth, Australia, [4]Sydney Spine and Pain, Hurstville, United States of America, [5]Brigham and Women's Hospital Harvard Medical School, Division Of Pain Medicine, Boston, United States of America, [6]Anesthesia Pain Care Consultants, Tamarac, United States of America

Introduction: Neuromodulation of nerve targets in the head including occipital (ON) and supraorbital trigeminal (SON) have shown promise in the treatment of chronic migraine. Prior research has demonstrated excellent clinical outcomes. However, the implantable systems utilized are not designed for the head/neck region. We describe the use of a novel, entirely head based, implantable system to stimulate ON and SON simultaneously in the treatment of chronic migraine.

Materials / Methods: A prospective, multi-center clinical trial is underway to examine the preliminary safety and performance of a novel, implantable neurostimulator designed to be fully located in the head region. Subjects were recruited at 4 clinical sites and will be followed for 12 months. Subjects suffering from chronic migraine according to ICHD-3 guidelines were initially screened by completing a 28-day headache diary. A trial phase was completed to screen if subjects were appropriate candidates for the implantable system. If they were, bilateral implantable pulse generators with integrated leads were placed at the nuchal ridge and leads were tunneled targeting right and left ON and SON targets. Both monthly migraine (MMD) and headache (MHD) days as well as secondary outcomes such as migraine specific quality of life (MSQ) and global impression of change (GIC) were collected.

Results: At submission 13 subjects underwent trials and 9 have received the implantable system with mean procedure times of 36 and 96 minutes respectively, and 2 awaiting implantation, representing a 83% trial conversion rate. Baseline values in implanted subjects for MMD and MHD were 17.7 and 19.0, respectively. Devices were programmed to optimize therapy to both ON and SON. At 4 weeks following activation, MMD decreased -9.0 (51%) and MHD reduced -10.4 (54%). Importantly, the occurrence of severe headache days dropped by 70%. Approximately 66% of the subjects demonstrated a 50% reduction in MHD, demonstrating a clinically significant responder rate. Subjects reported average increases of 26.2, 19.2 and 18.9 in RFR, RFP and EF MSQ domains, respectively at 4-weeks. Moreover, 83.4% of the subjects and clinicians noted a positive GIC at 4-weeks. Subjects responded well to the implant procedure and adverse events were minimal with all of them resolving spontaneously.

Discussion: ..

Conclusions: These early clinical results demonstrate promising safety and performance of a novel, fully-implantable head-based neuromodulation system in the treatment of chronic migraine. The ability to target both the ON and SON help account for the promising results and we anticipate this therapy will continue to show promise and perhaps even better outcomes as the therapy effects mature.

Supplemental Data: ..

References: ..

Acknowledgements: ..

Learning Objectives: NA

Financial Disclosures: Marc Russo, Matthew Green, John Salmon, James Yu are study investigators. Chris Gilligan and Robert Levy are advisors to ShiraTronics.

Disclosure: No significant relationships.

O115

Oral Presentations
NEUROMODULATION FOR GU, GI AND OTHER DISORDERS
15-05-2024 16:30 - 18:20

OCCIPITAL NERVE STIMULATION: LESSONS TO LEARN FROM THE 'VOLTAGE TUNERS'

Linda Kollenburg, BSc (Hons)[1], Erkan Kurt, MD[1], Hisse Arnts, MD[1], Mieke Heitkamp, BSc (Hons)[2], Suzanne Geerts, BSc (Hons)[2], Saman Vinke, MD[1], Christopher Robinson, MD, PhD[3], Wim Mulleners, MD[2]
[1]Radboud University Medical Center, Department Of Neurosurgery, Nijmegen, Netherlands, [2]Canisius Wilhelmina Hospital, Department Of Neurology, Nijmegen, Netherlands, [3]Beth Israel Deaconess Medical Center, Department Of Anesthesia, Critical Care, And Pain Medicine, Boston, United States of America

Introduction: Cluster headache (CH) is characterized by attacks of excruciating unilateral headache or facial pain (1). A subset of these patients is refractory to conventional pain treatments, and thus become eligible for interventional strategies e.g. occipital nerve stimulation (ONS). ONS is effective in 62-69% of patients and allows for personalized stimulation (2,3). Whereas most patients are consistent in their parameter settings as programmed by the physician, a subset of patients rapidly increases the voltage on a regular basis using their remote control, and are therefore referred to as 'Voltage Tuners' (figure 1). Anxiety and self-control are thought to be key aspects in this tendency to adjust the voltage. Research on this phenomenon could provide major insight into the determination of optimal parameter settings. Nevertheless, this group has never been defined before. Hence, we aim to determine the efficacy of ONS in CH patients, with emphasis on the parameter adjustments of the *Voltage Tuners*.

Materials / Methods: For this analysis, CH patients with ONS implantation received from 2020-2023 were included. All patients underwent bilateral ONS implantation. Information on the attack frequency and -intensity was retrieved from our patient database, and all patients were interviewed separately on their voltage adjustments.

Results: Twenty-eight patients (M=17; 43.8±12.64 years) were included in the current analysis. At 1y follow-up, 3 patients showed no response to ONS, 6 patients a reduction in attack frequency/intensity of <50%, 13 patients between 51-99% reduction, and 5 patients showed an excellent outcome having no attacks anymore. Overall, 51.9% of patients were categorized as *Voltage Tuners* and adjusted their voltage with an average increase of 3.4 V and frequency of 16 times/month for 383 minutes/attack. Mitigation and treatment of the CH attacks and background pain were the main reasons for the voltage adjustments (figure 1).

Discussion: Adjusting the amplitude is a phenomenon that is also seen in spinal cord stimulation, the main difference however is that CH is an unstable disorder of very diverse expressions because of its recurrence in cluster periods. Despite a good effect of ONS, some patients still need additional strategies to optimize their stimulation.

Conclusions: Rapid Voltage tuning is seen in a subset of patients with CH undergoing ONS and should be further researched as it could provide major insights into the optimization of parameter settings, thus allowing for further improvements in ONS outcomes and quality of life in CH patients.

Supplemental Data:

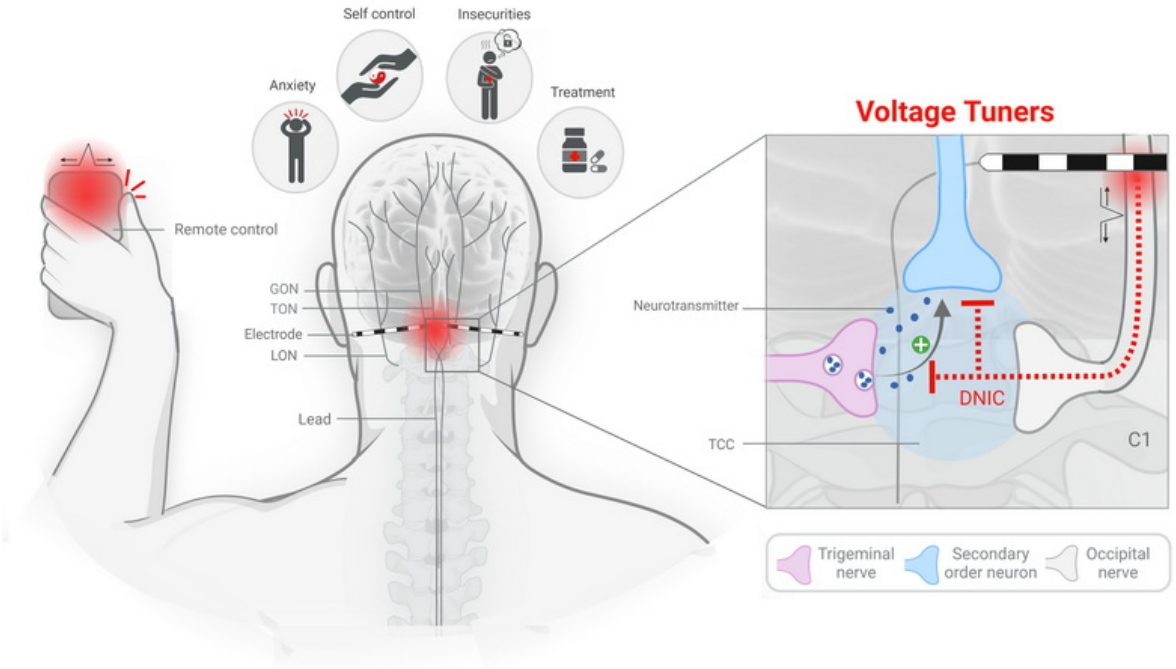


Figure 1: Overview of the rationale and underlying mechanism of the voltage adjustments seen in the group of the V*oltage Tuners*.

References: 1. Brandt RB, Doesborg PGG, Haan J, Ferrari MD, Fronczek R. Pharmacotherapy for Cluster Headache. CNS Drugs. 2020;34(2):171-84. 2. Wilbrink LA, de Coo IF, Doesborg PG, Mulleners WM, Teernstra OP, Bartels EC, et al. Safety and efficacy of occipital nerve stimulation for attack prevention in medically intractable chronic cluster headache (ICON): a randomised, double-blind, multicentre, phase 3, electrical dose-controlled trial. The Lancet Neurology. 2021;20(7):515-25. 3. Leplus A, Fontaine D, Donnet A, Regis J, Lucas C, Buisset N, et al. Long-term efficacy of occipital nerve stimulation for medically intractable cluster headache. Neurosurgery. 2021;88(2):375-83.

Acknowledgements: No acknowledgements.

Learning Objectives: 1. More than half of the patients with CH undergoing ONS adjust the voltage of their stimulation during their therapy 2. Adjusting the voltage in ONS is a real biological phenomenon with real effects 3. “Voltage Tuners” will provide us new insights in the treatment of ONS for CH

Financial Disclosures: No relationships.

Disclosure: No significant relationships.

O116

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 04
15-05-2024 16:30 - 18:20

CELLULAR QUANTIFICATION OF CEREBROSPINAL FLUID AND DORSAL ROOT GANGLION IN PATIENTS WITH CHRONIC NEUROPATHIC PAIN

Deborah Galvin, MB ChB, Connail McCrory, MB ChB
TRINITY TRANSLATIONAL MEDICINE INSTITUTE, Dept Of Surgery, DUBLIN, Ireland

Introduction: Chronic neuropathic pain (CNP) is notoriously resistant to current therapies available. Difficulty in treating CNP is due to a paucity of knowledge regarding the pathophysiology of pain chronicity. A shift to human research and investigation of current effective treatments is needed to further define the effects and benefits of pain treatments in humans. Glial cells, T lymphocytes, B lymphocytes and macrophages all have a role to play in nerve repair. It is known that binding of PD-1/PD-L1 in tumour cells and T cells allows painless proliferation of certain tumours. These findings suggest that PD-L1 is a previously unrecognised endogenous inhibitor of pain. The PD-1/PD-L1 checkpoint inhibitor pathway may be a previously unrecognised pain pathway in the initiation of pain chronicity. PD-L1 may be a potential biomarker and therapy thus potentially adding to the armamentarium in the treatment of pain.

Materials / Methods: After clinically assessing patients, DN4 questionnaire identified patients with CNP who were recruited to provide samples of cerebrospinal fluid (CSF) and dorsal root ganglion (DRG) washings before and after pulsed radiofrequency (PRF) pain procedures. Samples were centrifuged and stained with antibodies in preparation for flow cytometric analysis. We investigated the cellular composition of cerebrospinal fluid in patients with chronic neuropathic pain. In a novel analysis technique, we looked at the cellular composition of dorsal ganglion washings in these patients also. We performed flow cytometric analysis to quantify the levels of CD4+, CD8+, CD 56+ T cells in both sample types. We focused on T cells which expressed PD-1 and also investigated for presence of PD-L1. Multivariate ELISA testing is currently ongoing.

Results: A statistically significant difference was observed in CD4+ T cells levels in CSF and DRG pre-treatment (*p value* 0.0386). A statistically significant difference was observed in CD4+ T cells levels in CSF pre and post PRF treatment (*p value* 0.0217*).* A statistically significant difference was observed in CD4+ PD1+ T cells levels in DRG pre and post PRF treatment (*p value 0.0232*) A statistically significant difference was observed in CD8+ T cells levels in CSF pre and post PRF (*p value* 0.0268). A statistically significant difference was observed in CD45+ PD-L1+ cells in CSF pre and post PRF *(p value* 0.0167).

Discussion: Our study was most notable for the observation in changes in cellular quantification of both CSF and DRG pre and post treatment.

Conclusions: This study is the first report in the literature of cellular alterations in CSF compared to DRG.

Supplemental Data: Additional data available when ELISA completed

References: None

Acknowledgements: The participation of the patients in this study is gratefully acknowledged.

Learning Objectives: 1. Contribute to the further understanding of neuroimmunity in chronic neuropathic pain. 2. Identify a potential novel pathway (PD-1/PD-L1 pathway) for chronic neuropathic pain propagation 3. Contribute to the knowledge of pulsed radiofrequency and its pain-treating mechanism of action

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O117

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 04
15-05-2024 16:30 - 18:20

EXPLORING THE PATHOPHYSIOLOGY AND RESPONSE PATTERNS OF PERSISTENT SPINE PAIN SYNDROME TYPE 2 TO SPINAL CORD STIMULATION: A HUMAN GENOME-WIDE ASSOCIATION STUDY

Gustavo Fabregat-Cid, MD, MSc, PhD[1], David Cedeño, PhD[2], Jose De Andres, MD, PhD[1], Ricardo Vallejo, MD, PhD[2]
[1]General University Hospital, Anesthesia, Critical Care, And Multidisciplinary Pain Management Department, Valencia, Spain, [2]SGX Medical LLC, Bloomington, United States of America

Introduction: Spinal cord stimulation (SCS) has been shown to alleviate pain in a subset of patients suffering from persistent spine pain syndrome type 2 (PSPS 2). However, the exact mechanisms responsible for this relief and the factors predicting a positive pain response remain unclear. This in vivo human genome-wide association study sheds light on certain aspects of the underlying pathophysiology.

Materials / Methods: We performed a high density oligonucleotide microarray analysis of serum obtained from both, PSPS 2 cases and pain free controls who had undergone low back spinal surgery at the study site. mRNA transcripts with different expression between PSPS 2 patients relative to controls, SCS responders and non responders, or significantly modulated by SCS relative to baseline were identified using multivariate discriminant analysis. Gene ontology enrichment analysis was used to identify the biological processes that best discriminate between the groups of clinical interest.

Results: Our study encompassed 30 PSPS 2 patients, of whom 23 exhibited a positive response to SCS, and it included 15 pain-free controls. We identified 11 downregulated genes in PSPS 2 patients in comparison to pain-free controls, and two downregulated genes when the response to SCS became evident. All these genes were indicative of an intensified inflammatory response, enhanced tissue repair mechanisms, and proliferative reactions among PSPS 2 patients. Regrettably, we were unable to identify any specific genes that could differentiate between SCS responders and non-responders.

Discussion: In this study, a genome-wide association analysis was conducted to examine gene expression patterns in various contexts related to persistent spine pain syndrome type 2 (PSPS 2) and its response to spinal cord stimulation (SCS). We identified several genes that were downregulated in PSPS 2 patients compared to pain-free controls, particularly highlighting the involvement of G protein-coupled receptor (GPCR) signaling pathways, proinflammatory cytokines, and anti-inflammatory cytokines. Interestingly, the study also noted changes in the expression of genes associated with vascular endothelial growth factor (VEGF), dopamine receptors, and dopamine signaling pathways in SCS responders. However, the study did not find consistent differences between responders and non-responders to SCS. While the research has shed light on various biological processes related to PSPS 2 and SCS, it has limitations, including the need for further validation and more specific insight into the causality of gene modulation.

Conclusions: This study points out various biological processes that may underlie PSPS 2 pain and SCS therapeutic effects, including the modulation of neuroimmune response, inflammation and restorative processes

Supplemental Data:

References: 1. Christelis, N., Simpson, B., Russo, M., Stanton-Hicks, M., Barolat, G., Thomson, S., Schug, S., Baron, R., Buchser, E., Carr, D. B., Deer, T. R., Dones, I., Eldabe, S., Gallagher, R., Huygen, F., Kloth, D., Levy, R., North, R., Perruchoud, C., . . . Loeser, J. (2021). Persistent Spinal Pain Syndrome: A Proposal for Failed Back Surgery Syndrome and ICD-11. *Pain Med*, *22*(4), 807-

818. https://doi.org/10.1093/pm/pnab015 2. De Andres, J., Navarrete-Rueda, F., Fabregat, G., Garcia-Gutierrez, M. S., Monsalve-Dolz, V., Harutyunyan, A., Minguez-Marti, A., Rodriguez-Lopez, R., & Manzanares, J. (2021). Differences in Gene Expression of Endogenous Opioid Peptide Precursor, Cannabinoid 1 and 2 Receptors and Interleukin Beta in Peripheral Blood Mononuclear Cells of Patients With Refractory Failed Back Surgery Syndrome Treated With Spinal Cord Stimulation: Markers of Therapeutic Outcomes? *Neuromodulation*, *24*(1), 49-60. https://doi.org/10.1111/ner.13111 3. Fabregat-Cid, G., Cedeno, D. L., Harutyunyan, A., Rodriguez-Lopez, R., Monsalve-Dolz, V., Minguez-Marti, A., Hernandez-Cadiz, M. J., Escriva-Matoses, N., Villanueva-Perez, V., Asensio Samper, J. M., De Andres, J., & Vallejo, R. (2023). Effect of Conventional Spinal Cord Stimulation on Serum Protein Profile in Patients With Persistent Spinal Pain Syndrome: A Case-Control Study. *Neuromodulation*. https://doi.org/10.1016/j.neurom.2023.05.004 4. James, S. (2013). Human pain and genetics: some basics. *Br J Pain*, *7*(4), 171-178.https://doi.org/10.1177/2049463713506408 5. LaCroix-Fralish, M. L., Austin, J. S., Zheng, F. Y., Levitin, D. J., & Mogil, J. S. (2011). Patterns of pain: meta-analysis of microarray studies of pain. *Pain*, *152*(8), 1888-1898. https://doi.org/10.1016/j.pain.2011.04.014

Acknowledgements:

Learning Objectives: What does this study add? 1. We present a comparative analysis of genome-wide mRNA expression levels in the serum of patients with persistent spine pain syndrome type 2 (PSPS 2) and pain-free individuals who underwent spinal surgery, differentiating between patients who responded to conventional spinal cord stimulation (SCS) therapy and those who did not, while also exploring how SCS affects gene expression. 2. Notably, our study revealed significant in vivo regulation of specific genes, implying the importance of neuroimmune responses and inflammation in the pathophysiology of PSPS 2, potentially elucidating the factors contributing to the response to SCS. 3. Although the precise gene names may not align with those identified in previous preclinical pain models, it is remarkable that the associated biological processes consistently point to a pro-neuroinflammatory and immunoreactive environment as the underlying factor in the persistence of back pain.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O118

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 04
15-05-2024 16:30 - 18:20

SPINAL CORD STIMULATION NAÏVE PATIENTS VERSUS PATIENTS WITH FAILED PREVIOUS EXPERIENCES WITH STANDARD SPINAL CORD STIMULATION: TWO DISTINCT ENTITIES OR ONE POPULATION?

Lisa Goudman, PhD[1], Philippe Rigoard, MD[2], Maxime Billot, PhD[3], Manuel Roulaud, MSc[3], Discover Consortium, MSc[1], Maarten Moens, MD[1]
[1]Vrije Universiteit Brussel, Stimulus Research Group, Jette, Belgium, [2]Poitiers University, Spinal Neurosurgery, Neuromodulation, Poitiers, France, [3]CHU de Poitiers, Neurosurgery Departement/prismatics Lab, Poitiers, France

Introduction: Nowadays, the success of spinal cord stimulation (SCS) is evaluated separately in patients who have previous experiences with standard SCS and in SCS-naïve patients. According to our healthcare system, and according to the point of view of clinicians, both patient groups are completely different (inducing that research trials are separately conducted in SCS naïve patients and patients with previous SCS experiences). Nevertheless, it is yet to be evaluated whether both patient groups are effectively distinct patient groups. Therefore, the aims of this study are twofold: 1) Are there clusters in the data to distinguish between both patient groups? 2) Can we discriminate both patient groups based on routinely collected clinical parameters?

Materials / Methods: Baseline data from the Discover study were used, in which 263 patients with persistent spinal pain syndrome type 2 were included (185 neurostimulation-naïve patients and 78 patients with previous SCS experience). Pain intensity scores for low back and leg pain, functional disability, medication use, and health-related quality of life utility scores were used in the analysis. Model-based clustering was performed on standardized data. Discriminant analysis was performed with linear and quadratic discriminant analysis, with leave-one-out cross-validation to evaluate model performance.

Results: Model-based clustering revealed two different clusters in the data. None of the clusters clearly separated SCS-naïve patients from patients with previous SCS experience. Linear discriminant analysis resulted in a leave-one-out cross-validation error rate of 30.0% to discriminate between both patient groups, based on routinely collected clinical parameters.

Discussion: This is the first study using model-based clustering analysis to profile patients eligible for SCS from two different clinical patient populations (SCS naïve versus previous SCS experience) to identify differences based on clinical parameters. Clustering analysis did not result in clusters that separate SCS-naïve patients from patients with previous SCS experience.

Conclusions: This may suggest that both patient groups should not be considered as two different patient groups when comparing them on routine clinical parameters, with potentially profound implications for research and clinical settings.

Supplemental Data:

References: Goudman L, Rigoard P, Billot M, De Smedt A, Roulaud M, Consortium D, Moens M; Discover Consortium. Spinal Cord Stimulation-Naïve Patients vs Patients With Failed Previous Experiences With Standard Spinal Cord Stimulation: Two Distinct Entities or One Population? Neuromodulation. 2023 Jan;26(1):157-163.

Acknowledgements:

Learning Objectives: 1) To challenge our current clinical reasoning about patient profiling for SCS 2) To learn how to interpret machine learning models and to know the pitfalls of these models 3) To gain

insight in what the commonalities and differences are between SCS naïve patients and patients with previous SCS experience

Financial Disclosures: Maarten Moens has received speaker fees from Medtronic and Nevro. Lisa Goudman is a postdoctoral research fellow funded by the Research Foundation Flanders, Belgium (project number 12ZF622N). Philippe Rigoard reports grants and personal fees from Medtronic, Abbott, and Boston Scientific, outside the submitted work. STIMULUS received independent research grants from Medtronic. The remaining authors reported no conflict of interest.

Disclosure: No significant relationships.

O119

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 04
15-05-2024 16:30 - 18:20

EXAMINING THE DURATION OF CARRYOVER EFFECT IN CHRONIC PAIN PATIENTS TREATED WITH SPINAL CORD STIMULATION (ECHO STUDY). AN OPEN, INTERVENTIONAL, INVESTIGATOR-INITIATED, INTERNATIONAL MULTICENTER STUDY.

Kaare Meier, MD, PhD[1,2], Cecile De Vos, PhD[3], Martine Bordeleau, MSc, PhD[4], Sharon Van Der Tuin, MSc, RN[5], Bart Billet, MD[6], Thomas Ruland, MD[7], Morten Blichfeldt-Eckhardt, MD, PhD[8], Matthias Winkelmüller, MD[9], Helga Gulisano, MD[10], Kliment Gatzinsky, MD, PhD[11], Anne Lene Knudsen, MSc, RN[2], Jens Christian Sørensen, MD, PhD[2], Ioanna Milidou, MD, MSc, PhD[12], Sylvine Carrondo-Cottin, MSc, PhD[13]
[1]Aarhus University Hospital, Anesthesiology, Aarhus N, Denmark, [2]Aarhus University Hospital, Neurosurgery, Aarhus N, Denmark, [3]Erasmus MC, Rotterdam, Netherlands, [4]Université de Sherbrooke, Sherbrooke, Canada, [5]Medisch Spectrum Twente, Enschede, Netherlands, [6]AZ Delta, Roeselare, Belgium, [7]Sunderby Hospital, Luleå, Sweden, [8]Odense University Hospital, Odense, Denmark, [9]Friederikenstift, Hannover, Germany, [10]Aalborg University Hospital, Aalborg, Denmark, [11]Sahlgrenska, Göteborg, Sweden, [12]Gødstrup Hospital, Herning, Denmark, [13]Laval University, Neurosurgery, Quebec, Canada

Introduction: It has long been assumed that when temporarily deactivating a spinal cord stimulation (SCS) device, there is a variable interval before the patient perceives the return of the pain; a phenomenon often termed Echo or Carryover effect. Although the carryover effect has been problematized as a source of error in crossover studies, and has, indeed, been utilized in treatment regimens using automated ON/OFF cycles, no experimental investigation of the effect has, to our knowledge, been published. This open, prospective, international multicenter study aimed to systematically document, quantify and investigate the carryover effect in SCS.

Materials / Methods: Patients having good pain control from their SCS treatment were instructed to deactivate their SCS device in a home setting and to reactivate it when their pain returned. Primary outcome was duration of carryover time defined as the time interval from deactivation to reactivation. Central clinical parameters such as age, sex, indication for SCS, SCS treatment details, and pain score were registered and analysed for correlation with carryover time.

Results: 158 patients were included in the analyses. A median carryover time of 5 hours (IQR 2.5;21 hours) was found . Back pain as primary indication for SCS, high-frequency stimulation, and higher pain score at the time of deactivation seemed correlated with longer carryover time.

Discussion: This study was not aimed at exploring the effectiveness of SCS therapy but only at investigating the carryover effect. It should be noted that the participants were, in most cases, not pain free even with active stimulation. The study documents a remarkably large inter-individual variation in the carryover time, ranging from mere minutes to several hours, and even days. The results of this study point to the importance of including investigation of the individual study participant's carryover time when designing a study paradigm.

Conclusions: This study confirms the phenomenon often termed carryover or echo effect, and documents that the duration of the effect varies highly between individuals. The results also suggest that the effect may be determined by the nature of the pain condition.

Supplemental Data:

References:

Acknowledgements: The authors wish to thank the patients who consented to participate in this project. The authors are deeply grateful to RN Rian Wolters and RN Simone Hansler. This study was

supported by a grant from the Science Council, Aarhus University Hospital, the Health Research Fund, Central Denmark Region, and the Fondation du CHU de Québec. No other support was received for this work.

Learning Objectives: 1. In SCS, the carryover / echo effect does exist. 2. The duration of the carryover effect has a remarkably large inter-individual variation among SCS patients. 3. The effect shuld be taken into account when designing clinical experiments with changes in stimulation parameters.

Financial Disclosures: KM: Lecture fees from Abbott. Consultancy fees from Salvia. Co-owner of neuromodulation database company Neurizon. CdV: No conflicts of interest. MB: No conflicts of interest. SvdT: No conflicts of interest. BB: Consultancy for Abbott, Salvia Bioelectronics and Medtronic. TR: No conflicts of interest. MRBE: Travel support from Medtronic, Abbott and Boston Scientific MW: Lecture fees and travel support from Boston Scientific and Medtronic HAG: Fees for teaching and advisory board engagements from Medtronic. KG: Fees for teaching and advisory board engagements from Medtronic and Boston Scientific. ALK: No conflicts of interest. JCHS: Lecture fees from Abbott. Co-owner of neuromodulation database company Neurizon. IM: No conflicts of interest. SCC: Travel support from Medtronic and Boston Scientific. KM's and JCHS' institution (AUH) has received travel support from Abbott and Boston Scientific.

Disclosure: No significant relationships.

O120

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 04
15-05-2024 16:30 - 18:20

HIGH CERVICAL SPINAL CORD STIMULATION AS A NOVEL APPROACH FOR THE MANAGEMENT OF MEDICALLY INTRACTABLE CHRONIC CLUSTER HEADACHE (MICCH)

Casper Lansbergen, MD[1], Cecile De Vos, PhD[1], Frank Huygen, MD, PhD[2]
[1]Erasmus Medical Centre, Center For Pain Medicine, Department Of Anesthesiology, Rotterdam, Netherlands, [2]Erasmusmc, Centre Of Pain Medicine, Rotterdam, Netherlands

Introduction: Chronic cluster headaches pose significant management challenges, especially when standard drug treatments prove ineffective. Over the past decades, various forms of neuromodulation techniques have emerged as potential treatments for medically intractable chronic cluster headaches (MICCH), including sphenopalatine ganglion(SPG) stimulation and occipital nerve stimulation (ONS). (1-4) However, while ONS has shown to be effective and gained recognition in recent studies(4), only a little more than half of the patients were responders (≥50% headache frequency reduction. (4,5) The pursuit of additional treatment modalities for MICCH is therefore imperative. High-frequency (HF10) spinal cord stimulation (SCS) has demonstrated effectiveness in various pain conditions, including migraine and other primary headaches. (6-9) This case series explores the efficacy of high cervical SCS as a novel therapeutic approach for MICCH.

Materials / Methods: Ten MICCH patients, who were unresponsive to ONS, were implanted with a high cervical SCS system. High-frequency stimulation (10 kHz, HF10) was applied at the C2-C3 vertebral level. The patients have been followed up for at least 6 months. Clinical data was collected, including patient characteristics, comorbidities, treatment history, pain characteristics, attack frequency, duration, and stimulation parameters.

Results: Of the 10 patients, half reported attack frequency reduction of >50% with the HF10 SCS therapy. While pain intensity and attack duration showed less consistent improvements, the decrease in attack frequency correlated with patient satisfaction. The presence of facial autonomic symptoms, unaffected by the neuromodulation, suggests that HF10 SCS does not interfere with the trigeminal-autonomic reflex.

Discussion: This case series demonstrates potential efficacy of high cervical HF10 SCS in selected cases of MICCH, particularly in reducing attack frequency. However, additional research is required to elucidate the underlying mechanisms of MICCH and HF10 SCS to determine the therapy's effectiveness. This underscores the need for further phenotyping of cluster headache populations. Moreover, further investigations with larger, well-defined populations and randomized studies are warranted to validate the findings of this case series.

Conclusions: High cervical HF10 SCS reduces the frequency of cluster headache attacks in selected cases. Enhanced phenotyping of the cluster headache population is imperative for optimizing the utilization of neuromodulation modalities.

Supplemental Data: Not applicable.

References: 1. Goadsby PJ, Sahai-Srivastava S, Kezirian EJ, Calhoun AH, Matthews DC, McAllister PJ, et al. Safety and efficacy of sphenopalatine ganglion stimulation for chronic cluster headache: a double-blind, randomised controlled trial. Lancet Neurol. 2019;18(12):1081-90. 2. Jurgens TP, Barloese M, May A, Lainez JM, Schoenen J, Gaul C, et al. Long-term effectiveness of sphenopalatine ganglion stimulation for cluster headache. Cephalalgia. 2017;37(5):423-34. 3. Schoenen J, Jensen RH, Lanteri-Minet M, Lainez MJ, Gaul C, Goodman AM, et al. Stimulation of the sphenopalatine ganglion (SPG) for cluster headache treatment. Pathway CH-1: a randomized, sham-controlled study. Cephalalgia. 2013;33(10):816-30. 4. Wilbrink LA, de Coo IF, Doesborg PGG, Mulleners WM, Teernstra OPM, Bartels EC, et al. Safety and efficacy of occipital nerve stimulation for attack

prevention in medically intractable chronic cluster headache (ICON): a randomised, double-blind, multicentre, phase 3, electrical dose-controlled trial. Lancet Neurol. 2021;20(7):515-25. 5. Leone M, Proietti Cecchini A, Messina G, Franzini A. Long-term occipital nerve stimulation for drug-resistant chronic cluster headache. Cephalalgia. 2017;37(8):756-63. 6. Arcioni R, Palmisani S, Mercieri M, Vano V, Tigano S, Smith T, et al. Cervical 10 kHz spinal cord stimulation in the management of chronic, medically refractory migraine: A prospective, open-label, exploratory study. Eur J Pain. 2016;20(1):70-8. 7. Lambru G, Trimboli M, Palmisani S, Smith T, Al-Kaisy A. Safety and efficacy of cervical 10 kHz spinal cord stimulation in chronic refractory primary headaches: a retrospective case series. J Headache Pain. 2016;17(1):66. 8. Al-Kaisy A, Palmisani S, Carganillo R, Wesley S, Pang D, Rotte A, et al. Safety and Efficacy of 10 kHz Spinal Cord Stimulation for the Treatment of Refractory Chronic Migraine: A Prospective Long-Term Open-Label Study. Neuromodulation. 2022;25(1):103-13. 9. Wolter T, Kiemen A, Kaube H. High cervical spinal cord stimulation for chronic cluster headache. Cephalalgia. 2011;31(11):1170-80.

Acknowledgements: Not applicable.

Learning Objectives: 1. Despite its efficacy as a last resort treatment, Occipital Nerve stimulation falls short in achieving the desired outcome in approximately 40% of cases. 2. High-Frequency Cervical Spinal Cord Stimulation might be a viable treatment alternative when Occipital Nerves stimulation proves ineffective. 3. Enhanced phenotyping of the cluster headache population is imperative for optimizing the utilization of neuromodulation modalities.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O121

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 04
15-05-2024 16:30 - 18:20

SPINAL CORD STIMULATION WITH SURGICAL LEAD IS A SUFFICIENT SECONDARY TREATMENT OPTION FOR PATIENTS SUFFERING FROM PERSISTENT SPINAL PAIN SYNDROM

Anton Früh, MD, MSc, Laura Hallek, MD, Melanie Brüßeler, MD, Tarik Alp Sargut, MD, Simon Bayerl, MD
Charité, Berlin, Germany

Introduction: Persistent spinal pain syndrome (PSPS) poses a significant medical challenge, often leading to diminished quality of life for affected individuals. In response to this syndrome Spinal Cord Stimulation (SCS) is a promising intervention. In case a therapy with percutaneous lead (PL) fails (e.g., due to a dislocation), surgical lead (SL) can also be used. This is resulting in a more invasive procedure and do not allow for intraoperative monitoring. The aim of the study is to investigate the efficacy and safety of the use of SL, as there have been only a few case series published so far.

Materials / Methods: We prospectively included PSPS patients that were treated with SL. All implantations were performed with the SCS-SL-System (BostonScientific). Ethic was approved by the local-committee(EA2/093/13). Outcome scores concerning the quality of life (SF-36), pain related disability [ODI], sleeping quality [PSQI] and pain intensity (NRS) were obtained prior surgery and at outpatient visits after implantation.

Results: 34 patients with a median age of 66(IQR 56-75) years received a SCS-SL system. 32(94.1%) SL-Systems were implanted secondary after a treatment with PL failed. 2(5.9%) patients received SL as primary treatment. One patient showed postoperative a new neurological deficit (left-sided leg paresis), resulting in a morbidity rate of 2.9%. In 3(8.8 %) patients the electrodes were explanted within the first month (n=1: neurological deficit n=1: wound infection, n=1: negative trial phase). Thus follow-up data of 21 subjects were available. Median time of the latest follow-up was 28(IQR 15-47) months. The mean pain intensity ($NRS_{preop,rest.}$ =6.9 +/- 1.2;$NRS_{preop,motion.}$ =8.9 +/- 1.0) was reduced at the follow-up ($NRS_{follow-up,rest.}$= 2.6 +/- 2.3,$NRS_{follow-up,rest}$= 3.4 +/- 2.7). Further the pain depending disability improved ($ODI_{preop.}$ =42.9 +/- 17.5;$ODI_{follow-up.}$ =21.3 +/- 16.7). The quality of life improved physically ($SF\text{-}36_{physical,preop}$ = 23.0 +/- 8.0; $SF\text{-}36_{physical,follow-up}$ =39.4 +/- 9.6) and mentally ($SF\text{-}36_{mental,preop}$ = 42.7 +/- 19.1;$SF\text{-}36_{mental,follow-up}$ =52.2 +/- 14.7). Further an improvement concerning the sleeping quality was reported ($PSQI_{preop}$ = 11.5 +/- 3.6;$PSQI_{follow-up}$ =6.6 +/- 4.0)

Discussion: SCS with SL is a safe and sufficient technique for patients suffering from PSPS. The ,orbidity rate is low. The data reveal an improvement concerning pain, pain related disability, quality of life and sleeping quality. This is underlining the effectiveness of SCS SL treatment for these subjects.

Conclusions: SCS with SL is a safe secondary technique to treat PSPS, where treatment with percutaneous lead fail. The results show a promising long-term effect concerning pain intensity and functional outcome.

Supplemental Data:

Learning Objectives: (1) Surgical lead SCS is a safe procedure (no mortality, morbidity 2.9%) (2) Surgical lead SCS is improving pain in treated patients (23 Surgical lead SCS is improving quality of life, sleeping and pain related disability

Financial Disclosures: PD Dr. med. Simon Bayerl has a consulting agreement with Bostin Scientific, Abbot, Curonix and Nevro

Disclosure: No significant relationships.

O122

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 04
15-05-2024 16:30 - 18:20

REIMPLANTATION OF SCS PADDLE ELECTRODE: BENEFITS AND RISKS

Xenia Kuparinen, MD[1,2], Riku Kivisaari, MD, PhD[3], Nuutti Vartiainen, MD, PhD[3], Julio Resendiz-Nieves, MD, PhD[3]
[1]University of Helsinki, Doctoral Programme In Clinical Research, Helsinki, Finland, [2]Turku University Hospital, Department Of Neurosurgery, Turku, Finland, [3]Helsinki University Hospital, Department Of Neurosurgery, Helsinki, Finland

Introduction: Spinal cord stimulation (SCS) is a well-recognized treatment for chronic pain that does not respond to medication. Unfortunately, a significant number of patients have their stimulator explanted for various reasons i.e., infection, loss of benefit, malfunction, or need for MRI. Most of these patients continue suffering from their chronic, debilitating pain and although reimplantation remains an option, few publications are addressing the benefits and the risks of reimplantation of SCS paddle electrodes.

Materials / Methods: We recently reported the surgical outcomes of all the patients at the *Helsinki University Hospital Department of Neurosurgery* who underwent explantation of SCS paddle electrodes between February 2005 and October 2020[1]. Now we analysed all the patients who had their SCS paddle electrode re-implanted or relocated during the explantation procedure or after it. Patients' ability to reduce pain medication, the complication rate of the operation and the benefits of the new stimulator were evaluated.

Results: Out of 131 explanted electrodes, 60 (45,8%) were replaced by a new electrode and 16 (12,2%) were relocated. All 16 were relocated during the initial explantation, while 40 electrodes were replaced intraoperatively and 20 were reimplanted later. Patients suffered 22 complications during 19 operations, making the complication rate 25%; 15 (78.9%) were replacement operations and 4 (21.1%) relocations. Three patients suffered more than one complication; 81.2% of complications were considered minor and 18.2% were considered major. All, except one patient who suffered from permanent C8-paresthesia, recovered without sequels. (Table 1) Postoperatively 60% of the patients who received a new stimulator had equal or better (38%) pain relief during follow-up. In comparison, 56% of the patients who had their stimulator relocated had equal or better (44%) pain relief. The reason for relocation or re-implantation did not correlate with the benefits of the surgery (Table 2). 20 out of 76 (26.4%) patients could completely or partially reduce their pain medication.

Discussion: SCS is a valuable treatment form for chronic pain that does not respond to medication and has a deleterious effect on a patient's quality of life. Unfortunately, many patients have their electrodes explanted for various reasons. This study shows that over 50% of the patients who had their SCS paddle electrode explanted benefitted from reimplantation. We demonstrated that the procedure has an acceptable complication rate, thus reaffirming that reimplantation should remain an option.

Conclusions: Reimplantation or relocation of the SCS paddle electrode is beneficiary and carries an acceptable complication risk. Thus it should remain a valuable treatment option.

Supplemental Data:

Table 2. Reason for revision

	Total sample n (%)		**Level of pain relief**		
		Better n (%)	**Same n (%)**	**Worse n (%)**	**p-value**
Relocation n=16		n = 7	n =2	n = 7	

Loss of benefit	14 (87.5%)	6 (42.9%)	2 (14.3%)	6 (42.9%)	1
Malfunction	1 (6.3%)	1 (100%)	0 (0.0%)	0 (0.0%)	
Migration	1 (6.3)	0 (0.0%)	0 (0.0%)	1 (100%)	
Replacement	n = 60	n = 23	n =13	n = 24	
Need for MRI	2 (3.3%)	1 (50.0.%)	0 (0.0%)	1 (50.0%)	0.119
Infection	18 (30.0%)	5 (27.8%)	4 (22.2%)	9 (50.0%)	
Loss of benefit	21 (35.0%	9 (42.9%)	2 (9.5%)	10 (47.6%)	
Malfunction	16 (26.7%)	7 (43.8%)	7 (43.8%)	2 (12.5%)	
Migration	3 (5.0%)	1 (33.3%)	0 (0.0%)	2 (66.7%)	

Table 1. Complications

	Total sample n (%)	**Replacement n (%)**	**Relocation n (%)**
	n = 22	n = 14	n = 8
Major complications			
Epidural hematoma	2 (9.1 %)	2 (14.3%)	
Progressive paraparesis	1 (4.5%)	1 (7.1%)	
Infection with abscess formation	1 (4.5%)		1 (12.5%)
Minor complications			
Infection	9 (40.9%)	6 (42.9%)	3 (37.5%)
Migration	2 (9.1%)	2 (14.3%)	
Paresthesia	1 (4.5%)	1 (7.1%)	
Wound dehiscence	2 (9.1%)	2 (14.3%)	
Abdominal pain	1 (4.5 %)		1 (12.5%)
Subcutaneous hematoma/seroma	3 (13.6%)		3 (37.5%)

References: 1. Kuparinen X, Ahmed Haji Omar A, Vartiainen N, et al. Explantation and Simultaneous Explantation-Reimplantation of Spinal Cord Stimulation Paddle Electrodes: Complication Rate and Predisposing Factors. *Neurosurgery Practice*. 2023;4(3):e00055. doi:10.1227/neuprac.0000000000000055

Acknowledgements:

Learning Objectives: 1. Educating professionals on risks and benefits associated with the reimplantation of SCS paddle electrodes. 2. Provide clinicians with information to discuss with their patients when considering explantation/reimplantation of SCS paddle electrodes. 3. Reimplantation should remain an option in patients who have their SCS system explanted.

Financial Disclosures: No significant relationship.

Disclosure: No significant relationships.

O123

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 04
15-05-2024 16:30 - 18:20

AN EVALUATION OF INCIDENCE OF INFECTIONS, EXPLANTATIONS AND DISPLACEMENTS/MECHANICAL COMPLICATIONS OF SPINAL CORD STIMULATION DURING THE PAST 8 YEARS.

Lisa Goudman, PhD[1], Maarten Moens, MD[2], Christopher Young, BSc (Hons)[3], Sophie Kelly, BSc (Hons)[3], Julie Pilitsis, MD, PhD[4]
[1]Laarbeeklaan 103, Stimulus Research Group, Jette, Belgium, [2]Vrije Universiteit Brussel, Stimulus Research Group, Jette, Belgium, [3]Florida Atlantic University School of Medicine, Boca Raton, United States of America, [4]Florida Atlantic University School of Medicine, Neurosurgery, Boca Raton, United States of America

Introduction: The overall awareness and potential of real-world data has drastically increased in the medical field, with potential implications for postmarket medical device surveillance. The goal of this study was to evaluate real-world data on incidence of infections, explantations and displacements/mechanical complications of Spinal Cord Stimulation (SCS) during the past 8 years and forecast point estimates for the upcoming 3 years based on the identified patterns.

Materials / Methods: Based on electronic health records from 80 healthcare organizations within the TriNetX database in the USA, data of 11,934 patients who received SCS as treatment for Persistent Spinal Pain Syndrome Type 2 (PSPS T2) was extracted. Events of interest were explantations and displacements/mechanical complications of both the lead and implanted pulse generator (IPG), as well as infection rates from 2015 to 2022. Mann-Kendall tests were performed to detect monotonic trends in the time series. Forecasts were made for the upcoming 3 years for every event of interest.

Results: Statistically significant increasing time trends were revealed for the annual incidence of IPG and lead displacements/mechanical complications in patients with PSPS T2 over the past 8 years. These time trends were visible in both males and females as well as in smokers and non-smokers. For annual incidence of explantations and infections, no significant time effect was observed. In 2025, the incidence of displacements/mechanical complications of the lead (3.07%) is predicted to the highest, followed by explantations of the IPG (2.67%) and lead (2.02%).

Discussion: Real-world data from 80 healthcare organizations revealed increasing time trends for IPG and lead displacements/mechanical complications in patients with PSPS T2 over the past 8 years. Device explantation was the most frequent event of interest, with negative peaks in the time series in 2016 and 2020, presumably due to the introduction of rechargeable pulse generators and Covid-19 pandemic, respectively.

Conclusions: Real-world data provides a complementary estimate of displacements/mechanical complications, explantations and infections related to SCS, whereby longer time series will enable us to forecast future incidence rates to promptly address events with high estimates. The possibility of device explantation clearly points towards reversibility, a major advantage in term of safety of this therapeutic option with a medical device.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1) To gain insight in the value of real-world data, in comparison to data obtained from randomized controlled trials. 2) To learn about the incidence of adverse events during

the past 8 years in terms of SCS for PSPS-T2. 3) To interpret statistical findings from time series and to evaluate & translate the findings for clinical practice.

Financial Disclosures: Lisa Goudman is a postdoctoral research fellow funded by the Research Foundation Flanders (FWO), Belgium (project number 12ZF622N), with additional funding for a long stay abroad by Research Foundation Flanders (FWO), Belgium (project number V405123N) during which this manuscript was written. Maarten Moens has received speaker fees from Medtronic, Saluda and Nevro. STIMULUS received independent research grants from Medtronic. Julie Pilitsis received grant support from Medtronic, Boston Scientific, Abbott, NIH 2R01CA166379, NIH R01EB030324, NIH Blueprint 3U54EB015408 and NIH U44NS115111. She is part of the Board of Directors of Facial Pain Association, Board of Directors at Large of International Neuromodulation Society, President Elect of American Society of Stereotactic and Functional Neurosurgery and President of North American Neuromodulation Society. There are no other conflicts of interest to declare.

Disclosure: No significant relationships.

O124

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 04
15-05-2024 16:30 - 18:20

SPINAL CORD STIMULATION FOR BRACHIAL PLEXUS AVULSION PAIN - A CASE SERIES

Harry Soar, MBChB FRCA EDPM, David Cronin, MB ChB, Andrew Whelan, MB ChB, Sheila Black, MB ChB
Leeds Teaching Hospitals, Pain Department, Leeds, United Kingdom

Introduction: Data on the outcomes of patients with brachial plexus avulsion treated with SCS is limited to case reports. We present the follow up data for a series of 7 patients. Brachial plexus avulsion (BPA) is a traumatic injury that occurs when the cervical nerve roots that innervate the upper limb are severed from the spinal cord. Neuropathic pain is the most prevalent and debilitating symptom, occurring in 80% of BPA patients.1,2 Various neuromodulation techniques have been used to treat BPA-related pain, such as peripheral nerve stimulation, cervical spinal cord stimulation (SCS), dorsal root entry zone (DREZ) lesioning and deep brain stimulation (DBS) or motor cortex stimulation (MCS). SCS may have an advantage over other methods, due to its increased availability, reversibility and advances in stimulation paradigms.

Materials / Methods: A retrospective review of follow up data for 7 patients with traumatic brachial plexus avulsion treated with SCS. Brachial plexus injuries: the 7 patients had traumatic injuries resulting in unilateral complete avulsion of between 2-3 nerve roots. 2 patients had a 2 week trial period and 5 patients went directly to full implant. Data was recorded at routine patient follow up appointments with pain specialist nurses. SCS Systems used: •3 x Boston Scientific •4 x Nevro

Results: Figure 1: NRS - Pain Numerical Rating Scale for the 7 patients at follow up.

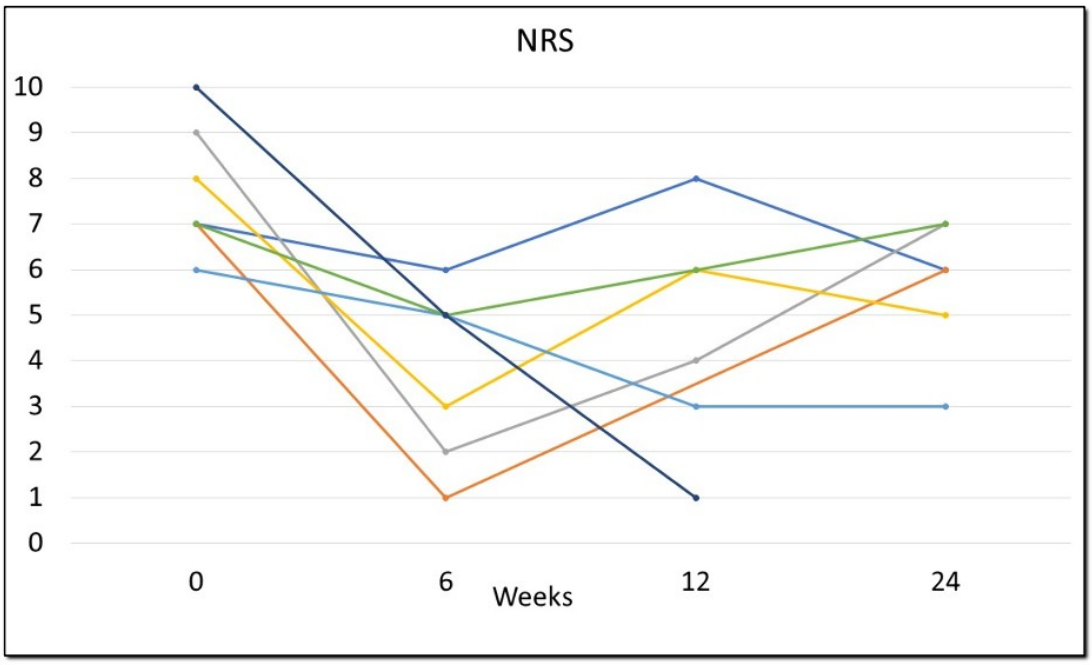
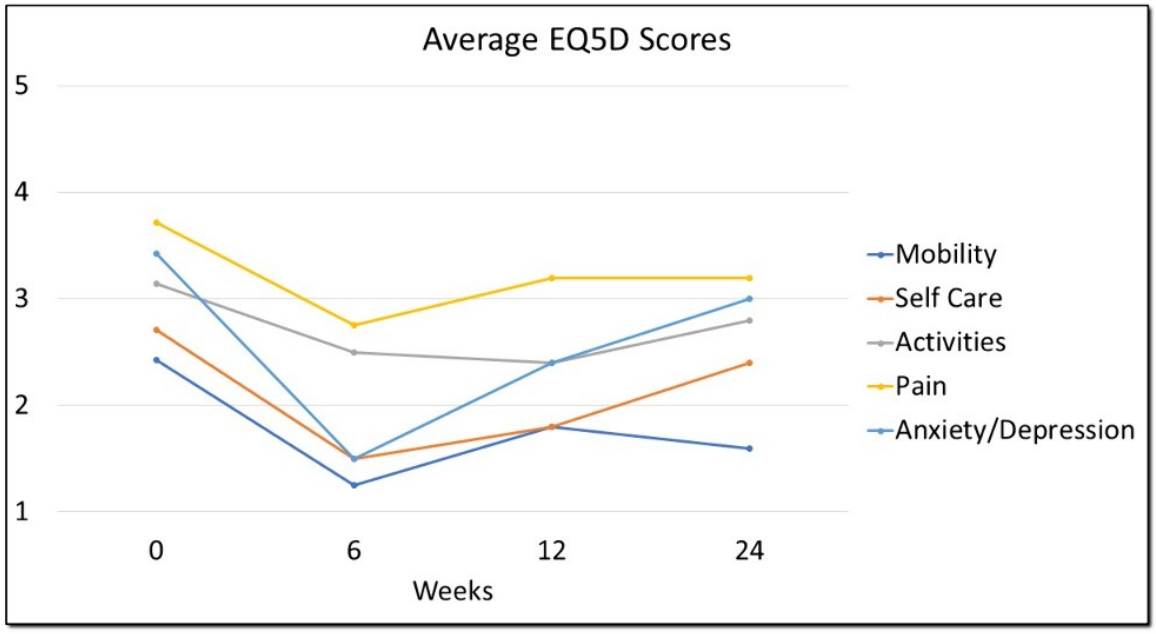


Figure 2: Average of EQ5D scores in each domain at follow

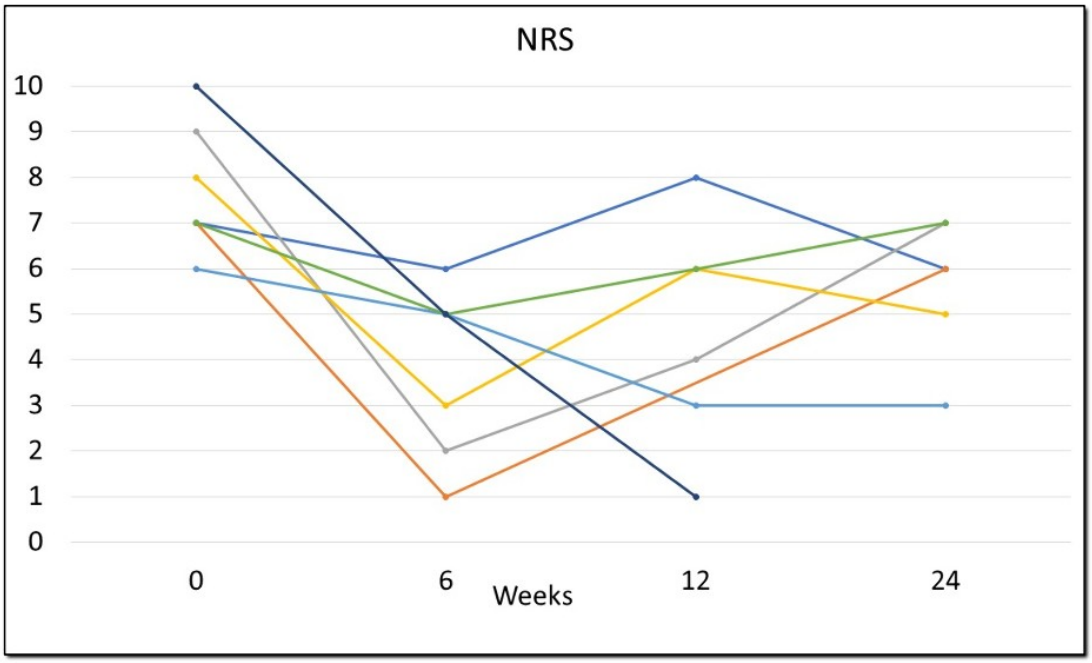
up.

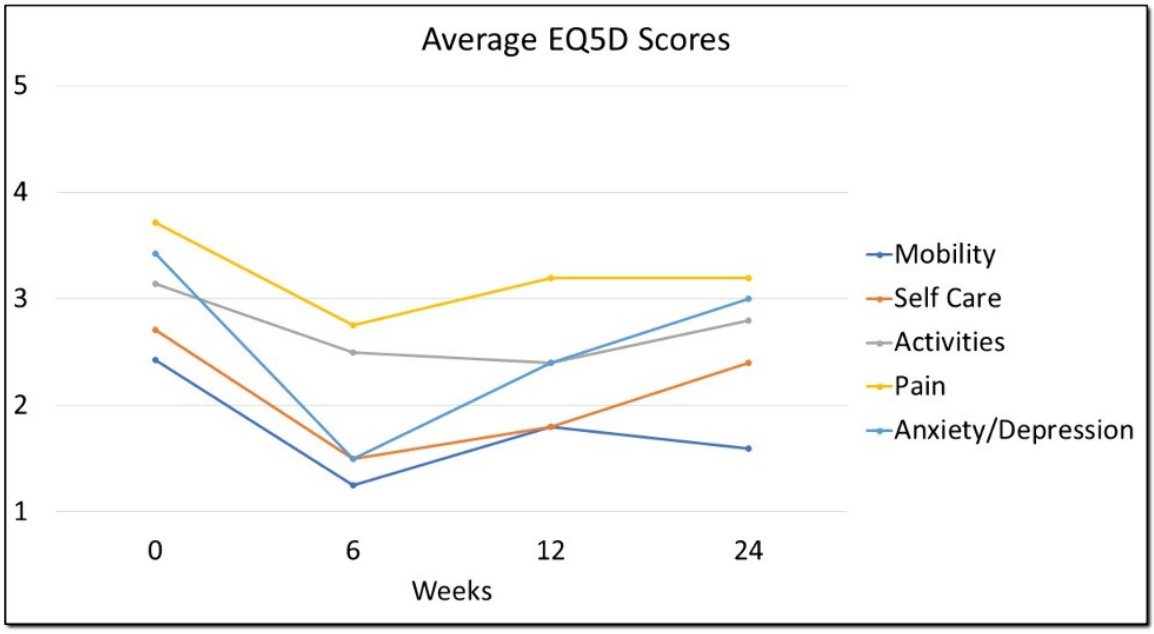


Discussion: 6 of the 7 patients saw an improvement in their NRS pain score at last follow up. The mean EQ5D scores fell in all domains across this patient group. We were not able to identify any potential factors for good responders based on either type of injury or type of stimulation used. BPA related neuropathic pain is a debilitating condition. Where pain is refractory to pharmacological agents, DREZ and DBS may be considered however, these are very invasive and risky procedures. SCS represents a reversible and lower risk alternative that has potential to bring relief to this patient group.

Conclusions: SCS is a viable treatment option for pain related to brachial plexus avulsion. Further research is required to better predict those who will benefit from SCS therapy and the optimal stimulation pattern.

Supplemental Data:





References: 1.Bertelli JA, Ghizoni MF. Use of clinical signs and computed tomography myelography findings in detecting and excluding nerve root avulsion in complete brachial plexus palsy. J Neurosurg 2006;105:835–42. 2.Teixeira MJ, da Paz MG da S, Bina MT, et al. Neuropathic pain after brachial plexus avulsion—Central and peripheral mechanisms. BMC Neurology. 2015;15:73.

Acknowledgements:

Learning Objectives: Describe the outcomes of patients with brachial plexus avulsion treated with SCS.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O125

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 04
15-05-2024 16:30 - 18:20

BIG ECAP DATA: A NOVEL "OBJECTIVE NEURAL PANEL" FOR SCS THERAPY OPTIMIZATION

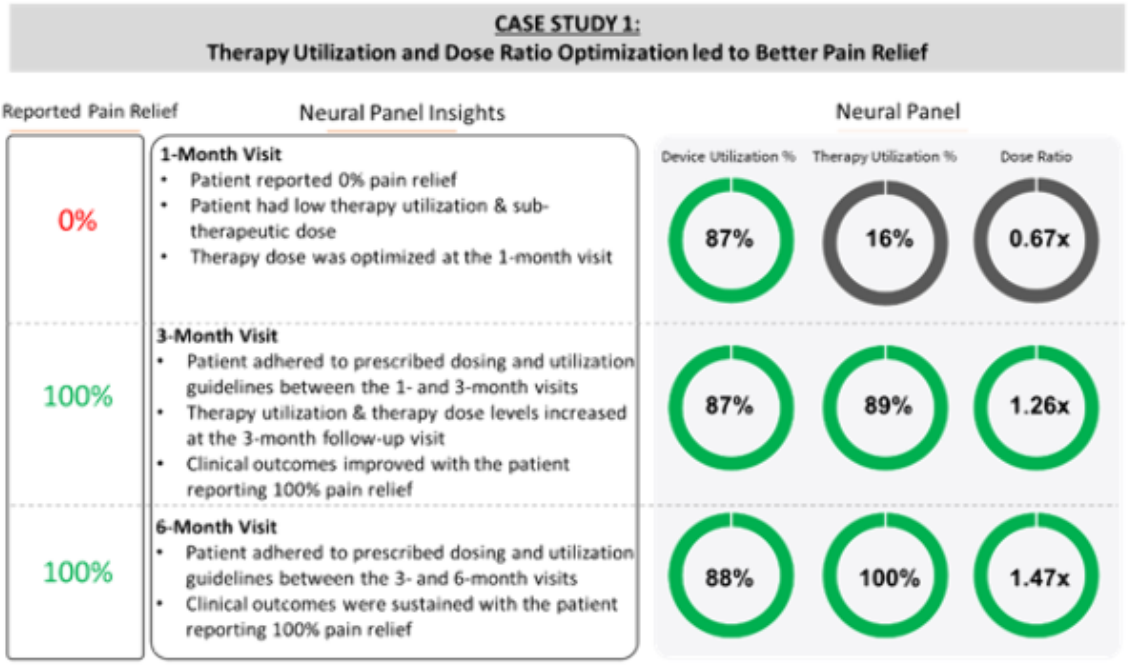
Erika Petersen, MD[1], Lawrence Poree, MD, PhD[2], Peter Staats, MD[3], Leonardo Kapural, MD[4], Ajay Antony, MD[5], Ian Gould, MSc, PhD[6], Dean Karantonis, MSBmE, MSBmE[6], Paul Verrills, MBBS[7], Jan Willem Kallewaard, MD[8,9], Leah Muller, PhD[6]
[1]University of Arkansas for Medical Sciences, Little Rock, United States of America, [2]Univeristy of California San Francisco, San Francisco, United States of America, [3]National Spine & Pain Centers, Shrewsbury, United States of America, [4]Carolinas Pain Institute and Wake Forest University School of Medicine, Winston-Salem, United States of America, [5]The Orthopaedic Institute, Gainesville, United States of America, [6]Saluda Medical, Macquarie Park, Australia, [7]Metro Pain Group, Melbourne, Australia, [8]Rijnstate Hospital, Arnhem, Netherlands, [9]Amsterdam Medical Centers, Amsterdam, Netherlands

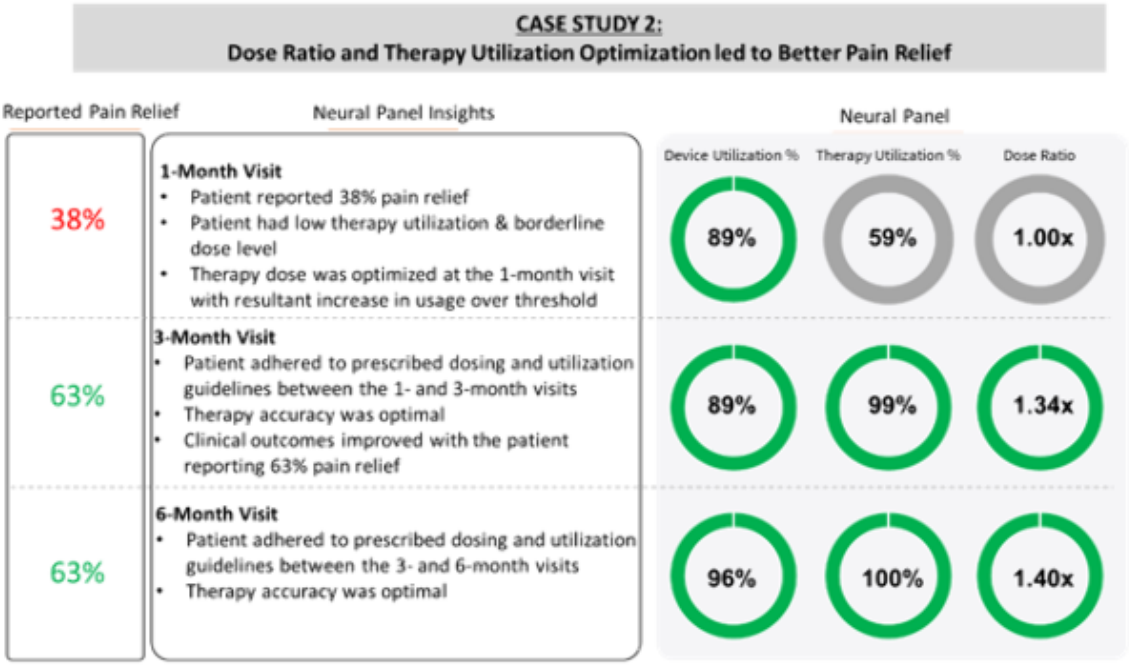
Introduction: In spinal cord stimulation (SCS) therapy, electricity is the medication delivered to the spinal cord for pain relief. In contrast to conventional medication where the dose is determined by therapeutic plasma concentration, the amount of electrical energy (charge) delivered in open-loop (OL) SCS has not been guided by objective measurement, despite the dynamic nature of the epidural space[1,2]. Physiologic evoked compound action potential (ECAP)-controlled closed-loop (CL) technology provides the ability to continuously measure neural activation and objectively inform SCS therapy optimization. Here we introduce a '*neural panel'* comprising three neurophysiologic indicator metrics relating to the therapy utilization, the therapy dose delivered, and the dose accuracy of SCS therapy. Relationships between these objective metrics and patient outcomes are reported, and its utility for guiding clinicians to optimize SCS therapy is explored.

Materials / Methods: Global study [EVOKE (NCT02924129), ECAP (NCT04319887), AVALON (ACTRN12615000713594), BRIGHTON (ACTRN12618001808235), DR (DR-UK: ISRCTN27710516;DR-NL: NL7889;DR-DE: NCT05272137), DURABILITY (NCT04627974), FRESHWATER (NCT04662905)] and real-world ECAP-controlled CL subjects (N>600; Evoke® SmartSCS™, Saluda Medical, USA) were included in this analysis. To identify relationships between *'neural panel'* indicator metrics and patient outcomes - neurophysiologic data (therapy utilization [percent usage over ECAP threshold], dose ratio [median stimulation level relative to ECAP threshold], and out-of-clinic dose accuracy [deviation from target therapy dose]) was analyzed for the week preceding the follow-up visit at which patients reported maximum percent pain relief from baseline. Each metric was grouped linearly in the anticipated range of values[3] and a Jonckheere-Terpstra test for trend performed. Case studies are presented.

Results: Therapy utilization, dose ratio, and dose accuracy show a statistically significant positive relationship with percent pain reduction ($p = 0.033$, 0.008, and $p<0.05$, respectively). Case studies (Figure 1) illustrate practical application of the neural panel to optimize therapy based on these objective

metrics.





Discussion: Physiologic ECAP-controlled closed-loop technology provides the ability to consistently measure neural activation and objectively inform SCS therapy optimization.

Conclusions: We demonstrate the utility of guiding therapy optimization using a novel ‘neural panel’ comprised of physiologic metrics including therapy utilization, dose, and dose accuracy. Pain relief improvement is associated with high device utilization over ECAP threshold, a dose ratio of 1.2-1.6, and a highly accurate optimized loop. Practical case studies illustrate that an objective neural panel with these physiologic metrics can provide therapy performance insights to maximize clinical benefit for SCS patients.

Supplemental Data:

References: 1. J. G. Pilitsis et al., “The Evoked Compound Action Potential as a Predictor for Perception in Chronic Pain Patients: Tools for Automatic Spinal Cord Stimulator Programming and Control,” *Front. Neurosci.*, p. 881, 2021. 2. J. L. Parker, D. M. Karantonis, P. S. Single, M. Obradovic, and M. J. Cousins, “Compound action potentials recorded in the human spinal cord during neurostimulation for pain relief,” *Pain*, vol. 153, no. 3, pp. 593–601, Mar. 2012, doi: 10.1016/j.pain.2011.11.023. 3. J. Holsheimer, “Which Neuronal Elements are Activated Directly by Spinal Cord Stimulation,” *Neuromodulation*, vol. 5, no. 1, pp. 25–31, Jan. 2002, doi: 10.1046/j.1525-1403.2002.

Acknowledgements:

Learning Objectives: 1. ECAP-controlled closed-loop SCS enables evaluation of spinal cord physiologic data and development of a potential neural panel to provide objective metrics to optimize SCS therapy 2. Pain relief improvement is associated with high device utilization over ECAP threshold, optimal dose ratio, and a highly accurate optimized loop 3. Objective neural panel data consisting of physiologic metrics has the potential to maximize clinical benefit for patients and better inform clinician and programmers with objective physiologic measurements

Financial Disclosures: Lawrence Poree, Saluda Medical, Consultant/Advisory Board Peter Staats, Saluda Medical, Consultant/Advisory Board, $5,001-$20,000 USD, Education/Research, $20,001-$100,000, Stock Options, $20,001-$100,000 Leonardo Kapural, Saluda Medical, Consultant/Advisory Board, $500-$5000 USD; Education/Research, $500-$5000 Ajay Antony, Saluda Medical, Consultant/Advisory Board, $20,001-$100,000 USD; Education/Research, $20,001-$100,000 USD Ian Gould, Saluda Medical, Employee, > $100,000 USD Dean Karantonis, Saluda Medical, Employee, > $100,000 USD Leah Muller, Saluda Medical, Employee, > $100,000 USD Paul Verrills, Saluda Medical, Speaker Program, $5,001-$20,000 USD, Consultant/Advisory Board, $5,001-$20,000 USD, Education/Research, $500-$5000 USD Jan-Willem Kallewaard, Saluda Medical, Consultant/Advisory Board, 6,000

Disclosure: Administrative support to authors funded by Saluda Medical.

O126

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 04
15-05-2024 16:30 - 18:20

NOVEL SENSING DEEP BRAIN STIMULATION IN NEUROPATHIC FACIAL PAIN: POTENTIAL PERIODIC AND APERIODIC BIOMARKERS OF SEVERE PAIN IN THE SENSORY THALAMUS

Christian Lopez Ramos, MD, Alex Rockhill, PhD, Maryam Shahin, MD, Hao Tan, BSc (Hons), Antonia Gragg, MSc, Erin Yamamoto, MD, Adeline Fecker, BSc (Hons), Mostafa Ismail, MD, Daniel Cleary, MD, Ahmed Raslan, MD
Oregon Health & Science University, Portland, United States of America

Introduction: Advancements in adaptive DBS devices offer a unique opportunity to record local field potentials (LFP) longitudinally and improve the efficacy of treatment. The longitudinal electrophysiological correlates of facial pain in the ventral posteromedial nucleus (VPM) thalamus and periaqueductal gray (PAG) have yet to be examined. Using a novel chronic sensing DBS pulse generator, we analyzed the periodic and aperiodic features of power spectra time-locked to ambulatory clinically relevant pain states to identify potential biomarkers of pain in the VPM and PAG.

Materials / Methods: We analyzed the power spectra of ambulatory pain-related events from one patient implanted with a chronic sensing generator (Medtronic Percept PC). Events represented different pain intensities (no pain, pain > 7, pain > 9) and pain qualities (burning, stabbing, and shocking pain). The power spectra were parametrized to separate oscillatory and aperiodic features and compared across the different pain states to explore for potential biomarkers of facial pain.[1] Analysis was restricted below 40 Hz. Data was analyzed offline in MNE-python using non-parametric tests.

Results: A total of 96 events were marked during a 16-month follow-up **(Figure 1)**. Parametrization of spectra revealed a total of 62 oscillatory peaks with the majority in the VPM (77.4%) **(Figure 2)**. The most prevalent peaks were in the beta (n=39) and theta (n=16) range. The pain-free condition did not demonstrate any oscillations in either the VPM or PAG. In contrast, beta peaks were observed in the VPM during all episodes (100%) associated with pain > 9, 56% of episodes with pain > 7, and 50% of burning pain events (center frequencies (CF): 28.4 Hz, 17.8 Hz, 20.7 Hz, respectively; p <0.001). Episodes of pain >9 demonstrated the highest relative beta band power in the VPM and lowest aperiodic exponents (denoting the slope of the power spectra) in both the VPM and PAG. (**Figure 3)**. A greater proportion of theta oscillations were observed in the PAG, generally during pain >7 (CF: 5.60 Hz). No prominent oscillations were observed during shocking or stabbing pain.

Figure 1. Parametrized Power Spectrum in VPM During Pain >9

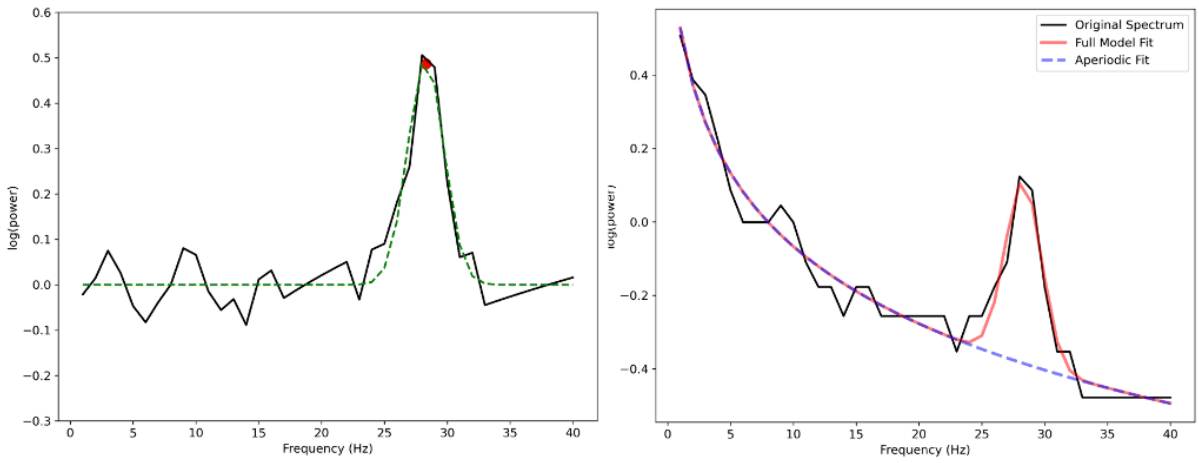


Figure 2. Oscillatory Peaks in the VPM Thalamus (left) and PAG (right)

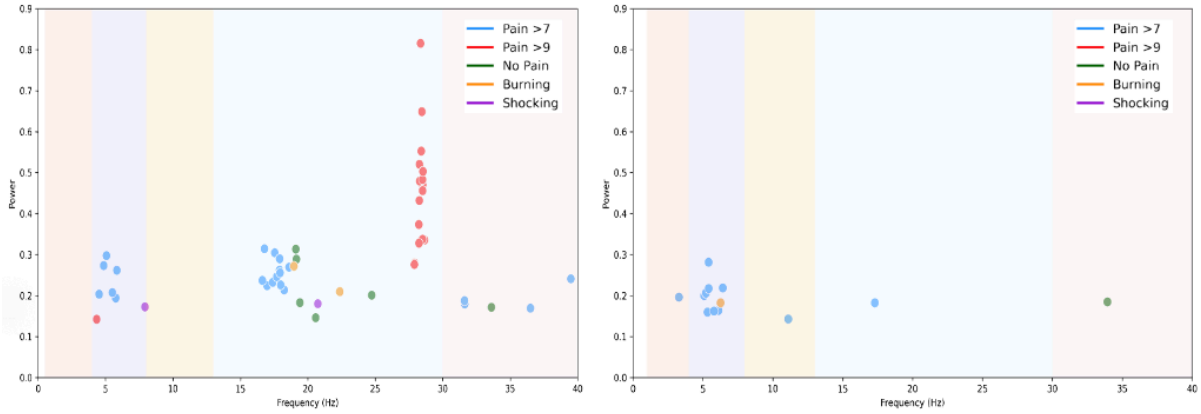
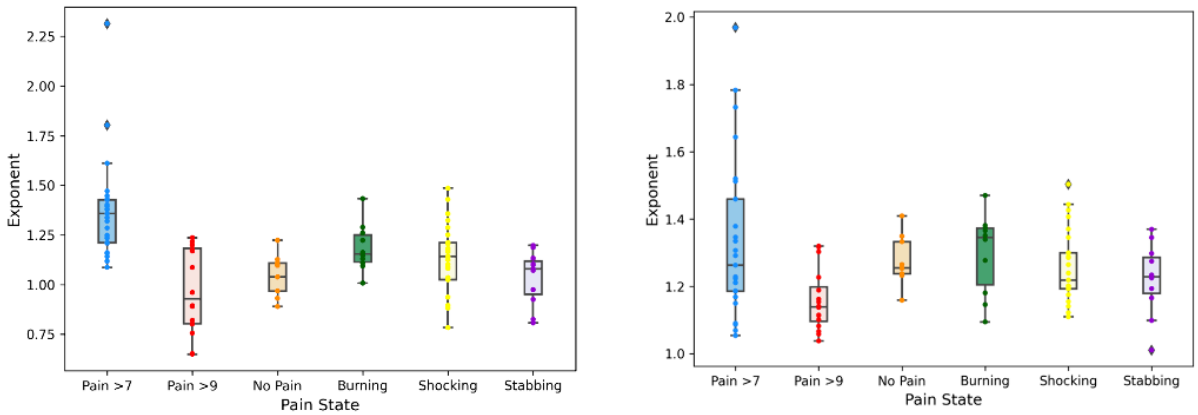


Figure 3. Aperiodic Exponents in VPM Thalamus (left) and PAG (right) by Pain State



Discussion: In our patient, we identified beta band peaks in the VPM thalamus during episodes of severe pain and facial pain characterized by burning sensations. Specifically, a robust increase in beta band power occurred in all episodes associated with severe pain above 9.

Conclusions: We demonstrate the feasibility of using chronic sensing DBS to identify potential biomarkers of clinically relevant pain states for the treatment of neuropathic facial pain.

Supplemental Data:

References: 1. Donoghue, T., Haller, M., Peterson, E.J. *et al.* Parameterizing neural power spectra into periodic and aperiodic components. *Nat Neurosci* **23**, 1655–1665 (2020)

Acknowledgements:

Learning Objectives: 1. To demonstrate features of chronic sensing devices for the exploration of electrophysiological biomarkers in neuropathic facial pain. 2. To identify potential periodic and aperiodic components as potential biomarkers of neuropathic facial pain. 3. To understand the parametrization of power spectra using a quantitative algorithm

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O127

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 05
15-05-2024 16:30 - 18:20

LONG-TERM SAFETY OF ULTRA LOW FREQUENCY WAVEFORM SHOWN IN LARGE ANIMALS

Nishant Verma, PhD[1], Makaela Rietman, BSc (Hons)[2], Daniel Merrill, PhD[3], Andrew Sullivan, MD[2], James Harris, PhD[2]
[1]Presidio Medical, Science & Technology, South San Francisco, United States of America, [2]Presidio Medical, South San Francisco, United States of America, [3]Dan Merrill Consulting, Salt Lake City, United States of America

Introduction: The mechanisms of how action potentials are initiated with short pulses and inhibited with longer pulses was established by the pioneering work of Hodgkin and Huxley[1]. Although the nervous system functions via an exquisite balance of inhibitory and excitatory drives, technologies to directly inhibit activity of the nervous system have not been well developed to-date. Previous technologies have been unable to deliver long pulses or static fields due to tissue damage concerns including necrosis and demyelination.

Materials / Methods: These previous constraints are alleviated by the Ultra Low Frequency (ULF^{TM}) therapy to safely inhibit neural tissue. The ULF (Presidio Medical, South San Francisco, California, USA) waveform is a proprietary, biphasic waveform (alternating positive and negative polarity). We implanted multi-contact electrodes into an ovine model, for up to 180 days, to evaluate the long-term safety of ULF therapy. Leads were implanted in the epidural space, resting in the lumbar/thoracic range of spinal segments. The ULF waveform was applied chronically, and at the end of the therapy period, spinal cord and epidural tissues were harvested and histologically assessed by a pathologist blinded to treatment versus sham.

Results: Tissue adjacent to electrodes that delivered the long pulse width waveform was compared to tissue adjacent to inactive electrodes. The analysis revealed neither group showed significant findings of necrosis, neovascularization, fibrosis, gliosis, demyelination, or neuronal loss. The novel waveform avoids impact to neural tissue, despite its long pulse width and high charge, while emulating the inhibitory effects of the static currents employed by Hodgkin and Huxley.

Discussion: In several large animal trials, we investigated the safety of a novel long pulse width neuromodulation system designed to safely attenuate activity in neural tissue. In the novel therapy, the period of each cycle is multiple seconds long to inhibit neural activity. This is in contrast to traditional neurostimulators that use sub-millisecond pulses. The novel waveform system leverages decades of electrochemistry practice and principles to avoid damage to the tissue while providing a novel mechanism to inhibit neural activity.

Conclusions: This work has shown that long-term application of the novel long pulse width waveform is well-tolerated in the sheep model, displaying no detectable signs of neurological impact over many months. Overall, the long pulse width therapy offers a notable and alternative method to treat diseases of the nervous system by inhibiting activity, enabling a new class of neuromodulation therapies.

Supplemental Data:

References: [1] The Nobel Prize in Physiology or Medicine 1963. NobelPrize.org. Nobel Prize Outreach AB 2022. Sun. 2 Jan 2022

Acknowledgements: Presidio Medical sponsored this project that was executed by an accredited CRO.

Learning Objectives: 1 – Educate audience regarding electrochemistry principles of neuromodulation 2 – Provide basic scientific principles regarding safety of ULF therapy 3 – Describe the sheep model for safety and pathology results of ULF therapy

Financial Disclosures: Nishant Verma - Role: Company Employee Makaela Rietman - Role: Company Employee Daniel Merrill – Role: Consultant Andrew Sullivan - Role: Company Employee James P. Harris - Role: Company Employee

Disclosure: No significant relationships.

O128

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 05
15-05-2024 16:30 - 18:20

REMOTE DEVICE MANAGEMENT FOR PROACTIVE AND RAPID OPTIMIZATION OF SPINAL CORD STIMULATION: 12-MONTH RESULTS FROM A PROSPECTIVE MULTICENTER STUDY

Marc Russo, MBBS[1], James Yu, MD[2], Kasra Amirdelfan, MD[3], Leonardo Kapural, MD[4], Paul Verrills, MBBS[5]
[1]Hunter Pain Specialists, Broadmeadow, Australia, [2]Sydney Spine and Pain, Hurstville, Australia, [3]Boomerang Healthcare, Pain Management, Walnut Creek, United States of America, [4]Carolinas Pain Institute, Winston-Salem, United States of America, [5]Monash House Private Hospital, Metro Pain Group, Clayton, Australia

Introduction: A recently published expert recommendation article highlighted that remote management of spinal cord stimulation (SCS) may benefit patients with chronic pain.[1] Specifically, remote management may allow prompt issue resolution and improve clinical outcomes, although more evidence is needed. BENEFIT-03 (NCT04683718) is an ongoing, long-term study of an SCS system with proactive care made available by automatic daily transmission of objective device monitoring data and remote programming. Here, we report analysis of the impact of proactive care on time to intervention to optimize SCS in BENEFIT-03.

Materials / Methods: BENEFIT-03 is a prospective, single-arm, multicenter study ongoing in Australia with Human Research Ethics Committee approval in consenting participants with chronic low back and/or leg pain. Post-implant follow-up consists of in-office visits (3, 6, 12, and 24 months) and remote visits that may be initiated by participants, investigators, proactive triggers (based on automatic daily device monitoring), or patient-reported outcomes. Primary endpoints are responder rate (at least 50% overall pain relief, VAS) and freedom from device-related complications at 6 months. Additional outcomes include system usage, proactive care triggers, time to interventions, and questionnaires.

Results: As of this March 2024 interim analysis, 34 participants were trialed, 31 were implanted, and 25 had completed the 12-month follow-up. Out of 209 remote device management sessions conducted, 1 session transmitted new SCS programs during the trial period, 40 transmitted new programs post-implant, and 168 allowed for real-time monitoring. Remote device management sessions were utilized more frequently in early intervals post implant versus later stages. For daily device monitoring, data transmission rate was 94.75% overall. Proactive care triggers from automated monitoring occurred for 100% of implanted patients, with the most common triggers related to low device usage, charging compliance, and therapeutic window. Following a trigger, mean response time—including review, action, and confirmation the SCS issue was addressed—was 2.96 days. All participants agreed/strongly agreed they felt reassured with routine checks and 100% agreed/strongly agreed remote device management was convenient.

Discussion: Proactive care triggers detected potential device-related issues for 100% of participants, which enabled prompt review and intervention by the care team that was convenient for patients.

Conclusions: Automatic daily remote device monitoring and remote programming capabilities allowed for proactive identification of potential SCS device-related issues to optimize participant's SCS therapy.

Supplemental Data: None

References: 1. Staats P, Deer TR, Hunter C, et al. Remote Management of Spinal Cord Stimulation Devices for Chronic Pain: Expert Recommendations on Best Practices for Proper Utilization and Future Considerations. *Neuromodulation*. 2023;26(7):1295-1308.

Acknowledgements: BIOTRONIK sponsors the study and funded writing/editorial support.

Learning Objectives: 1. To discuss the potential benefits of remote device management and proactive identification of potential SCS device-related issues 2. To distinguish various remote SCS management capabilities, such as remote monitoring and automatic daily transmission of objective device monitoring data 3. To describe participant questionnaire data from BENEFIT-03, which included almost all participants reporting their experience with proactive care and remote device management was reassuring and convenient

Financial Disclosures: Marc Russo: SPR Therapeutics, historical stockholder <1%; Saluda Medical, stock options <0.5%; and Presidio Medical, stock options <0.5%. **James Yu:** Abbott, consultant; Nevro, consultant, research; Medtronic, consultant, research; Boston Scientific, consultant, research; Saluda, research; Biotronik, research; and Nalu, research. **Kasra Amirdelfan:** Medtronic, consultant; Boston Scientific, consultant; Nevro, consultant; Biotronik, consultant; and Nalu, consultant, stock options. **Leonardo Kapural:** Nevro, consultant, research; Abbott, consultant; Medtronic, consultant, research; Nalu, consultant; Saluda, consultant, research; Biotronik, consultant, research; Gimer Medical, research; Neuros, research; and SPR Therapeutics, research. **Paul Verrills:** Presidio, consultant, research, $500 – $5,000; Biotronik, consultant, research, $1 - $500; Saluda, consultant, $5,000 - $20,000; and Nalu, consultant, $1 – $500.

Disclosure: Jacob Hicks is an employee at Biotronik INC.

O129

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 05
15-05-2024 16:30 - 18:20

SINGLE SITE LONG TERM OUTCOMES USING MULTI-WAVEFORM SPINAL CORD STIMULATION FOR CHRONIC NEUROPATHIC PAIN

Sarah Love Jones, MBBS BSc FRCA FFPMRCA EDPM, Adam Williams, MD, Janet Clark, BSc (Hons), Gaurav Chhabra, MBBS, Nicola Wade, BSc (Hons)
Southmead Hospital, Pain Clinic, Gloucester House, Bristol, United Kingdom

Introduction: Long term outcomes in Spinal Cord Stimulation (SCS) are vital to demonstrate the sustained effectiveness of stimulation devices for the treatment of chronic neuropathic pain. In this poster, retrospective real world outcome data over five plus years is presented from a single site using a multi-waveform device capable of both paraesthesia-based and paraesthesia-free therapy.

Materials / Methods: Data from patients implanted with a multi-waveform SCS device was collected by the site clinical team. From January 2023 all patients were contacted for an up-to-date percentage pain reduction. Patients were also asked to report which waveforms they were using. Patients who were achieving sub-optimal pain relief at time of contact were invited to an optimisation clinic as per standard of care. After optimisation, patients were re-contacted for percentage pain reduction and waveform use. Patients were considered responders to SCS therapy if achieving a ≥50% pain reduction.

Results: At last follow-up, 86% of patients were responding to SCS therapy and the average pain reduction was 71%. Of patients who were responding to SCS therapy, 82% reported ≥70% pain relief at last follow up, and half were reporting ≥80% pain relief. The majority of patients chose to use more than one waveform as opposed to a single waveform alone. Furthermore, the majority of patient preferred to use both paraesthesia-based and paraesthesia- free options.

Discussion: The outcomes form this cohort demonstrate that patients are still achieving significant long term pain relief up to five plus years post implantation. In line with other research, the data presented also demonstrates that when given the option patients prefer to use multiple waveforms consisting of both paraesthesia-based and paraesthesia-free therapy (1)(2).

Conclusions: Patients in this cohort using multi-waveform SCS for chronic pain have sustained long-term outcomes while utilising both paraesthesia-based and paraesthesia-free waveforms.

Supplemental Data:

References: *Berg AP, Mekel-Bobrov N, Goldberg E, Huynh D, Jain R. Utilization of multiple spinal cord stimulation (SCS) waveforms in chronic pain patients. Expert Rev Med Devices. 2017 Aug;14(8):663-668. Wallace MS, North JM, Phillips GM, Calodney AK, Scowcroft JA, Popat-Lewis BU, Lee JM, Washabaugh EP 3rd, Paez J, Bolash RB, Noles J, Atallah J, Shah B, Ahadian FM, Trainor DM, Chen L, Jain R. COMBO RCT: Combining Mechanisms for Better Outcomes. NANS. 2022*

Acknowledgements:

Learning Objectives: 1. multi wave form spinal cord stimulation gives patients further choice of therapy. 2. Long term efficacy of SCS for neuropathic pain

Financial Disclosures: Dr Love-Jones has received travel and honoraria for Medical advisory board to Boston Scientific, Medtronic, Saluda Medical, Pfizer and research funding from Boston Scientific, Saluda Medical, Nalu Medical, Mainstay Medical, Abbot. Mr Williams has received travel and

honoraria for Medical advisory board to Boston Scientific, Medtronic, Saluda Medical, and research funding from Boston Scientific, Saluda Medical, Mainstay Medical, Abbot.

Disclosure: I have received research funding and medical advisory board honorarium form Boston Scientific, the SCS devices used in this study

O130

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 05
15-05-2024 16:30 - 18:20

MULTI-DIMENSIONAL IMPROVEMENTS WITH CLOSED-LOOP SCS THERAPY AT 6-MONTHS WITH PERSONALIZED WAVEFORMS

Vahid Mohabbati, MD[1], Richard Sullivan, MB ChB[2], James Yu, MD[3], Peter Georgius, MBBS[4], Charles Brooker, MB ChB[5], Malgorzata Straka, PhD[6], Andrew Cleland, MD[6], Glenn Butler, BS[6], Michelle Knight, BSc[6], Zachary Kyle-Little, BSc[6], Justin Morey, BS[6], Nancy McClelland, BSN[6], Charles Cain, PhD[6], Abi Franke, PhD[6], Marc Russo, MBBS[7]
[1]Sydney Pain Management Centre, Sydney, Australia, [2]Precision Brain Spine and Pain Center, Kew Vic, Australia, [3]Australian Medical Research, Hurstville, Australia, [4]Sunshine Coast Clinical Research, Noosa Heads, Australia, [5]Royal North Shore Hospital, St Leonards, Australia, [6]Medtronic, Minneapolis, United States of America, [7]Hunter Pain Specialists, Hunter Pain Specialists, Broadmeadow, Australia

Introduction: Closed loop (CL) spinal cord stimulation (SCS) systems adjust stimulation output based on sensed positional or physiologic signals with the goal of minimizing therapy dosage fluctuations and preventing overstimulation. Evoked compound action potentials (ECAPs) are a measure of the depolarization of nerve axons elicited by an SCS pulse. In this study, ECAPs were used to modulate stimulation intensity, and provide continuous, closed-loop stimulation on a pulse-by-pulse basis.[1] Here we present therapy outcomes using various CL-SCS waveforms in individuals with chronic low back and/or leg pain.

Materials / Methods: The primary objective of the Closed Loop SCS study is to demonstrate reduction in overstimulation with the CL feature versus open loop SCS at 1-month; the in-clinic testing for the primary endpoint has a randomized, crossover, single blind design. Secondary objective is to characterize the proportion of subjects with ≥50% reduction in overall, back and/or leg pain visual analogue score (VAS) at 3 months; follow-up for the pain outcomes has a single-arm design with devices programmed with waveforms tailored to individual needs, with the CL feature added to ensure consistent dosing. Study is being conducted at 7 sites in Australia (NCT05177354).

Results: Ninety subjects with back/leg pain have been enrolled, 71 trialed and 57 have been implanted with the study device; 92% of those trialed had ≥50% reduction in pain and were eligible for study device implant. At enrollment, mean age of subjects was 58.6 (SD: 13.5) years, 46.4% were female and 50% were on opioids; overall back/leg pain VAS was 79.2 (SD: 11.1) mm and 86% of subjects were severely disabled or worse per ODI. The study successfully met its primary endpoint with 89% of subjects reporting reduction in overstimulation with the CL feature enabled, significantly more than a null hypothesis of 50% ($p < 0.001$; binomial exact test). Follow ups are ongoing and patient reported outcomes at 6 months including proportion with ≥50% reduction in pain, and clinically meaningful improvements in physical function and health related quality of life will be presented at the congress.

Discussion: Offering a preferred and more consistent therapy experience to patients may lead to increased therapy utilization, reliable long-term therapy outcomes, and thereby reduce explants for lack of efficacy.

Conclusions: will be added once 6-month data are available.

Supplemental Data:

References: 1. Vallejo et al. Journal of Pain Research, 2021; vol.14, 3909 – 3918.

Acknowledgements:

Learning Objectives: 1. Understand the benefits of closed loop, polymodal SCS for those with chronic pain with prior history of surgery. 2. Understanding the instances of under- or overstimuation with open-loop SCS. 3. Understanding how patient preference for closed-loop SCS may contribute to better compliance and thereby lead to sustained benefits in the long term.

Financial Disclosures: This study was sponsored by Medtronic Plc.

Disclosure: Employed by Medtronic.

O131

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 05
15-05-2024 16:30 - 18:20

ECAPS FROM A MULTICOLUMN DIRECTIONAL PERCUTANEOUSLY IMPLANTED LEAD IN A LARGE ANIMAL MODEL

Steven Falowski, MD[1], Maria Celeste Cantone, MSc[2], Omar Caspani, MSc[2], Matteo Saini, MSc[2], Federica Montrone, MSc[2], Mahima Sharma, PhD[3], Mohamad Fallahrad, PhD candidate[4], Vividha Bhaskar, BSc (Hons)[4], Thomas Bianchi, MSc[2], Sandro Ferrari, PhD[2], Valentina Ferpozzi, PhD[2], Marom Bikson, Dr.[4]
[1]Center for Interventional Pain and Spine, Lancaster, United States of America, [2]WISE Srl, Cologno Monzese, Italy, [3]Buck Institute for Research on Aging, Novato, United States of America, [4]City College of New York, Neural Engineering Group, New York, United States of America

Introduction: The advent of closed-loop Spinal Cord Stimulation (SCS) systems requires the use of electrodes with increased sensing capabilities, coupled with high stimulation efficiency to ensure focal stimulation and consistent feedback. In response to this need, a multicolumn directional percutaneously implanted lead was conceived. It provides an array of electrodes distributed across two columns, situated on two wings extending from the cable; these wings are designed to rest against the *dura* when in place. During insertion, the wings are coiled into a cylindrical shape within a delivery sheath so that the lead can be inserted through a percutaneous procedure and navigated to the target. To illustrate the advantages offered by the multicolumn directional lead, we present the findings of an *in-vivo* neurophysiological study conducted on a large animal model. This study is aimed at demonstrating the stimulating and sensing capabilities of the multicolumn directional lead to assess its potential in connection to closed-loop systems. We tested the hypothesis that the directional stimulation enables a reduction in the current required for eliciting Evoked Compound Action Potentials (ECAPs) when compared to a cylindrical lead with equivalent electrode length and inter-electrode spacing.

Materials / Methods: In a sheep model, two multicolumn directional (manufactured by WISE) and two cylindrical leads were implanted in epidural space between L1 and L3. Stimulation and recording electrodes for both lead types were positioned at the same anatomical midline. In case of the multicolumn directional lead, additional recording electrodes were placed on a dorsal column. The aim was to consistently elicit ECAPs and compare the stimulation intensities required to achieve this with both lead types.

Results: ECAPs were recorded by both leads. The stimulus intensity necessary to elicit ECAPs from the same anatomical position was 0.7 mA for the multicolumn directional lead and 1 mA for the cylindrical lead.

Discussion: The multicolumn directional lead's capacity to deliver directional stimulation was demonstrated. The ECAPs recorded with the multicolumn directional lead suggest its suitability for its use in closed-loop systems. Notably, a lead configuration comprising a total of eight electrodes (four in each column) turned to be sufficient to record ECAPs. By allowing a reduced stimulation intensity required to elicit ECAPs compared to a traditional cylindrical lead, the multicolumn directional percutaneously implanted lead potentially translates into a more efficient SCS therapy, without adding any burden on the insertion procedure.

Conclusions: The study's results underscore the multicolumn directional lead's potential to enhance the precision and efficiency of SCS treatments.

Supplemental Data:

References:

Acknowledgements: This work was funded by: European Commission – European Innovation Council and SMEs Executive Agency. PercPad - GA No. 959546. MiMit - Agreements for Innovation. SCS Expert - B29J23000210005

Learning Objectives: 1- Two multicolumn directional leads seem to be sufficient to record ECAPs. 2- A multicolumn directional lead can be used in closed-loop systems. 3- A multicolumn directional lead may transmit a more efficient and sustainable SCS therapy.

Financial Disclosures: S. Falowski is consultant for WISE, Abbott, Medtronic, Saluda Medical, Vertos, COrnerLoc, Mainstay; equity for BackStop Neural, SurgenTec, SynerFuse, Aurora Spine, Thermaquil, SPR Therapeutics, Saluda Medical, CornerLoc, PainTeq, SpineThera. M. C. Cantone, O. Caspani, M. Saini, F. Montrone, S. Ferrari and V. Ferpozzi are employees of WISE. WISE is the manufacturer of the new multicolumn directional lead. M. Sharma, M. FallahRad, and V. Bhaskar are consultants for WISE. M. Bikson is consultant for WISE and Boston Scientific.

Disclosure: I am an employee of WISE S.r.l.

O132

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 05
15-05-2024 16:30 - 18:20

DIFFERENTIAL TARGET MULTIPLEXED SPINAL CORD STIMULATION FOR INDICATED CHRONIC BACK PAIN PATIENTS INELIGIBLE FOR SPINE SURGERY: US RCT OUTCOMES

Thomas White, MD[1], Rafael Justiz, MD[2], Wilson Almonte, MD[3], Velimir Micovic, MD[4], Binit Shah, MD[5], Eric Anderson, MD[6], Leonardo Kapural, MD[7], Harold Cordner, MD[8], Amr El-Naggar, MD[9], Michael Fishman, MD[10], Yashar Eshraghi, MD[11], Philip Kim, MD[10], Al Abd-Elsayed, MD[12], Krishnan Chakravarthy, MD, PhD[13], Yoann Millet, MD[1], Mahendra Sanapati, MD[14], Nathan Harrison, MD[11], Brandon Goff, DO[15], Mayank Gupta, MD[16], Prabhdeep Grewal, MD[15], Indy Wilkinson, MD[17], Richard Bundschu, MD[18], Andrew Will, MD[19], Pankaj Satija, MD[20], Sean Li, MD[21], Scott Dulebohn, MD[17], John Broadnax, MD[6], Gennady Gekht, MD[22], Kenneth Wu, MD[1], Steven Falowski, MD[10], Wesley Park, MPH[23], David Cedeño, PhD[23], Ricardo Vallejo, MD, PhD[23]
[1]Procura Pain and Spine, The Woodlands, United States of America, [2]Oklahoma Pain Physicians, Oklahoma City, United States of America, [3]Victoria Pain and Rehabilitation, Victoria, United States of America, [4]Pain Management Consultants, Fort Myers, United States of America, [5]Carolinas Pain Center, Pain Management, Huntersville, United States of America, [6]Advance Pain Institute of Texas, Lewisville, United States of America, [7]Carolina's Pain Institute and Center for Clinical Research, Winston-Salem, United States of America, [8]Florida Pain Management Associates, Sebastian, United States of America, [9]DREZ One, Somerset, United States of America, [10]Center for Interventional Pain and Spine, Lancaster, United States of America, [11]Ochsner Medical Center, New Orleans, United States of America, [12]University of Wisconsin, Madison, United States of America, [13]Coastal Research Institute, Department Of Anesthesiology And Pain Medicine., San Diego, United States of America, [14]Global Scientific Innovations, Evansville, United States of America, [15]Burkhart Research Institute for Orthopaedics, San Antonio, United States of America, [16]Neuroscience Research Center, Overland Park, United States of America, [17]Pain Medicine Associates Surgery Center, Johnson City, United States of America, [18]Coastal Orthopedics, Pain Management, Bradenton, United States of America, [19]Twin Cities Pain Clinic, Edina, United States of America, [20]Pain & Headache Centers of Texas, Houston, United States of America, [21]National Spine and Pain Centers, Shrewsbury, United States of America, [22]Coastal Orthopedics and Pain Management, Bradenton, United States of America, [23]SGX Medical LLC, Bloomington, United States of America

Introduction: There are few treatment options for Persistent Spinal Pain Syndrome Type 1 (PSPS-T1) patients with refractory low back pain (LBP) who are ineligible for surgical interventions. A randomized controlled trial (RCT)[1] showed long-term superior efficacy of Differential Target Multiplexed SCS (DTM SCS) to conventional SCS (Conv-SCS) for LBP in Failed Back Syndrome (Persistent Spinal Pain Syndrome Type 2, PSPS-T2) subjects. A European RCT studying the effect of DTM SCS vs conventional medical management in the treatment of this population reported primary endpoint results consistent with published outcomes for PSPS-T2[2] with DTM SCS. The current RCT evaluated the efficacy of DTM SCS versus Conv-SCS in PSPS-T1 patients with chronic LBP, ineligible for spine surgery, with degenerative disc disease, herniated disc, or radiculopathy.

Materials / Methods: This is a post-market, multicenter RCT study comparing DTM™ SCS to Conv-SCS in PSPS-T1 patients ineligible for spine surgery. Table 1 shows key eligibility criteria. Subjects underwent temporary SCS trial with their assigned treatment, followed by permanent implantation in those reporting ≥40% pain relief. Primary endpoint was percentage of LBP responders (≥50% relief) at 3-month in subjects who completed the trial. Patients were followed up to 12 months. Secondary endpoints included LBP and leg pain, responder rates, disability, quality of life, and patient satisfaction and global impression of change. An optional two-way crossover was available on the 6-month visit.

Results: 105 randomized subjects at 20 US sites completed the trial phase. LBP responder rates with DTM SCS were superior to Conv-SCS at study timepoints (Figure 1A). Similarly, mean LBP reduction from baseline with DTM SCS was superior to Conv-SCS at study timepoints (Figure 1B). DTM SCS resulted in significantly greater leg pain responder rate, reduction of leg pain, functional disability (ODI), quality of life (EQ-5D-5L index), satisfaction, and patient global impression of change. About

47% of subjects treated with Conv-SCS opted to crossover to DTM SCS, with 91% of them being LBP responders by study end. No patient crossed over from DTM SCS to Conv-SCS.

Discussion: This RCT demonstrated the superior efficacy of DTM SCS relative to Conv-SCS for treating chronic LBP in non-surgical PSPS-T1 patients. Clinical improvements provided by DTM SCS were sustained over the study period and provided significant benefits in the management of PSPS-T1 patients who are ineligible for spine surgery.

Conclusions: DTM SCS is efficacious for treatment of LBP and leg pain in PSPS-T1 patients not eligible for spine surgery.

Supplemental Data:

TABLE 1. Key eligibility criteria.

Inclusion	Exclusion
Adult subjects	Previous lumbar spine surgery
Non-eligible for spine surgery	Contraindications for SCS
≥ 5 cm LBP VAS with or without leg pain	Mechanical spine instability.
SCS candidate per approved labeling*	
Under a stable pain medication regime.	

*Indications included degenerative disc disease or herniated discs refractory to conservative and surgical interventions or patients with radicular pain syndrome.

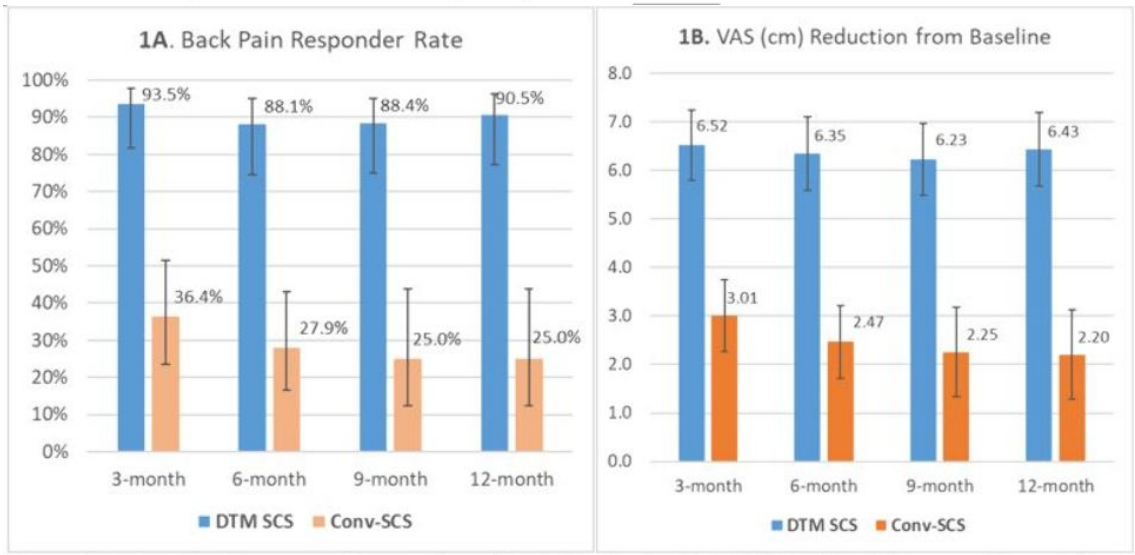


Figure 1. A. Back pain responder rate in subjects treated with DTM SCS (N=51) versus Conventional SCS, Conv-SCS (N=54) **B.** Mean back pain VAS reduction from baseline in subjects treated with DTM SCS (N=51) versus Conventional SCS, Conv-SCS (N=54). Results for implanted subjects who completed the trial phase using imputation (repeated measures) for missing data. Error bars are 95%CI. Crossover data was censored in these analyses. DTM SCS was superior to Conv-SCS at all time points ($P < 0.0001$).

References: 1. Fishman M, Cordner H, Justiz R, Provenzano D, Merrell C, Shah B, et al. Twelve-Month results from multicenter, open-label, randomized controlled clinical trial comparing differential target multiplexed spinal cord stimulation and traditional spinal cord stimulation in subjects with chronic intractable back pain and leg pain. Pain Pract. 2021 Nov;21(8):912-923. 2. Kallewaard JM, Billet B, Van Paesschen R, Smet I, Mendiola A., Peña I, et al. European randomized controlled trial to study the effects of differential target multiplexed SCS in treating intractable chronic back pain without previous lumbar spine surgery. INS 15th World Congress. 21-26 May 2022. Barcelona, Spain.

Acknowledgements: This study has been sponsored by SGX NOVA (acquired by Medtronic).

Learning Objectives: 1. Understand the benefits of SCS in patients with chronic low back pain, ineligible for spine surgery, with degenerative disc disease, herniated disc, or radiculopathy. 2. Evaluate level-1 evidence provided by a study with a randomized controlled trial design. 3. Interpret 12-month results from a randomized controlled trial evaluating SCS for chronic low back and leg pain in candidates with degenerative disc disease, herniated disc, or radiculopathy who are not candidates for spine surgery.

Financial Disclosures: David L. Cedeno, PhD. SGX Medical, Consultant, >$100,000 Ricardo Vallejo MD, PhD, SGX Medical, Consultant, >$100,000 Ricardo Vallejo, MD, PhD, Medtronic Inc, Consultant/Advisory Board, >$100,000

Disclosure: I am an employee of Medtronic.

O133

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 05
15-05-2024 16:30 - 18:20

DIFFERENTIAL TARGET MULTIPLEXED SCS FOR INTRACTABLE UPPER LIMB AND NECK PAIN: RESULTS FROM A 12-MONTH PROSPECTIVE STUDY

Thomas White, MD[1], Rafael Justiz, MD[2], Michael Fishman, MD[3], David Schultz, MD[4], Aaron Calodney, MD[5], Harold Cordner, MD[6], Wilson Almonte, MD[7], Yoann Millet, MD[1], Kenneth Wu, MD[1], Gennady Gekht, MD[8], Andrew Will, MD[9], Philip Kim, MD[3], Richard Bundschu, MD[10], Justin Sirianni, MD[8], Amr El-Naggar, MD[11], Mayank Gupta, MD[12], Wesley Park, MPH[13], David Cedeño, PhD[13], Ricardo Vallejo, MD, PhD[13]
[1]Procura Pain and Spine, The Woodlands, United States of America, [2]Oklahoma Pain Physicians, Oklahoma City, United States of America, [3]Center for Interventional Pain and Spine, Lancaster, United States of America, [4]Nura Research Institute, Minneapolis, United States of America, [5]Precision Spine Care, Pain Management, Tyler, United States of America, [6]Florida Pain Management Associates, Sebastian, United States of America, [7]Victoria Pain and Rehabilitation, Victoria, United States of America, [8]Coastal Orthopedics and Pain Management, Bradenton, United States of America, [9]Twin Cities Pain Clinic, Minneapolis, United States of America, [10]Coastal Orthopedics, Pain Management, Bradenton, United States of America, [11]DREZ One, Somerset, United States of America, [12]Neuroscience Research Center, Overland Park, United States of America, [13]SGX Medical LLC, Bloomington, United States of America

Introduction: Radicular upper limb pain (ULP) is a common chronic pain condition for which spinal cord stimulation (SCS) may be considered when conventional medical management fails. Treatment of chronic ULP using conventional SCS can be challenging. Differential target multiplexed SCS (DTM SCS) has proven successful for the treatment of low back and lower limb pain[1,2]. A recent prospective, multicenter, post market study evaluated the efficacy of DTM in the treatment of ULP. We report the outcomes of subjects who had a diagnosis of neck pain in addition to upper limb pain from this study.

Materials / Methods: This post-market, prospective, cohort, multicenter study evaluated DTM™ SCS in patients with a primary diagnosis of ULP. Informed, consented, eligible subjects were enrolled in 11 centers in the US. Key inclusion criteria included: adult (≥18 y/o), ULP Visual Analog Scale (VAS) ≥5 cm, SCS candidate as per indication, stable pain medication. Key exclusion criteria included: contraindications for SCS, conditions that could interfere with evaluation, active implanted device, cervical stenosis, facet spondylosis, mechanical instability, previous surgery of posterior elements of the cervical spine. All enrolled subjects underwent an SCS trial, and those with successful trials were implanted with cervically placed leads and a permanent neurostimulator and followed-up for 12-months. Secondary outcomes included neck pain VAS where applicable, functional disability (PDI), Patient Global Impression of Change (PGIC), and satisfaction.

Results: 58 patients with a ULP primary diagnosis were enrolled, 52 completed trial, and 46 were permanently implanted. Of those implanted, 43, 40, and 39 subjects reported concomitant neck pain at 3-, 6- and 12-month follow-ups, respectively. The primary endpoint was met with a 92% ULP responder rate (≥50% pain relief) at 3-months. The average neck pain VAS (cm) at baseline was 7.70, which was reduced by 81% to 1.48 at 3-months, 82% to 1.41 at 6-months, and 78% to 1.70 at 12-months. Average neck pain responder rates were 92%, 93% and 86% at 3-, 6-, and 12-months, respectively. Subjects reported reduced disability and reported >97% therapy satisfaction at 12-months.

Discussion: This study demonstrates that DTM SCS is a feasible treatment for chronic intractable ULP and suggests the potential benefit of DTM SCS for neck pain. More research is needed to confirm these findings.

Conclusions: DTM SCS can effectively reduce upper limb and neck pain in this patient demographic, however more data is needed.

Supplemental Data:

References: 1. Fishman M, Cordner H, Justiz R, Provenzano D, Merrell C, Shah B, et al. Twelve-month results from multicenter, open-label, randomized controlled clinical trial comparing differential target multiplexed spinal cord stimulation and traditional spinal cord stimulation in subjects with chronic intractable back pain and leg pain. Pain Pract. 2021 Nov;21(8):912-923. 2. Fishman MA, Calodney A, Kim P, Slezak J, Benyamin R, Rehman A, et al. Prospective, multicenter feasibility study to evaluate differential target multiplexed spinal cord stimulation programming in subjects with chronic intractable back pain with or without leg pain. Pain Pract. 2020 Sep;20(7):761-768.

Acknowledgements: This study has been sponsored by SGX Procura (acquired by Medtronic).

Learning Objectives: 1. Assess safety and efficacy of Differential Target Multiplexed SCS for upper limb pain. 2. Assess safety and efficacy of Differential Target Multiplexed SCS for neck pain. 3. Evaluate feasibility study data in support of SCS for the treatment of upper limb and neck pain.

Financial Disclosures: David L. Cedeno, PhD. SGX Medical, Consultant, >$100,000 Ricardo Vallejo MD, PhD, SGX Medical, Consultant, >$100,000 Ricardo Vallejo, MD, PhD, Medtronic Inc, Consultant/Advisory Board, >$100,000

Disclosure: I am an employee of Medtronic.

O134

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 05
15-05-2024 16:30 - 18:20

PREDICTION OF RESPONSE TO TRANSCRANIAL MAGNETIC STIMULATION IN THE MOTOR CORTEX IN PATIENTS WITH FIBROMYALGIA: PRELIMINARY STUDY

Catarina Lins, MD[1], Alessandra Fonseca, NURSING[2], Pedro Martins, MEDICAL STUDENT[3], Júlio Cesar Oliveira, MD[4], Daniel Andrade, PhD[5]
[1]Pain Center, University of São Paulo School of Medicine, São Paulo – SP, SAO PAULO, Brazil, [2]Pain Center, University of São Paulo School of Medicine, SAO PAULO, Brazil, [3]Federal University of Juiz de Fora School of Medicine, JUIZ DE FORA, Brazil, [4]Precision Data, SAO PAULO, Brazil, [5]University of Aalborg, Aalborg, Denmark

Introduction: Reduced gray matter volumes in specific areas, such as the left medial prefrontal cortex and the right dorsal posterior cingulate cortex, are present in individuals with fibromyalgia(1). We hypothesized that values of these cortical areas may predict the response to the analgesic effect of M1-rTMS in people with fibromyalgia.

Materials / Methods: 62 participants with fibromyalgia from a multicenter, randomized, double-blind, placebo-controlled clinical trial "Transcranial magnetic stimulation of the precentral gyrus in the relief of FM pain: a controlled adaptive trial" were included in a secondary analysis, and the prediction of response to transcranial magnetic stimulation in the motor cortex was assessed, were evaluated during the baseline and at the 8th week. They received the intervention conventional rTMS (i.e., 10Hz TMS session) or sham rTMS (i.e., sham TMS), based on the randomization assignment. The following baseline and at the 8th week variables were assessed: Charlson Comorbidity index, Visual Analogue Scale, Brief Pain Inventory, Hospital Anxiety and Depression Scale, Fibromyalgia Impact Questionnaire. In addition to the data collected in the clinical trial, the collection of Conditioned Pain Modulation and Magnetic Resonance Imaging was performed in both the active group and the sham group of participants.

Results: All participants were women, and the median VAS was 8 points. Baseline and Week 8 assessments for disease-related scales. 15 (N=32) participants in the intervention arm reached a ≥ 50% reduction in VAS, against 7 (N=30) in the sham arm (p = 0.053).
Although not statistically significant in this subsample, treatment effect was deemed present in the full trial sample. So far, we evaluated baseline scales that might predict the response to TMS: HADS; BPI; FIQ; TAS and CPM, as well as their subscales, when appliable. None had a statistically significant association with the primary endpoint either in the full sample or in the TMS group.
None of the MRI imaging volumes assessed was significantly associated with the primary outcome (Table 1).
Table 1. Comparison of MRI volume assessments according to VAS improvement ≥50% (TMS Only)

Characteristic	Responder, N = 12[1]	Non responder, N = 11[1]	p-value[2]	Responder, N = 12[1]	Non responder, N = 11[1]	p-value[2]
Insula	5916 (5630 – 6084)	6071 (5487 – 6604)	0.449	5843 (5529 – 5974)	5885 (5429 – 6309)	0.413
Precentral gyrus	10714 (9983 – 11848)	11016 (10419 – 11322)	0.976	10388 (10087 – 11077)	10156 (9728 – 11650)	>0.999
Postcentral gyrus	7853 (7590 – 8410)	8108 (6905 – 8586)	0.880	7724 (6821 – 7943)	7710 (6922 – 8751)	0.651
Paracentral gyrus	2889 (2551 – 3135)	2658 (2373 – 2811)	0.230	2839 (2727 – 3531)	3161 (2691 – 3613)	0.525
Rostral anterior cingulate gyrus	1998 (1819 – 2241)	2075 (1870 – 2290)	0.880	1486 (1294 – 1561)	1499 (1226 – 1645)	0.976
Caudal anterior cingulate gyrus	1361 (1216 – 1494)	1460 (1262 – 1611)	0.608	1649 (1442 – 1752)	1549 (1319 – 1947)	0.608
Cingular isthmus	2092 (1955 – 2242)	2234 (1951 – 2411)	0.525	2046 (1799 – 2192)	2006 (1877 – 2092)	0.902

[1]Median (IQR); [2]Wilcoxon rank sum test

Discussion: Thirteen studies investigating fMRI associated with pain thresholds found that individuals with FM exhibited increased cortical blood flow to brain regions involved in pain processing, even with lower levels of stimulation. Additionally, there was evidence of reduced connectivity within the descending pain-modulation system in FM patients, particularly between the

ACC and the amygdala, hippocampus, and brainstem(3). The ACC, periaqueductal gray, and rostral ventromedial medulla are key components of the descending pain processing pathway(4).

Conclusions: The analysis of our sample regarding the association between cortical thickness and the analgesic effects of motor cortex stimulation has not been completed yet.

Supplemental Data:

References: 1. Burgmer M, Gaubitz M, Konrad C, Wrenger M, Hilgart S, Heuft G, Pfleiderer B. Decreased gray matter volumes in the cingulo-frontal cortex and the amygdala in patients with fibromyalgia. Psychosom Med. 2009 Jun;71(5):566-73. doi: 10.1097/PSY.0b013e3181a32da0. Epub 2009 May 4. PMID: 19414621. 2. Fischl B. FreeSurfer. Vol. 62, NeuroImage. 2012. p. 774–81. 3. Jensen KB, Loitoile R, Kosek E, Petzke F, Carville S, Fransson P, et al. Patients with fibromyalgia display less functional connectivity in the brain's pain inhibitory network [Internet]. Vol. 8, Molecular Pain. 2012. Available from: http://www.molecularpain.com/content/8/1/32 4. Kong J, Tu PC, Zyloney C, Su TP. Intrinsic functional connectivity of the periaqueductal gray, a resting fMRI study. Behavioural Brain Research. 2010 Aug;211(2):215–9. 5. Lin C, Lee SH, Weng HH. Gray Matter Atrophy within the Default Mode Network of Fibromyalgia: A Meta-Analysis of Voxel-Based Morphometry Studies. Biomed Res Int. 2016;2016:7296125. doi: 10.1155/2016/7296125. Epub 2016 Dec 26. PMID: 28105430; PMCID: PMC5220433. 6. Mhalla A, Baudic S, De Andrade DC, Gautron M, Perrot S, Teixeira MJ, et al. Long-term maintenance of the analgesic effects of transcranial magnetic stimulation in fibromyalgia. Pain. 2011;152(7):1478–85. 7. Murillo-Garcia A, Leon-Llamas JL, Villafaina S, Gusi N. Fibromyalgia impact in the prefrontal cortex subfields: An assessment with MRI. Clin Neurol Neurosurg. 2022 Aug;219:107344. doi: 10.1016/j.clineuro.2022.107344. Epub 2022 Jun 18. PMID: 35750020.

Acknowledgements:

Learning Objectives: DISCUSS ABOUT TMS IN PAIN INCREASE KNOWLEDGE ABOUT NON INVASIVE NEUROMODULATION IN PAIN INCREASE KNOWLEDGE ABOUT FIBROMYALGIA AND TMS

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O135

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 05
15-05-2024 16:30 - 18:20

DAILY PAIN INTENSITY AND SLEEP QUALITY ASSESSED AT HOME IN A PROSPECTIVE MULTICENTER SPINAL CORD STIMULATION STUDY

Marc Russo, MBBS[1], James Yu, MD[2], Kasra Amirdelfan, MD[3], Leonardo Kapural, MD[4], Paul Verrills, MBBS[5]
[1]Hunter Pain Specialists, Broadmeadow, Australia, [2]Sydney Spine and Pain, Hurstville, Australia, [3]Boomerang Healthcare, Pain Management, Walnut Creek, United States of America, [4]Carolinas Pain Institute, Winston-Salem, United States of America, [5]Monash House Private Hospital, Metro Pain Group, Clayton, Australia

Introduction: Recent evidence from spinal cord stimulation (SCS) studies suggests traditional pain assessments do not fully capture patient experience due to inconsistencies between pain levels assessed in clinic versus at home.[1,2] Therefore, SCS studies supplementing in-clinic measures with at-home patient-reported outcomes (PROs) may better reflect real-world patient experience. The BENEFIT-03 study (NCT04683718) is evaluating safety and effectiveness of an implantable SCS system with remote device management and multiphase stimulation. Here, we report 12-month results of daily at-home assessments of sleep quality and pain intensity from BENEFIT-03.

Materials / Methods: BENEFIT-03 is a prospective, single-arm, multicenter study ongoing in Australia with Human Research Ethics Committee approval in consenting participants with chronic low back and/or leg pain. Post-implant follow-up consists of in-office visits (3, 6, 12, and 24 months) and remote visits that may be initiated by participants, investigators, proactive triggers (based on automatic daily device monitoring), or PROs. Primary endpoints are responder rate (at least 50% overall pain relief, VAS) and freedom from device-related complications at 6 months. Additional novel outcomes include daily PROs (Numerical Rating Scale [NRS] pain intensity and sleep quality) collected via diaries for 14 days at baseline and 28 days following post-implant visits.

Results: As of this March 2024 interim analysis, 21 of 31 implanted participants had at-home PROs available at baseline and 12 months post-implant. Participants averaged 6.1 nights/week with good/excellent sleep (NRS sleep quality at least 6) at 12 months versus 2.4 nights/week at baseline (mean per-patient improvement=59.1%). At-home mean pain intensity (NRS) decreased from 7.3 at baseline to 2.2 at 12 months; mean percentage pain relief was 69.3%. Participants averaged 5.5 days/week with mild/no pain (NRS=3 or less) at 12 months compared with 0.4 days/week at baseline. Trends in at-home results were consistent with in-clinic reporting. Mean overall VAS decreased from 78.0mm at baseline to 18.4mm at 12 months.

Discussion: In BENEFIT-03, traditional in-clinic assessments are augmented by longitudinal at-home diaries to assess daily patient experiences. Notably, at-home and in-clinic pain relief was more consistent in BENEFIT-03 than in previous studies.[1,2]

Conclusions: These results provide evidence that an SCS system with multiphase stimulation and proactive remote care provides long-term at-home daily pain relief and improved sleep quality. Additionally, this novel study design may better characterize real-world SCS patient experiences.

Supplemental Data: None

References: 1. Thomson S, Tavakkolizadeh M, Love-Jones S, et al. Effects of Rate on Analgesia in Kilohertz Frequency Spinal Cord Stimulation: Results of the PROCO Randomized Controlled Trial. *Neuromodulation*. 2018;21(1):67-76. 2. Kapural L, et al. At-Home Versus In-Clinic Pain Reporting for SCS Patients: Post Hoc Analysis of the BENEFIT-02 Study [NANS abstract 214538]. *Neuromodulation*. 2023;26(4):S66

Acknowledgements: BIOTRONIK sponsors the study and funded writing/editorial support.

Learning Objectives: 1. To describe the potential benefits of at-home daily pain assessment for characterizing real-world SCS patient experiences 2. To summarize improvements in daily pain relief and nightly sleep quality with multiphase stimulation and proactive remote care, as assessed the at-home setting in BENEFIT-03 3. To compare at-home versus in-clinic pain relief outcomes in the BENEFIT-03 clinical trial, which are more consistent than in previous studies

Financial Disclosures: Marc Russo: SPR Therapeutics, historical stockholder <1%; Saluda Medical, stock options <0.5%; and Presidio Medical, stock options <0.5%. **James Yu:** Abbott, consultant; Nevro, consultant, research; Medtronic, consultant, research; Boston Scientific, consultant, research; Saluda, research; Biotronik, research; and Nalu, research. **Kasra Amirdelfan:** Medtronic, consultant; Boston Scientific, consultant; Nevro, consultant; Biotronik, consultant; and Nalu, consultant, stock options. **Leonardo Kapural:** Nevro, consultant, research; Abbott, consultant; Medtronic, consultant, research; Nalu, consultant; Saluda, consultant, research; Biotronik, consultant, research; Gimer Medical, research; Neuros, research; and SPR Therapeutics, research. **Paul Verrills:** Presidio, consultant, research, $500 – $5,000; Biotronik, consultant, research, $1 - $500; Saluda, consultant, $5,000 - $20,000; and Nalu, consultant, $1 – $500.

Disclosure: Jacob Hicks is an employee at Biotronik Inc.

O136

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 05
15-05-2024 16:30 - 18:20

TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION IN CHRONIC LOW BACK PAIN: EFFECTS AND MECHANISMS IN A RANDOMIZED CONTROLLED STUDY

Tingting Li, MBBS, Amy Ursitti, BSc (Hons), Sveta Reddy, BSc (Hons), Valeria Sacca, PhD, Meixuan Zhu, BSc (Hons), Jian Kong, MBBS
Massachusetts General Hospital, Charlestown, United States of America

Introduction: Chronic low back pain (cLBP) is a widespread health condition, requiring more treatment options..The purpose of this study is to investigate the modulation effects of transcutaneous auricular vagus nerve stimulation (taVNS) on cLBP as well as its potential underlying mechanisms.

Materials / Methods: 71 cLBP patients were recruited and randomly assigned to two groups [either four weeks of 20 Hz taVNS or transcutaneous greater auricular nerve stimulation (tGANS, applied to the earlobe as control)]. Resting-state functional magnetic resonance imaging data were acquired at baseline and at the end of the four-week treatment (5 sessions / week, 30 minutes / session). Static (sFC) and dynamic (dFC) functional connectivity analyses were conducted, using the nucleus tractus solitarius (NTS), raphe nucleus (RN), and locus coeruleus (LC) as seed regions. Spectral dynamic causal modeling (DCM) was applied to further explore the effective connectivity patterns between taVNS and tGANS.

Results: 51 patients (taVNS: n=25; tGANS: n=26) completed the study. Within-group comparisons revealed a significant alleviation of pain-related outcomes in both groups, illustrated by patients' pain intensity, pain bothersomeness, and pain interference scores. Between-group comparisons revealed no significant difference in pain reduction. The sFC analysis showed that both taVNS and tGANS could modulate the sFC between the seed regions and pivotal brain regions associated with cLBP pathology and modulation including the thalamus, insula, postcentral gyrus, anterior cingulate cortex (ACC), and medial prefrontal cortex (mPFC). DCM revealed that taVNS was associated with reduced effective connectivity from the left amygdala to the left ACC, which was positively correlated with pain bothersomeness. Between-group comparisons showed that taVNS was associated with a significant increase in effective connectivity from the RN to both the left amygdala and right insula, from the left amygdala to the NTS, as well as from the LC to the left ACC, in comparison to tGANS.

Discussion: The limitations of this study include: 1) the sample size is relatively small, further research with larger sample sizes is necessary to validate our findings; and 2) the present study was performed over a duration of four weeks, indicating that the observed effects can only be attributed to short- and mid-term effects.

Conclusions: Our findings suggest that both taVNS and tGANS have the potential to relieve cLBP by modulating both functional and effective connectivity of key brainstem nuclei along the central vagus nerve pathway.

Supplemental Data: None

References: None

Acknowledgements: The support of NIH HEAL Initiative (R34DA046635) for this project is gratefully acknowledged.

Learning Objectives: 1) introducing the peripheral nerve stimulation (particularly the transcutaneous auricular vagus nerve stimulation) 2) introducing the effects of peripheral nerve stimulation on chronic low back pain 3) introducing the brain mechanisms underlying the peripheral nerve stimulation

Financial Disclosures: J.K has a disclosure to report (holding equity in startup companies (MNT, BTT) and a patent on applying neuromodulation), but declares no significant relationships. All other authors declare no conflict of interest.

Disclosure: No significant relationships.

O137

Oral Presentations
NEUROSTIMULATION FOR PAIN – CLINICAL UPDATE 05
15-05-2024 16:30 - 18:20

DIFFERENTIAL TARGET MULTIPLEXED SPINAL CORD STIMULATION FOR INDICATED CHRONIC BACK PAIN PATIENTS INELIGIBLE FOR SPINE SURGERY: EU RANDOMIZED CONTROLLED TRIAL

Jan Willem Kallewaard, MD[1], Bart Billet, MD[2], Raf Van Paesschen, MD[3], Iris Smet, MD[4], Agustin Mendiola, MD[5], Isaac Peña, MD[6], Pablo Lopez, MD[7], Javier Carceller, MD[7], Carlos Tornero, MD[8], Xander Zuidema, MD[9,10], Jan Vesper, MD[11], Jens Lehmberg, MD[12], Wim Laloo, MSc[13], David Cedeño, PhD[13], Ricardo Vallejo, MD, PhD[13]
[1]. Rijnstate, Anesthesiology, arnhem, Netherlands, [2]AZ Delta, Roeselare, Belgium, [3]GZA Hospitals, Wilrijk, Belgium, [4]Vitaz, St Niklaas, Belgium, [5]Hospital Universitario Puerta de Hierro, Madrid, Spain, [6]Hospital Virgen Del Rocio, Pain Unit, Seville, Spain, [7]Hospital Clínico Universitario de Santiago, Santiago de Compostela, Spain, [8]Hospital Clínico Universitario de Valencia, Valencia, Spain, [9]Diakonessenhuis, Zeist, Netherlands, [10]Maastricht UMC+, Maastricht, Netherlands, [11]Uniklinik Düsseldorf, Düsseldorf, Germany, [12]München Klinik Bogenhausen, Bogenhausen, Germany, [13]SGX Medical LLC, Bloomington, United States of America

Introduction: A randomized controlled trial (RCT)[1] showed that Differential Target Multiplexed SCS (DTM SCS) provided superior long-term low back pain (LBP) responder rate (RR, percent subjects with ≥50% relief) relative to conventional SCS in subjects diagnosed with persistent spinal pain syndrome type 2 (PSPS-T2). Previously, we reported 6-month outcomes of DTM SCS in the treatment of LBP PSPS-T1 patients ineligible for spine surgery in multiple sites in Europe (EU-RCT)[2]. The 24-month outcomes of this EU-RCT are presented.

Materials / Methods: This post-market, multicenter RCT compares DTM™ SCS to optimized conventional medical management (CMM) in PSPS-T1 patients suffering from chronic LBP who are ineligible for spine surgery. Table 1 shows key eligibility criteria. Subjects were randomized 1:1 to either treatment. Primary endpoint was LBP RR to therapy at 6-month. An optional two-way crossover was available on the 6-month visit. Subjects who were treated with DTM SCS underwent a therapy trial, followed by permanent implantation in those reporting ≥50% LBP relief. Subjects were followed-up through 24-months.

Results: 12 European centers enrolled 115 subjects, with 55 and 57 subjects randomized to DTM SCS and CMM, respectively. DTM SCS was superior to CMM for LBP with RR of 85.6%,80.0%, 82.2% and 88.4%at 6-, 12-, 18- and 24-month follow-ups, respectively. Mean LBP VAS reduction from baseline to 6-, 12-, 18- and 24-month follow-ups were 5.85, 5.42, 5.52, and 5.98 cm, respectively, corresponding to 73.3%, 69.6%, 71.3% and 76.9%LBP reduction. Leg pain was also reduced by 5.17, 5.39, 5.46, and 6.14 cm, with a responder rate of 83.3%,80.0%, 80.0% and 93.1% at 6-, 12-, 18- and 24-month follow-ups. Improvements in functional disability (Oswestry Disability Index, ODI) and quality of life (EQ-5D-5L) were also sustained. A reduction of 24.3,22.7, 25.2 and 25.7 points in ODI, relative to a 49 (severely disabled) baseline, was observed at 6-, 12-, 18- and 24-month follow-ups, respectively. EQ-5D-5L index improved to 0.71 (6- and 12-month), 0.72 and 0.73 (18- and 24-month, respectively) from 0.40 at baseline. Fifty subjects receiving CMM opted to cross

over.

Table 1. Key eligibility criteria of the EU RCT.

Inclusion	Exclusion
• Adult subjects • Non-eligible for spine surgery • ≥ 6 cm LBP VAS with or without leg pain • SCS candidate per approved labeling • Under a stable pain medication regime	• Previous lumbar spine surgery • Contraindications for SCS • Mechanical spine instability

Discussion: DTM SCS was superior to CMM for LBP RR through 24-months. Sustained benefits of DTM SCS for LBP and leg pain and improvements in functional disability and quality of life were also observed.

Conclusions: DTM SCS is efficacious for treatment of LBP and leg pain in PSPS-T1 patients not eligible for spine surgery.

Supplemental Data:

References: 1. Fishman M, Cordner H, Justiz R, Provenzano D, Merrell C, Shah B, et al. Twelve-Month results from multicenter, open-label, randomized controlled clinical trial comparing differential target multiplexed spinal cord stimulation and traditional spinal cord stimulation in subjects with chronic intractable back pain and leg pain. Pain Pract. 2021 Nov;21(8):912-923. 2. Kallewaard JM, Billet B, Van Paesschen R, Smet I, Mendiola A., Peña I, et al. European randomized controlled trial to study the effects of differential target multiplexed SCS in treating intractable chronic back pain without previous lumbar spine surgery. INS 15th World Congress. 21-26 May 2022. Barcelona, Spain.

Acknowledgements: The support of SGX International, the sponsor for this project, is gratefully acknowledged

Learning Objectives: 1. Understand the benefits of SCS in patients with intractable chronic back and leg pain who are ineligible for spine surgery. 2. Evaluate level-1 evidence provided by a study with a randomized controlled trial design. 2. Interpret long-term results from a randomized controlled trial evaluating SCS for chronic low back and leg pain.

Financial Disclosures: David L. Cedeno, PhD. SGX Medical, Consultant, >$100,000 Ricardo Vallejo MD, PhD, SGX Medical, Consultant, >$100,000 Ricardo Vallejo, MD, PhD, Medtronic Inc, Consultant/Advisory Board, >$100,000

Disclosure: I am a co-inventor of patents related to Differential Target Multiplexed SCS assigned to Medtronic

O138

Oral Presentations
NEUROPSYCHIATRIC DISORDERS: BEHAVIORAL NEUROMODULATION
16-05-2024 10:30 - 11:20

REAL-TIME REGULATION OF AROUSAL AND PERFORMANCE IN HEALTHY NONHUMAN PRIMATES USING THE BIDIRECTIONAL NEUROMODULATION RESEARCH PLATFORM, DYNEUMO-X.

Jonathan Baker, PhD[1], Alceste Deli, MD, MSc, DPhil[2], Robert Toth, PhD[3], Mayela Zamora, PhD[4], John Fleming, PhD[4], Moaad Benjaber, PhD[3,4], Jae-Wook Ryou, PhD[1], Nicholas Schiff, MD[1], Tim Denison, PhD[4,5], Keith Purpura, PhD[1]
[1]Weill Cornell Medicine, Brain And Mind Research Institute, New Work, United States of America, [2]University of Oxford, Nuffield Department Of Surgical Sciences, Oxford, United Kingdom, [3]University of Oxford, Nuffield Department Of Clinical Sciences, Oxford, United Kingdom, [4]Oxford University, Institute Of Biomedical Engineering, Department Of Engineering Science, Oxford, United Kingdom, [5]University of Oxford, Nuffield Department Of Clinical Neurosciences, Oxford, United Kingdom

Introduction: The development and application of bidirectional neuromodulation, using closed-loop deep brain stimulation (DBS) and brain-computer interfaces (BCI), holds great promise for advancing our understanding of the brain and developing novel, fully implantable systems, to restore lost function. Treatment-resistant brain disorders are manifestations of pathophysiology across widely distributed brain networks and invasive approaches like DBS and BCI are emerging as promising therapeutic options. In a recent clinical study [1] (NCT02881151), we used daytime central thalamic DBS (CT-DBS) to treat chronic dysregulation of arousal and executive attention in five moderate-to-severe traumatic brain injury (msTBI) patients. However, the local and network effects of CT-DBS are not well understood, due to our inability to monitor and modulate the circadian dynamics of arousal regulation within the anterior forebrain network, in both the intact and damaged brain [2], and due to key limitations of approved clinical-grade systems. To address these limitations, we explored the use of closed-loop CT-DBS in healthy behaving non-human primates (NHP) using a novel bidirectional neuromodulation research platform, the DyNeuMo-X.

Materials / Methods: These studies were approved by the IACUC at Weill Cornell Medicine. NHPs were trained to perform a visuomotor and working memory task for liquid rewards and we used eye movements, pupillometry, behavioral performance measures, and real-time analysis of cortical and subcortical neurophysiological signals to initiate brief periods of CT-DBS. The various signals were analyzed using custom hardware/software to initiate closed-loop CT-DBS and the approach was then validated using the DyNeuMo-X research platform.

Results: Real-time closed-loop CT-DBS in behaving NHPs markedly enhanced cortical arousal by significantly reducing power within the theta-alpha frequency bands (4-12Hz), which led to the restoration of performance, but only when the animals were motivated to work.

Discussion: Rapid and robust power reduction within the theta-alpha frequency band (4-12Hz) of cortical signals, using the clinical-grade DyNeuMo-X, demonstrates the safety and feasibility of developing closed-loop CT-DBS approaches in large animal models. The internal DyNeuMo system has been used to promote wakefulness and alter sleep stages in patients [3] and its being used in several UK clinical trials (NCT05437393, NCT05197816, NC03837314). Overall, the results and approach developed in this study further support clinical trials aimed at treating dysfunction in arousal and executive attention in humans.

Conclusions: This study supports our long-term goal of developing a fully implantable bidirectional neuromodulation system to monitor and modulate arousal regulation in humans; ultimately to treat dysfunction in arousal and executive attention in patients with structural brain injuries and further etiologies.

Supplemental Data:

References: 1) Schiff, ND, Giacino, JT, Butson, CR, Choi, EY, Baker, JL, O'Sullivan, KP, Janson, AP, Bergin, M, Bronte-Stewart, HM, Chua, J, DeGeorge, L, Dikmen, S, Fogarty, A, Gerber, LM, Krel, M, Maldonado, J,Radovan, M, Shah, SA, Su, J, Temkin, N, Tourdias, T, Victor, JD, Waters, A, Kolakowsky-Hayner, SA, Fins, JJ, Machado, AG, Rutt, BK, Henderson, JM (2023) Thalamic deep brain stimulation in traumatic brain injury: a phase 1, randomized feasibility study. *Nature Medicine*. 2) Schiff, N.D., (2008) Central thalamic contributions to arousal regulation and neurological disorders of consciousness. *Annals of the New York Academy of Sciences*, *1129*(1), pp.105-118. 3) Deli A, Zamora M, Fleming J, Divanbeighi AP, Benjaber M, Green AL, Denison T. (2023) Bioelectronic Zeitgebers: targeted neuromodulation to re-establish circadian rhythms. *bioRxiv*. 2023:2023-04.

Acknowledgements: This work was funded by the National Institute of Neurological Disorders and Stroke (NS111019) and the Daedalus Fund for Innovation at Weill Cornell Medicine to J.L. Baker and from the Royal Academy Chair in Emerging Technology to T. Denison.

Learning Objectives: 1) Learn about the latest advances in closed-loop deep brain stimulation for all indications. 2) Learn about the latest advances in Brain-Computer Interfaces. 3) Learn about the minaturation and power constraints of current and future fully implantable neuromodulation devices.

Financial Disclosures: The University of Oxford has research agreements with Bioinduction Ltd. and Tim Denison (Co-Author) is a director and shareholder in Amber therapeutics, which has a controlling stake in Bioinduction.

Disclosure: No significant relationships.

O139

Oral Presentations
NEUROPSYCHIATRIC DISORDERS: BEHAVIORAL NEUROMODULATION
16-05-2024 10:30 - 11:20

DEEP BRAIN STIMULATION FOR THE AFFECTIVE COMPONENT IN NEUROPATHIC PAIN: RESULTS IN 5 PATIENTS

Gloria Villalba, MD, PhD[1,2], Juan Ramon Castaño, MD[3], Nazaret Infante, MD[2], Luis Miguel Martin, PhD[3], Victor Perez-Sola, PhD[3,4], Cristina Vieta, MD[5], Elisa Cuadrado, PhD[6], Alba Leon, MD[7], Killian Amadeus Abellaneda, DPsych[8,9], Jaume Capellades, MD[10], Brigitte Beltran, MD[10], Carmina Ribas, MD[5,11]
[1]Research Institute Hospital del Mar, Systems Neurologics And Neurotherapeutics Group, Barcelona, Spain, [2]Hospital del Mar, Neurosurgery, Barcelona, Spain, [3]Hospital del Mar, Psychiatry, Barcelona, Spain, [4]Research Institute Hospital del Mar, Mental Health, Barcelona, Spain, [5]Hospital de Bellvitge, Anesthesia, Hospitalet, Spain, [6]Hospital del Mar, Neurology, Barcelona, Spain, [7]Hospital del Mar, Neurophysiology, Barcelona, Spain, [8]Instituto Guttmann, Research Group, Barcelona, Spain, [9]Universidad Autonoma de Barcelona, Psycology, Bellaterra, Spain, [10]Hospital del Mar, Neurorradiology, Barcelona, Spain, [11]Instituto de investigacion de Hospital de Bellvitge, Neuroscience Program, Hospitalet, Spain

Introduction: When motor cortical stimulation (MCS) and/or deep brain stimulation (DBS) in thalamus and/or periventricular/periaqueductal gray matter (PVA,PGA) are not effective in patients with severe neuropathic pain, usually no other treatments are contemplated in neuropathic pain protocols.However, treatment of the affective component of neuropathic pain or DBS in the dorsal anterior cingulum shows some degree of efficacy in the few series reported in the literature

Materials / Methods: Five patiens with severe neuropathic pain of different etiologies , three of whom with previous MCS failure, were treated with DBS in the dorsal anterior cingulum bilaterally. Tetrapolar electrodes were used with bipolar stimulation, 2-4 mAmp, 240 Hz, 60 µs .Protocol implies a psychotherapeutic approach using acceptance and commitment therapy (ACT) .The primary goal is to evaluate efficacy and safety at 6 months of follow-up. The main variable is the interference of pain in activities of daily living.Other variables to be assessed include: pain intensity score, pain catastrophizing, quality of life, anxiety and depression.

Results: All five patients showed efficacy and there were no complications related to stimulation. Although the reduction in the numerical pain scale is not very significant (20-25 %) the improvement was highly significant in the pain interference in activities of daily living scale (60-70 %),which is the main variable, pain catastrophizing (60-70 %), quality of life (60-65 %), anxiety (60 %) and depression (65-70%).

Discussion: The treatment of the affective component of pain aims to make the experience of pain less uncomfortable and to reduce suffering. For this reason, the evaluation of efficacy after DBS in the dorsal anterior cingulum cannot have the numerical pain scale or the visual analogue scale as the main efficacy variable, as occurs with other neuromodulation treatments. Although the mechanism of action of MCS and DBS in the thalamus and/or PVA-PGA is unknown, they are considered to be effective to treat the sensory component of pain. We consider that if the treatment of the sensory component of pain with MCS or DBS has failed, and patient is experiencing severe suffering, treating the affective component with DBS in the dorsal anterior cingulum should be considered.

Conclusions: Although evidence is very scarce, the treatment of the affective component of pain by means of DBS in the dorsal anterior cingulum should be considered in patients with very severe pain without response to other neuromodulation techniques. Specialized psychology visits in addressing pain is mandatory for patients with DBS in dorsal anterior cingulum.

Supplemental Data:

References: . Alamri A, Pereira EAC " Deep brain stimulation for chronic pain" Neurosurg Clin N Am 2022;33(3):311-321 .Moisset X, Lanteri-Minet M, Fontaine D " Neurostimulation methods in the treatment of cronic pain" J Neural Transm 2020;127(4):673-686 . Pereira EA,Aziz TZ "Neuropathic pain and deep brain stimulation" Neurotherapeutics,2014;11(3):496-507 .Hann KEJ, McCrachen LM " A systematic review of randomized controlled trails of acceptance and commitment therapy for adults with chronic pain: outcome domains, design quality and efficacy". J Contextual Behav Sci,2014,3,17-227

Acknowledgements:

Learning Objectives: 1-Incorporation of the neuromodulation of the affective component of pain into the therapeutic algorithm for patients with severe neuropathic pain. 2-How to evaluate the effectiveness of DBS in the dorsal anterior cingulum.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O140

Oral Presentations
NEUROPSYCHIATRIC DISORDERS: BEHAVIORAL NEUROMODULATION
16-05-2024 10:30 - 11:20

TUNING HUMAN AROUSAL: METHODOLOGICAL CONSIDERATIONS BASED ON STATE-DEPENDENT NETWORK ACTIVITY

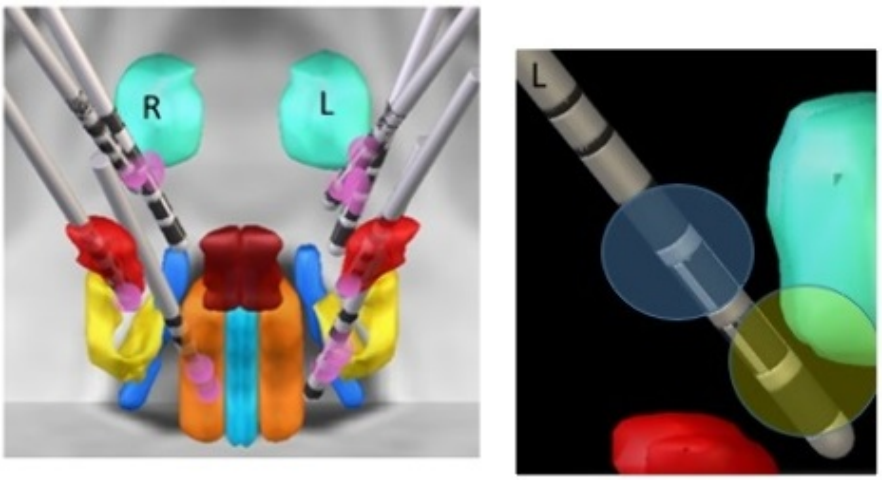
Alceste Deli, MD, MSc, DPhil[1], Michiel Cottaar, PhD[2], Sean Martin, FRCS(SN)[3], Amir Divanbeighi Zand, BA BM BCh[3], Mayela Zamora, PhD[4], Nagaraja Sarangmat, MD[5], Benoit Duchet, DPhil[2], Tim Denison, PhD[6], Alexander Green, PhD FRCS(SN)[7]
[1]University of Oxford, Sir Jules Thorn Sleep And Circadian Neuroscience Institute And Nuffield Department Of Surgical Sciences, Oxford, United Kingdom, [2]University of Oxford, Nuffield Department Of Clinical Neurosciences, Oxford, United Kingdom, [3]University of Oxford, Nuffield Department Of Surgical Sciences, Oxford, United Kingdom, [4]Oxford University, Institute Of Biomedical Engineering, Oxford, United Kingdom, [5]Oxford University Hospitals, Neurology, Oxford, United Kingdom, [6]University of Oxford, Mrc Brain Networks Unit, Oxford, United Kingdom, [7]University of Oxford, Nuffield Department Of Clinical Neurosciences (ndcn), Medical Sciences Division, Oxford, United Kingdom

Introduction: Despite advances in both theoretical approaches and device development in the field of deep brain stimulation (DBS)[1,2], parameter selection in clinical practice remains an empirical process based on trial-and-error. The development of strategic programming approaches incorporating electrophysiological biomarkers is especially crucial in emerging DBS indications[3], where evidence and prior cases can be sparse. Our work focuses on arousal modulation through DBS, as it is also impacted by neurodegeneration.[4] Herein we assess neuroanatomical correlates, longitudinal efficacy and implementability across device platforms of a targeted contact selection strategy, based on state-dependent neurophysiology.

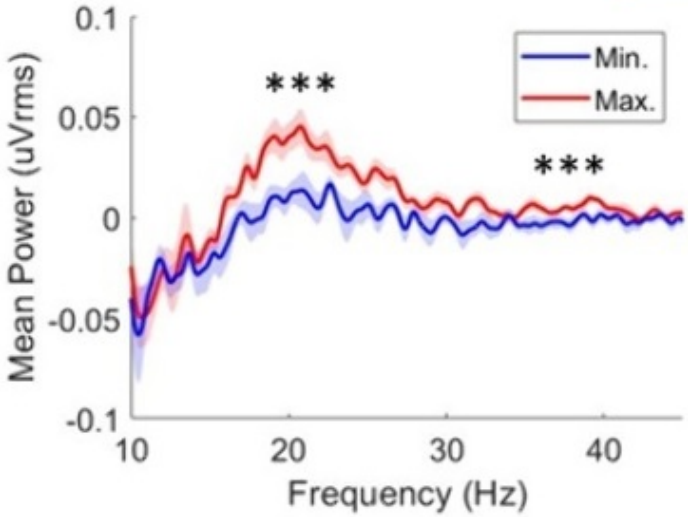
Materials / Methods: Firstly, oscillatory profiles in the beta (13-29 Hz) and low gamma (30-45 Hz) range, recorded during multiple periods of continuous slow wave activity, were compared to equivalent periods of quiet wake in four patients with externalised directional brainstem leads. Two contact groups were identified: one minimally and one maximally modulated by arousal state. The latter contact group was stimulated to induce arousal shifts. The anatomical locations of contacts were compared and their projections explored through neuroimaging analysis. To further confirm feasibility and results of targeted contact selection on arousal, lead configurations from each group were stimulated in a longitudinal cross-over design, in an additional patient with sleep-wake pathology, implanted with a novel neurostimulation device.

Results: The two contact groups differed in terms of anatomical location and cortical projections, with maximally modulated contacts (MMC) having a greater adjacency to arousal-promoting subcortical structures. The groups showed significant differences in beta (especially centered around 20Hz) ($p= 1.6 \times e^{-82}$) and gamma activity ($p= 1.6 \times e^{-38}$), results also present in within-patient analyses. When stimulated at a harmonic of the peak beta frequency and within the modulated gamma range, MMC stimulation induced transitions to wake[5]. Additionally, the main principles of this strategy were replicated in a patient with a novel device, resulting in a significant reduction of excessive daytime sleepiness compared to the control strategy, during the longitudinal cross-over design.

A.

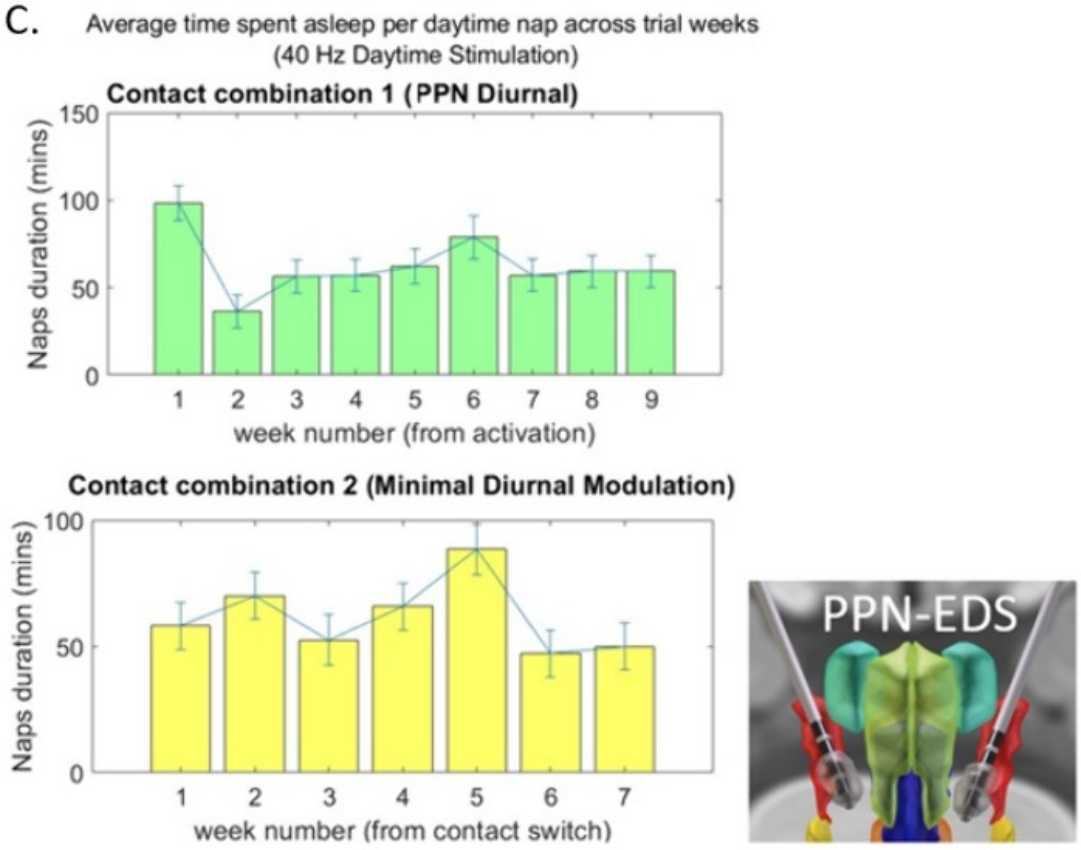


B.



A. Maximally modulated contacts (MMC) are located adjacent to subcortical arousal nuclei. MMCs shown for all four externalized cases (left), while location and connectivity were compared to contacts with low arousal state oscillatory modulation (right, within patient).

B. Differences in network activity between groups persisted across all cases. One group (MMC) showed significantly higher beta and gamma modulation compared to the other (comparison of differential averages across states, between groups – levels of significance reported in body of abstract).



C. Efficacy comparison of stimulation strategy, based on longitudinal cross-over in a patient with excessive daytime sleepiness (PPN-EDS case). Reduction occurred in nap number during MMC/PPN Diurnal contact stimulation (p= 0.0279, MMC contacts shown in grey). For the cross-over period of stimulation of contacts with minimal state modulation, nap frequency increased (p=0.0036). Total nap duration also fluctuated in these two conditions as shown. PPN: Pedunculopontine Nucleus, contact implantation site, visualized in red.

Discussion: The exploration of state-dependent modulation of brainstem oscillatory profiles resulted in an efficient, effective and anatomically meaningful strategy of contact selection for stimulation. Furthermore, the arousal-promoting effects of MMC stimulation at frequencies predicted to entrain wake-related oscillations[6] can be translated across device platforms and ameliorate daytime symptoms.

Conclusions: We propose a strategic approach to subcortical network stimulation, directly applicable to disorders of arousal regulation. This method can be integrated in treatment methodology in these cases, in lieu of multiple programming attempts based on trial-and-error.

Supplemental Data: Devices/neuromodulation platforms used: Abbott/St Jude (four cases, STAGG-MSA Trial, Clinical Study Identifier: NCT03593512) and DyNeuMo/BioInduction (one case, MINDS Trial, Clinical Study Identifier: NCT05197816). All five patients were male, diagnosed with Multiple Systems Atrophy (MSA-P). At time of recording, the four STAGG-MSA cases were not diagnosed as actively suffering from associated sleep pathology. In the MINDS case, pathological (excessive) daytime sleepiness was confirmed with repeated Epworth Sleepiness Scale measurements as well as patient and carer observational logs. In terms of analyses, recordings were pre-processed and analysed in Matlab using in-house scripts, the FieldTrip toolbox and code related to the Boundedline function. Additionally, imaging (MRI and CT) acquired pre- and post-operatively was processed in Matlab and Python, with utilisation of LeadDBS, FSLEyes and fslpy. Subcortical structures were

visualised in MNI and patient-native space using the Harvard Ascending Arousal Network Atlas. All statistical analyses, including students ttest and analyses of variance (ANOVA), were corrected for multiple comparisons (Bonferroni). Supplemental References: Johns, Murray W. "A new method for measuring daytime sleepiness: the Epworth sleepiness scale." *sleep* 14.6 (1991): 540-545. Oostenveld, R., Fries, P., Maris, E., & Schoffelen, J. M. (2011). FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. Computational Intelligence and Neuroscience, 2011. https://doi.org/10.1155/2011/156869 Kelly Kearney (2023). boundedline.m (https://github.com/kakearney/boundedline-pkg), GitHub. Retrieved October 17, 2023. Horn, Andreas, et al. "Lead-DBS v2: Towards a comprehensive pipeline for deep brain stimulation imaging." *Neuroimage* 184 (2019): 293-316. McCarthy, Paul. "FSLeyes (Version 0.33. 0)." *Zenodo http://doi. org/105281/zenodo3858136* (2020). McCarthy, P., Cottaar, M., Webster, M., Fitzgibbon, S., & Craig, M. (2023). fslpy (3.15.0). Zenodo. https://doi.org/10.5281/zenodo.8376794 Edlow, Brian L., et al. "Neuroanatomic connectivity of the human ascending arousal system critical to consciousness and its disorders." *Journal of Neuropathology & Experimental Neurology* 71.6 (2012): 531-546.

References: 1. Boutet, Alexandre, et al. "Predicting optimal deep brain stimulation parameters for Parkinson's disease using functional MRI and machine learning." *Nature communications* 12.1 (2021): 3043. 2. Toth R, Zamora M, Ottaway J, Gillbe T, Martin S, Benjaber M, Lamb G, Noone T, Taylor B, Deli A, Kremen V, Worrell G, Constandinou TG, Gillbe I, De Wachter S, Knowles C, Sharott A, Valentin A, Green AL, Denison T. DyNeuMo Mk-2: An Investigational Circadian-Locked Neuromodulator with Responsive Stimulation for Applied Chronobiology. Conf Proc IEEE Int Conf Syst Man Cybern. 2020 Oct;2020:3433-3440. doi: 10.1109/SMC42975.2020.9283187. Epub 2020 Dec 14. PMID: 33692611; PMCID: PMC7116879. 3. Sheth, Sameer A., et al. "Deep brain stimulation for depression informed by intracranial recordings." *Biological psychiatry* 92.3 (2022): 246-251. 4. Deli A, Zamora M, Fleming J, Divanbeighi AP, Benjaber M, Green AL, Denison T. (2023) Bioelectronic Zeitgebers: targeted neuromodulation to re-establish circadian rhythms. *bioRxiv*. 2023:2023-04. 5. Deli, Alceste, et al. "Tailoring human sleep: selective alteration through brainstem arousal circuit stimulation." *medRxiv* (2023): 2023-01. 6. Duchet B, Sermon JJ, Weerasinghe G, Denison T, Bogacz R. How to entrain a selected neuronal rhythm but not others: open-loop dithered brain stimulation for selective entrainment. *J Neural Eng*. 2023;20(2). doi:10.1088/1741-2552/ACBC4A

Acknowledgements:

Learning Objectives: 1. Present a comprehensive method of DBS parameter selection in an emerging clinical indication (disorders of arousal), backed by neuroanatomical and neurophysiological correlates and drastically different from empirical approaches, commonly used in the DBS field. 2. Showcase methodological principles in the programming of neuromodulation devices, that transcend device platform and are generally applicable across systems. 3. Present neurophysiological aspects of human arousal network activity, that can be harnessed for therapeutic modulation of arousal state.

Financial Disclosures: Alceste Deli, Timothy Denison and Alexander Green jointly hold intellectual property related to invasive neuromodulation of arousal (Oxford University Innovation). No financial compensation is received as of present in relation to this IP. Denison and Green are shareholders in Amber Therapeutics, with a total joint percentage that does not exceed 15%. Furthermore, they receive honoraria from various companies in the invasive neuromodulation space, however no such fees are directly related to this presentation material.

Disclosure: No significant relationships.

O141

Oral Presentations
NEUROPSYCHIATRIC DISORDERS: BEHAVIORAL NEUROMODULATION
16-05-2024 10:30 - 11:20

STUDY ON ANTI-DEPRESSION OF TRANSCUTANEOUS AURICULAR VAGUS STIMULATION

Junying Wang, PhD[1,2], Yu Wang, MD[2], Peijing Rong, PhD[2]
[1]Institute of Acupuncture and Moxibustion, China Academy of Chinese Medical Sciences, Beijing, China, [2]nstitute of Acupuncture and Moxibustion, China Academy of Chinese Medical Sciences, Beijing, China

Introduction: Depression is a serious disabling disease worldwide. Accumulating evidence supports that there is a close relationship between depression and inflammation, then inhibition of neuroinflammation may be another mechanism for the treatment of depression. Transcutaneous Auricular Vagus Stimulation(taVNS), as a non-invasive transcutaneous electrical stimulation, could effectively treat depression, but its mechanism is unclear.

Materials / Methods: In this study, rats with depression-like behavior were induced by intraperitoneal injection of lipopolysaccharide (LPS). The rats were randomly divided into a Control group, LPS group, taVNS+LPS group and the same as the α7 nicotinic acetylcholine chloride receptor(α7nAChR) (-/-) gene knockout rats. The expressions of tumor necrosis factor-alpha (TNF-α) and phosphorylated-Janus kinase2(p-JAK2),phosphorylated-signal transducer and activator of transcription3(p-STAT3) in the hypothalamus, amygdala and hippocampus were detected by Western Blot.

Results: We observed that LPS significantly decreased the sucrose preference, the time of into the open arms in the elevated plus maze, and the number of corssing and reaing in the open field test. TaVNS treatment improves these depression-like behaviors, but taVNS is not effective in α7nAChR (-/-) gene knockout rats. The expression of TNF-α signifciantly increased, and the expression of p-Jak2 and p-STAT3 markedly decreased in the hypothalamus and amygdala induced by LPS. TaVNS could significantly reverse the above-mentioned phenomena but had rare improvement effect for α7nAChR(-/-) rats.

Discussion: In the periphery, the vagus nerve anti-inflammatory pathway works through the activation of Jak2-STAT3 mediated by α7nAChR[1]. Electroacupuncture.activated the α7nAChR-mediated JAK2/STAT3 signaling pathway in macrophages which reduced the production of inflammatory cytokines to suppressed intestinal inflammation and promoted gastrointestinal motility[2]

Conclusions: Our research shows that taVNS can inhibit the inflammation of the central hypothalamus and amygdala by activating the a7nAchR/p-Jak2 signaling pathway, and also improve the depression-like behavior of rats. Therefore, the central anti-inflammatory effect of taVNS may be one of its antidepressant mechanisms.

Supplemental Data:

References: 1.de Jonge WJ, van der Zanden EP, The FO, Bijlsma MF, van Westerloo DJ, Bennink RJ, Berthoud HR, Uematsu S et al (2005) Stimulation of the vagus nerve attenuates macrophage activation by activating the Jak2-STAT3 signaling pathway. Nat Immunol 6(8):844-851 2. Yang NN, Yang JW, Ye Y, Huang J, Wang L, Wang Y, Su XT, Lin Y et al (2021) Electroacupuncture ameliorates intestinal inflammation by activating α7nAChR-mediated JAK2/STAT3 signaling pathway in postoperative ileus. Theranostics 11(9):4078-4089

Acknowledgements:

Learning Objectives: 1. **Transcutaneous Auricular Vagus Stimulation has an effect on depression 2. The** mechanism of Transcutaneous Auricular Vagus Stimulation for depression. 3. the

antidepressant effect of taVNS for LPS-induced depressive rats is related to α7nAchR/JAK2 signal pathway in the hypothalamus and amygdala

Financial Disclosures: This work was supported by the National Key R&D Program of China (2022YFC3500500,2022YFC3500501, 2018YFC1705800, 2018YFC1705803), Scientific and technological innovation project of China Academy of Chinese Medical Sciences(C12021A03405), Natural Science Foundation of Beijing Municipal (7212184), and the Fundamental Research Funds for the Central public welfare research institutes (ZZ20211803, ZZ20191603, ZZ13-YQ-062).

Disclosure: No significant relationships.

O142

Oral Presentations
NEUROPSYCHIATRIC DISORDERS: BEHAVIORAL NEUROMODULATION
16-05-2024 10:30 - 11:20

MACHINE-LEARNING-BASED PREDICTION OF PHOTOBIOMODULATION EFFECTS FOR OLD ADULTS WITH COGNITIVE DECLINE USING FUNCTIONAL NEAR-INFRARED SPECTROSCOPY BEFORE TREATMENT

Kyeonggu Lee, phD candidate[1], Minyoung Chun, MS student[1], Seung-Hwan Lee, PhD[2], Chang-Hwan Im, PhD[1]
[1]Hanyang university, Seoul, Korea, Republic of, [2]Inje university, Goyang, Korea, Republic of

Introduction: With the expansion of the elderly demographic, there is growing concern on addressing neurological disorders associated with cognitive decline. Transcranial photobiomodulation (tPBM) is gaining attraction as a promising treatment modality owing to its non-invasive, safe, and portable properties, especially for patients exhibiting subjective cognitive decline (SCD) or mild cognitive impairment (MCI). However, its consistent efficacy remains yet to be established for all users. In this study, we hypothesized that the effectiveness of tPBM may be predictable using functional near-infrared spectroscopy (fNIRS), before starting the tPBM treatment.

Materials / Methods: The psychiatrist assessed the cognitive function of 41 elder adults with cognitive decline who underwent tPBM stimulation more than 25 times over a span of three months. Using the Global Cognitive Score (GCS), significant pre- and post-stimulation changes were measured. A ΔGCS threshold greater than 0.5 was set as the threshold for determining the effectiveness of the stimulation [1,2]. The fNIRS data recorded during the resting state, verbal memory task, and Stroop task were preprocessed, with feature extraction covering temporal (statistical values) and spatial (connectivity values) features. The prediction accuracy and F1 score were subsequently assessed based on three distinct feature groups: temporal attributes, spatial attributes, and a combination of both. To predict treatment efficacy, a regularized support vector machine (rSVM) was utilized, and the validation was done using a leave-one-subject-out cross-validation strategy.

Results: fNIRS data recorded during the verbal memory task demonstrated the most promising results, with an accuracy of 0.8293 and an F1 score of 0.8205. The best performance was achieved when both temporal and spatial features were utilized.

Discussion: While our study has shown the feasibility of predicting tPBM efficacy using fNIRS prior to the tPBM treatment, further studies need to be conducted with additional data to generalize our results.

Conclusions: To the best of our knowledge, this study is the first to demonstrate the feasibility of predicting tPBM efficacy for elderly adults with cognitive decline by employing machine learning algorithms in conjunction with fNIRS data recorded before the tPBM treatment. It is expected that our approach would contribute to the reduction of the burden on patients and increase of cost-effectiveness in the treatment of cognitive decline.

Supplemental Data:

❖ ***Performance***

T: Temporal feature / S: Spatial feature

	Resting-state			Stroop task			Recognition task		
	T	S	T+S	T	S	T+S	T	S	T+S
Accuracy (%)	**70.73**	41.46	39.02	48.78	**75.61**	58.54	78.05	63.41	**82.93**
F1-score	**0.7143**	0.4	0.4186	0.6557	**0.7619**	0.5854	0.7805	0.6512	**82.05**
Sensitivity (%)	71.43	38.1	42.86	95.24	76.19	57.14	76.19	66.67	76.19
Specificity (%)	70	45	35	0	75	60	80	60	90
# feature	5	13	3	1	9	18	18	15	5

References: 1. Heseltine, P.N., et al., *Randomized double-blind placebo-controlled trial of peptide T for HIV-associated cognitive impairment.* Archives of neurology, 1998. **55**(1): p. 41-51. 2. McKhann, G.M., et al., *Cognitive outcome after coronary artery bypass: a one-year prospective study.* The Annals of thoracic surgery, 1997. **63**(2): p. 510-515.

Acknowledgements: The support of the Korea Medical Device Development Fund grant funded by the Korean government (the Ministry of Science and ICT, the Ministry of Trade, Industry, and Energy, the Ministry of Health & Welfare, Republic of Korea, the Ministry of Food and Drug Safety) (Project Number: 202013B10) for this project is gratefully acknowledged.

Learning Objectives: 1. Demonstration of the efficacy of tPBM with various cognitive tests. 2. Providing the technique to reduce the burden on patients with cognitive decline. 3. Providing the technique to enhance the cost-effectiveness of the tPBM treatment.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O143

Oral Presentations
STIMULATION FOR EPILEPSY
16-05-2024 10:30 - 11:20

OPTOGENETIC CLOSED-LOOP THERAPY FOR INTERICTAL DISCHARGES IN A MOUSE MODEL

Elisabeth Adetta Heynold, MD, Thomas Hainmueller, MD, PhD, György Buzsàki, MD, PhD
NYU Langone Health, Neuroscience, New York City, United States of America

Introduction: The neurocognitive impairment in temporal lobe epilepsy and early Alzheimer's is linked to interictal epileptiform discharges (IEDs) in the hippocampus[1–4] . The hippocampus comprises different anatomical subfields that are connected predominantly in a feed-forward loop in which excitation from the entorhinal cortex reaches the dentate gyrus and then progresses through the CA2/3 and 1 areas. In addition to the specialized principal cells in the respective hippocampal subfields, different types of GABAergic interneurons help to regulate and coordinate hippocampal networks[7]. Specifically, dendritic inhibition from somatostatin-expressing interneurons and soma-inhibiting, parvalbumin-expressing interneurons may have differential impact on neuronal network functions. The DG is thought to be a 'gate' for both pathological, hypersynchronized activity as well as physiological activity. The most important of the latter is the 'dentate spike' which plays an important role in memory consolidation and maintenance [8–10]. This project has two objectives: First describing the effect of optogenetic activation of different classes of inhibitory interneurons in the dentate gyrus. Second explore the feasibility of selectively inhibiting pathological but not physiological activity patterns.

Materials / Methods: In healthy mice the two different classes of inhibitory interneurons were selectively transfected with a light-excitatory opsin. Subsequently these mice were implanted with high density silicon probes and optic fibers. Interneurons were stimulated optogenetically while the entire network was recorded with the silicon probes. We used this recording setup to establish closed-loop coupling between recorded electrophysiological events and optogenetic stimulation.

Results: While parvalbumin-interneuron stimulation has a modest and biphasic effect, optogenetic somatostatin-interneuron activation causes a drastic reduction in dentate spike rate. Preliminary results indicate that closed loop optogenetic interneuron stimulation with microsecond precision is feasible and can be used to powerfully suppress hippocampal population activity. It may therefore be a promising tool to disrupt pathological network activation during IEDs.

Discussion: We proved that physiological patterns of hippocampal activity can reliably be altered and that closed-loop stimulation of hippocampal interneurons contingent on physiological activity patterns is feasible. We aim to apply this knowledge in disease mouse models displaying IEDs with the ultimate goal of developing a closed-loop optogenetic treatment approach to disrupt IEDs and improve memory.

Conclusions: While taking optogenetics to the human hippocampus is still far it might open up an avenue of new treatment options for cognitive impairment.

Supplemental Data:

References: 1. Soula, M. *et al.* Interictal epileptiform discharges affect memory in an Alzheimer's Disease mouse model. 2023.02.15.528683 Preprint at https://doi.org/10.1101/2023.02.15.528683 (2023). 2. Warsi, N. M. *et al.* Which is more deleterious to cognitive performance? Interictal epileptiform discharges vs anti-seizure medication. *Epilepsia* **64**, (2023). 3. Henin, S. *et al.* Spatiotemporal dynamics between interictal epileptiform discharges and ripples during associative memory processing. *Brain* **144**, 1590–1602 (2021). 4. Kleen, J. K. *et al.* Hippocampal interictal epileptiform activity disrupts cognition in humans. *Neurology* **81**, 18–24 (2013). 5. Buzsáki, G. Two-stage model of memory trace formation: A role for "noisy" brain states. *Neuroscience* **31**, 551–570

(1989). 6. Hainmueller, T. & Bartos, M. Dentate gyrus circuits for encoding, retrieval and discrimination of episodic memories. *Nat Rev Neurosci* **21**, 153–168 (2020). 7. Roux, L. & Buzsáki, G. Tasks for inhibitory interneurons in intact brain circuits. *Neuropharmacology* **0**, 10–23 (2015). 8. Lensu, S., Waselius, T., Penttonen, M. & Nokia, M. S. Dentate spikes and learning: disrupting hippocampal function during memory consolidation can improve pattern separation. *Journal of Neurophysiology* **121**, 131–139 (2019). 9. Bragin, A., Jandó, G., Nádasdy, Z., van Landeghem, M. & Buzsáki, G. Dentate EEG spikes and associated interneuronal population bursts in the hippocampal hilar region of the rat. *J Neurophysiol* **73**, 1691–1705 (1995). 10. Dvorak, D., Chung, A., Park, E. H. & Fenton, A. A. Dentate spikes and external control of hippocampal function. *Cell Reports* **36**, 109497 (2021).

Acknowledgements:

Learning Objectives: IEDs are deleterious and should be considered a treatment target in temporal lobe epilepsy and Alzheimer's. A subset of inhibitory interneurons in the dentate gyrus could be selectively targeted by a optogenetic closed-loop system to improve cognition.

Financial Disclosures: no significant relationships

Disclosure: No significant relationships.

O144

Oral Presentations
STIMULATION FOR EPILEPSY
16-05-2024 10:30 - 11:20

DEVELOPMENT OF CHRONIC VAGUS NERVE STIMULATION CUFF ELECTRODES IN MICE

Chris Phillips, MSc
University of Texas at Dallas, Neuroscience, Richardson, United States of America

Introduction: Vagus Nerve Stimulation (VNS) is an FDA-approved therapeutic option used to treat epilepsy, cortical injuries, and depression. While pre-clinical VNS models have been broadly studied in rats, few labs have studied the efficacy of VNS in mice due to the challenges associated with their small size. In this study, we aim to develop an in-house, low-cost chronic VNS cuff electrode in mice.

Materials / Methods: Miniaturized mouse VNS cuff electrodes were constructed using a similar approach to rat VNS cuff electrodes that have been previously published from our lab Briefly, 1.5 mm of micro-renathane tubing (BrainTree Scientific, MRE 040320, Diameter 1.016 mm) is cut and used to form the cuff. Two 5 cm silk sutures are placed bilaterally at the center of the tubing and secured with UV glue, allowing for flexible manipulation during cuff assembly. Next, two platinum-iridium wire (MEDWIRE, Part NO: 10IR9/49T) leads are de-insulated and secured in the cuff with UV glue. Lastly, the platinum-iridium wires are soldered to headcaps (Omnetics).

Results: Our preliminary results suggest that vagus-mediated physiological responses can be reliably evoked using the miniaturized cuffs at the time of implantation. To test the long-term viability of our cuff electrodes, mice were chronically implanted with the miniaturized devices and VNS-evoked physiological responses were re-tested under anesthesia every 2 weeks for up to 2 months.

Discussion: Several modifications to the original cuff design were made to improve the long-term functionality of the miniaturized cuffs.

Conclusions: Successful development of a low-cost VNS cuff electrodes for mice will enable the leveraging of a broad range of genetic tools to better understand the mechanism of VNS.

Supplemental Data: N/A

References: 1. Sanchez, C. et al. (2020). Preparation of peripheral nerve stimulation electrodes for chronic implantation in rats. *Journal of Visualized Experiments*

Acknowledgements: This work is funded by R21 DA055166 and R01 NS126816. We thank Chris Driskill and Sven Kroener for their help in data collection and interpretation.

Learning Objectives: 1. We question whether we can develop in-house, low cost mouse VNS cuff electrodes. 2. We question whether we can evoke physiological responses as seen in rat models of VNS with our miniturized cuff electrodes. 3. We question the long-term stability of chronic VNS cuff electrodes.

Financial Disclosures: 'No significant relationships'

Disclosure: No significant relationships.

O145

Oral Presentations
STIMULATION FOR EPILEPSY
16-05-2024 10:30 - 11:20

VAGUS NERVE STIMULATION LEAD DURABILITY: REAL-WORLD INSIGHTS FROM AN EXTENSIVE FRENCH MONO-OPERATOR SERIES.

Sami Barrit, MD[1], Maxine Dibue-Adjei, PhD[2], Steffen Fetzer, PhD[3], Romain Carron, MD, PhD[4]
[1]Université Libre de Bruxelles, Neurosurgery, Brussels, Belgium, [2]Brandenburg Medical School — Berlin Campus, Centre For Palliative And Neuro-palliative Care, Brandenburg, Germany, [3]LivaNova, Medical Affairs Neuromodulation, London, United Kingdom, [4]Aix-Marseille University/INSERM — APHM — Timone Hospital, Functional, And Stereotactic Neurosurgery,, Marseille, France

Introduction: Vagus nerve stimulation (VNS) for drug-resistant epilepsy and depression treatment can be disrupted by lead failures. With over 130,000 VNS implants worldwide, understanding lead durability is crucial. However, the multifaceted interplay of technical and surgical variables introduces confounding factors. A mono-operator, single-center series can offer insights to mitigate these complexities.

Materials / Methods: We retrieved all VNS-related surgeries performed at a French national referral center from November 30, 2011, to March 30, 2023. All surgeries performed according to the manufacturer's guidelines by one experienced surgeon, whose detailed surgical technique has been thoroughly documented in a previous technical note, were selected for analysis. Survival analysis was conducted using the Kaplan-Meier estimator.

Results: 267 patients (144 females; average age 36.56 years, SD: 12.92) underwent 340 surgeries, which included 233 primo-implantations, 74 generator replacements (four attributed to generator failures and one due to infection), 22 system removals (with one instance of lead fracture), three complete replacements (all resulting from lead failures, of which two were diagnosed as lead fractures), two lead replacements (both stemming from lead failures with one being a lead fracture), and three revisions (each undertaken for generator repositioning for patient comfort). No other perioperative complications, such as vagus nerve or vascular injury, hematoma, or lasting laryngeal dysfunction, were found. Of these patients, 230 had their primo-implantation by the same neurosurgeon. Four cases of lead failure were documented, all associated with abnormally high impedance (i.e., above 10,000 ohms). The cumulative 5-year and 10-year lead survival probabilities were 98.14% (95% CI: 96.06% - 100%) and 97.33% (95% CI: 94.75% - 100%), with a lead failure rate of 0.00295 events per DY.

case number	sex	putative cause retrieved	VNS surgery (n)	time to last surgery + lead lifetime
1	M	none	2	3 years (idem)
2	M	surgical complication	3	3 months + 4 years
3	M	fatigue/kinking	3	1 month + 5 years
4	F	pin-disconnection	3	9 months + 5.5 years

Discussion: While technological advancements may enhance lead durability, the potential role of surgical practices is raised. Surgeons, while considering the durability of newer lead models, must also navigate the ease of implantation and their own surgical preferences and abilities. Balancing lead durability with other pivotal factors, such as minimal vagus nerve manipulation, is crucial to optimizing VNS implementation.

Conclusions: Our study emphasizes the necessity for clinicians to adopt surgical best practices and stay versed in the latest models to optimize lead longevity and patient outcomes.

Supplemental Data:

References: 1. Rychlicki F, Zamponi N, Cesaroni E, Corpaci L, Trignani R, Ducati A and Scerrati M (2006). Complications of vagal nerve stimulation for epilepsy in children. Neurosurg Rev; 29: 103–7 2. Spuck S, Tronnier V, Orosz I, Schönweiler R, Sepehrnia A, Nowak G and Sperner J (2010). Operative and Technical Complications of Vagus Nerve Stimulator Implantation. Neurosurgery 67: 489-94 3. Hamdi, H., Spatola, G., Lagarde, S., McGonigal, A., Paz-Paredes, A., Bizeau, A., Bartolomei, F., & Carron, R. (2019). Use of Polyvinyl Alcohol Sponge Cubes for Vagal Nerve Stimulation: A Suggestion for the Wrapping Step. Technical Note and Step-by-Step Operative Technique. In Operative Neurosurgery (Vol. 18, Issue 5, pp. 487–495). Ovid Technologies (Wolters Kluwer Health). https://doi.org/10.1093/ons/opz227 4. Fetzer St. & Ortler M. (2021). A simple electrical approach to diagnosing a suspected lead break in patients with implanted vagus nerve stimulators – Technical note. Clinical Neurology and Neurosurgery 206:106707

Acknowledgements: The support of LivaNova PLC (London, United Kingdom) for this project is gratefully acknowledged.

Learning Objectives: 1. Recognize the Significance of VNS Lead Durability: Understand the implications of lead failures and the challenges posed by confounding factors in real-world settings. **2. Assess the Role of Surgical Practices:** Appreciate the influence of surgical techniques on lead longevity and the balance with other surgical considerations. **3. Optimize VNS Implementation:** Learn the importance of adopting surgical best practices and staying updated with the latest lead models to improve patient outcomes.

Financial Disclosures: Concerning authors: BARRIT Sami; CARRON, Romain a) LivaNova PLC b) For what role? Consultant & Education / Research c) Level of Compensation? $501 - $5,000 USD Concerning authors: DIBUE-ADJEI, Maxine; FETZER, Steffen a) LivaNova PLC b) For what role? Company Employee
c) Level of Compensation? $501 - $5,000 USD (monthly wage)

Disclosure: No significant relationships.

O146

Oral Presentations
STIMULATION FOR EPILEPSY
16-05-2024 10:30 - 11:20

LONG-TERM ANTISEIZURE EFFECTS OF EPICTRANIAL FOCAL CORTEX STIMULATION (FCS) USING THE EASEE SYSTEM IN PHARMACORESISTANT FOCAL EPILEPSY

Andreas Schulze-Bonhage, MD[1], Martin Hirsch, MD[1], Susanne Knake, MD[2], Elisabeth Kaufmann, MD[3], Josua Kegele, MD[4], Michael Rademacher, MD[5], Kristl Vonck, MD[6], Volker Coenen, MD[7], Martin Glaser, MD[8], Carolin Jenkner, PhD[9], Sergiu Groppa, MD[10], Yaroslaw Winter, MD[11]
[1]University Hospital Freiburg, Epileptology, Freiburg, Germany, [2]University Hospital Marburg, Neurology, Marburg, Germany, [3]Ludwig-Maximilan's University, Munich,, Neurology, Munich, Germany, [4]University of Tübingen, Department Of Neurology And Epileptology,, Tuebingen, Germany, [5]University of Bonn, Epileptology, Bonn, Germany, [6]University of Ghent, Neurology, Ghent, Belgium, [7]University of Freiburg, Neurosurgery, Freiburg, Germany, [8]University of Mainz, Neurosurgery, Mainz, Germany, [9]University of Freiburg, Study Center, University Medical Center, Freiburg, Germany, [10]University of Mainz, Neurology, Mainz, Germany, [11]University of Mainz, Epilepsy Center, Neurology, Mainz, Germany

Introduction: One third of patients with focal epilepsy are pharmacoresistant, and only a small proportion are candidates for epilepsy surgery. Stimulation of the epileptic focus has been reported to effectively reduce seizure frequency using an intracranially implanted device. We here for the first time report long-term treatment efficacy of a novel implantable, CE-certified device allowing to perform epicranial focal cortex stimulation based on the pooled-analysis of two prospective, multicenter, single-arm trials (EASEE II and PIMIDES I).

Materials / Methods: In both trials, a total of 33 patients (18 male, 15 female, age 18-75 y, mean age 34.6 y) from seven epilepsy centers in Germany and Belgium were implanted with a neurostimulation system (EASEE®) consisting of a pulse generator and a 5-channel electrode array. The system delivers FCS via the stimulation electrode implanted epicranially above the individual epileptic focus region. Stimulation was turned on in an unblinded fashion one month after implantation and consisted of a combination of high-frequency stimulation (HFS) and a direct current–like stimulation (DLS) for 20 min/day. Patients were followed for 2 years in terms of monthly responder rate (RR: ≥ 50% seizure frequency reduction), monthly seizure frequency (SF), and safety reporting.

Results: 81% of patients initially stimulated choose to continue epicranial focus stimulation for a period of 2 years. The responder rate was 41.4 % (95% CI, 23.5%-61.1%; n=29) at 1 year follow-up and 65.4 % at 2 years follow-up (95% CI, 44.3%-82.8%; n=26).
The median monthly seizure frequency decreased from a median baseline of 12/month, to 8/month at 1 year and to 5/month at 1.5 and 2 years follow-up, corresponding to a median seizure frequency reduction by 33% at 12 months follow-up (n=29), and 68% after 18 and 24 months follow-up (n=26). There were no serious adverse events considered related to the neurostimulation procedure also during the prolonged stimulation period.

Discussion: This pooled-analysis of long-term outcomes from two unblinded, prospective trials with FCS corroborate a reduction in seizure frequency and increase in responder rate over a period of 2 years of treatment, consistent with early positive outcomes of neuromodulation with this novel treatment approach in focal epilepsy (Schulze-Bonhage et al., JAMA Neurology 2023).

Conclusions: Long-term outcomes suggest that epicranial electrical stimulation of the epileptic focus using the EASEE System is an effective and well tolerated new treatment approach for patients with pharmacoresistant focal epilepsy.

Supplemental Data:

References: Schulze-Bonhage A, Hirsch M, Knake S, Kaufmann E, Kegele J, Rademacher M, Vonck K, Coenen VA, Glaser M, Jenkner C, Winter Y, Groppa S; EASEE Study Group. Focal Cortex Stimulation With a Novel Implantable Device and Antiseizure Outcomes in 2 Prospective Multicenter Single-Arm Trials. JAMA Neurol. 2023;80:588-596.

Acknowledgements: The support by BFARM, Country Baden-Württemberg and of the Company PRECISIS for support of this project is gratefully acknowledged.

Learning Objectives: 1. Epicranial Focal Cortex Stimulation is a new CE-certified neurostimulation approach used in European Countries since the end of 2022 which has antiseizure effects with stimulations of the focus area is stimulated transcranially via an implanted electrode array.
2. Long-term outcomes suggest a gradual neuromodulatory effect with growing responder rates over a period of 2 years of neurostimulation.
3. The safety profiele of epictranial Focal Cortex Stimulation is excellent with absent serious adverse events considered related to device implantation or neurostimulation.

Financial Disclosures: The first and presenting author and co-authors except Dr. Jenkner have received research support for performing two clinical trials using the EASEE device performing Epicranial Focal Cortex Stimulation.

Disclosure: No significant relationships.

O147

Oral Presentations
STIMULATION FOR EPILEPSY
16-05-2024 10:30 - 11:20

LONG-TERM EFFICACY OF PALLIDAL STIMULATION IN 20 PATIENTS WITH HUNTINGTON DISEASE

Witold Libionka, MD, PhD
Medical University of Gdansk, Department Of Neurosurgery, Gdansk, Poland

Introduction: Deep brain stimulation (DBS) is a well established treatment for hyperkinetic movement disorders. However, its role in Huntington disease (HD) requires further studies to establish optimal anatomical target and timing of the procedure. The aim of this prospective study is to assess effectiveness and safety of DBS in HD and to show how target selection and stimulation parameters affect motor and non-motor symptoms of HD.

Materials / Methods: 20 patients with genetically confirmed HD, with motor symptoms resistant to medications (15 women, 5 men, aged 27-50 years), who underwent DBS with octapolar electrodes implanted in the GPi-GPe, were followed up for 12-96 months. Symptoms were present 3-8 years before surgery and included choreatic movements (16 cases), muscle rigidity (4), dysarthria (16), dysphagia (11), gait disturbance (11), mild dementia (16). Patients with psychiatric symptoms were excluded. Surgical procedures were performed under local anesthesia, with microrecording and macrostimulation, using frame-based stereotaxy. Assessments with UHDRS and neuropsychologic tests were performed before and 1, 3, 12, 24, 36, 48, 60, 72, 84 and 96 months after surgery. The study was approved by ethics committee.

Results: In all patients significant motor improvement was observed during the stimulation at the consecutive follow-up examinations (motor score improved on average of 35-45%; chorea of 51-62%). We also noted reduction of dysarthria (12 patients), dysphagia (6), imbalance (6) and subcortical dementia (2). There were no hemorrhagic or infectious complications. GPi-GPe stimulation at 30-130 Hz, 65-110 μs and 1,5-3,5 mA was optimal.

Discussion: In the early phase of HD loss of striatal neurons disinhibits GPe and manifests as chorea. Later, loss of direct pathway neurons disinhibits GPi leading to akinesia. Therefore, a potential therapeutic approach for chorea is GPe inhibitory stimulation. However, majority of reports investigated a historically ablated target - GPi. Chorea reduction was generally immediate and maintained during the follow up. The effects on other symptoms were inconsistent. In recent randomized trial comparing GPi- and GPe-DBS, the latter was more effective. Similarly, in GPi-DBS active contacts were more often located dorsally, at GPi-GPe border, as expected based on the patomechanism. The authors proposed combined GPi-GPe stimulation with single octapolar electrode using current-steering to cover both targets and personalize therapy without increasing the surgical risk. Importantly, the observed improvement included not only motor, but also cognitive symptoms. This is in line with studies on GPe-DBS in HD.

Conclusions: Pallidal stimulation is an effective and safe long-term treatment for motor symptoms in Huntington disease.

Supplemental Data:

References: 1. Zittel S et al. Prospective evaluation of Globus pallidus internus deep brain stimulation in Huntington's disease. Parkinsonism Relat Disord. 2018;51:96-100. 2. Wojtecki L et al. Deep Brain Stimulation in Huntington's Disease-Preliminary Evidence on Pathophysiology, Efficacy and Safety. Brain Sci. 2016;6:E38. 3. Delorme C et al. Deep brain stimulation of the internal pallidum in Huntington's disease patients: clinical outcome and neuronal firing patterns. J Neurol. 2016;263:290-298. 4. Gonzalez V et al. Deep brain stimulation for Huntington's disease: long-term results of a prospective open-label study. J Neurosurg. 2014;121:114-22. 5. Velez-Lago FM et al.

Differential and better response to deep brain stimulation of chorea compared to dystonia in Huntington's disease. Stereotact Funct Neurosurg. 2013;91:129-33. 6. Moro E et al. Bilateral globus pallidus stimulation for Huntington's disease. Ann Neurol. 2004;56:290-4.

Acknowledgements:

Learning Objectives: 1. To support efficacy of DBS in drug-resistant chorea in Huntington disease. 2. To support use of intraoperative microelectrode recording and macrostimulation as a method of optimalization of targeting in difficult chorea cases. 3. To support safety of DBS in Huntington disease regarding dementia and psychiatric symptoms.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O148

Oral Presentations
TOPICS IN NON-INVASIVE STIMULATION
16-05-2024 10:30 - 11:20

TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION (TAVNS): EFFECTS ON ATTENTION, CONCENTRATION AND REACTION TIMES IN HEALTHY VOLUNTEERS

Zane Dastoor, 4th Year Medical Student[1], Tiago Costa, MSc[1,2,3], Billy Smith, MSc[1], Hannah Cave, BSc (Hons)[1,2], Sharmin Ahmed, MBBS[1], Sarah Gascoigne, MSc[1], Yujiang Wang, PhD[1], Mark Baker, MBBS, PhD[1,4], Stuart Watson, MBBS, MD[1,2], Hamish McAllister-Williams, MBBS, MD, PhD[1,2,3]
[1]Newcastle University, Newcastle upon Tyne, United Kingdom, [2]Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust, Newcastle upon Tyne, United Kingdom, [3]National Institute for Health and Care Research (NIHR) Newcastle Biomedical Research Centre, Newcastle Upon Tyne, United Kingdom, [4]Newcastle Hospitals NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom

Introduction: Transcutaneous auricular vagus nerve stimulation (taVNS) is a non-invasive neurostimulation technique, associated with improvements in cognitive measures and depressive symptoms in small samples (1,2). The mechanisms for this are not clear. Cognitive symptoms are common and debilitating in severe depression, but we have no targeted treatments for this. It is therefore clinically relevant to explore the associations between taVNS and cognition. We aimed to explore the effects of taVNS on cognitive performance of healthy volunteers, focusing on measures of reaction time and working memory.

Materials / Methods: A double-blind, randomized, sham-controlled, cross-over study of at-home taVNS in healthy volunteers, over a 7-day period. Each active or sham stimulation period was self-administered for 1 hour, in both morning and evening, over 2 consecutive days, followed by a 24-hours washout period before crossing over to the other intervention. Cognition was measured using the THINC-it tool, at baseline and after each 2-day intervention period. THINC-it includes a self-reported measure of cognition (Perceived Deficits Questionnaire for depression 5-item version, PDQ5) and gamifies 4 standardised cognitive tasks: Choice reaction time (CRT), N-Back, Digit Symbol Substitution Test (DSST), Trail Making Test-part B (TMT-B). We compared baseline with post-intervention measures using paired samples t-test and linear mixed-effects models.

Results: In 18 participants, 8 started with active leads. When compared to baseline, PDQ5 scores improved (decreased) after both active and sham periods but differences were not significant. For CRT, when compared to mean baseline (441.3ms, SD = 106.9ms), CRT average reaction times significantly improved post-active (392.9ms, SD=80.7ms; $p<0.05$) but not post-sham stimulation (408.3ms, SD=67.2ms; p=ns). Compared to baseline, both N-Back and DSST reaction times showed significant and larger average reductions post-active stimulation, relative to sham stimulation, although post-sham measures also significantly reduced from baseline and confidence intervals partially overlapped with post-active stimulation. TMT-B completing time had greater reduction post-sham than post-active stimulation, with both measures being significant.

Discussion: Objective cognitive measures such as reaction times (measured with CRT) and working memory (measured with DSST and N-Back) appear to have significant improvements, with taVNS. Sham stimulation was also associated to significant reductions from baseline on DSST and N-Back reaction times, albeit to a smaller magnitude. Conversely, subjective measures (PDQ5) did not show significant improvements.

Conclusions: In healthy volunteers, there were significant improvements with active taVNS on reaction times and working memory. The mixed-effects model accounted for effects of repeated testing, group and period. These results require replication in larger samples.

Supplemental Data: Raw data is available on reasonable request to Dr Tiago Costa (Tiago.da-Silva-Costa@newcastle.ac.uk). Below are tables for the paired sample t-tests.

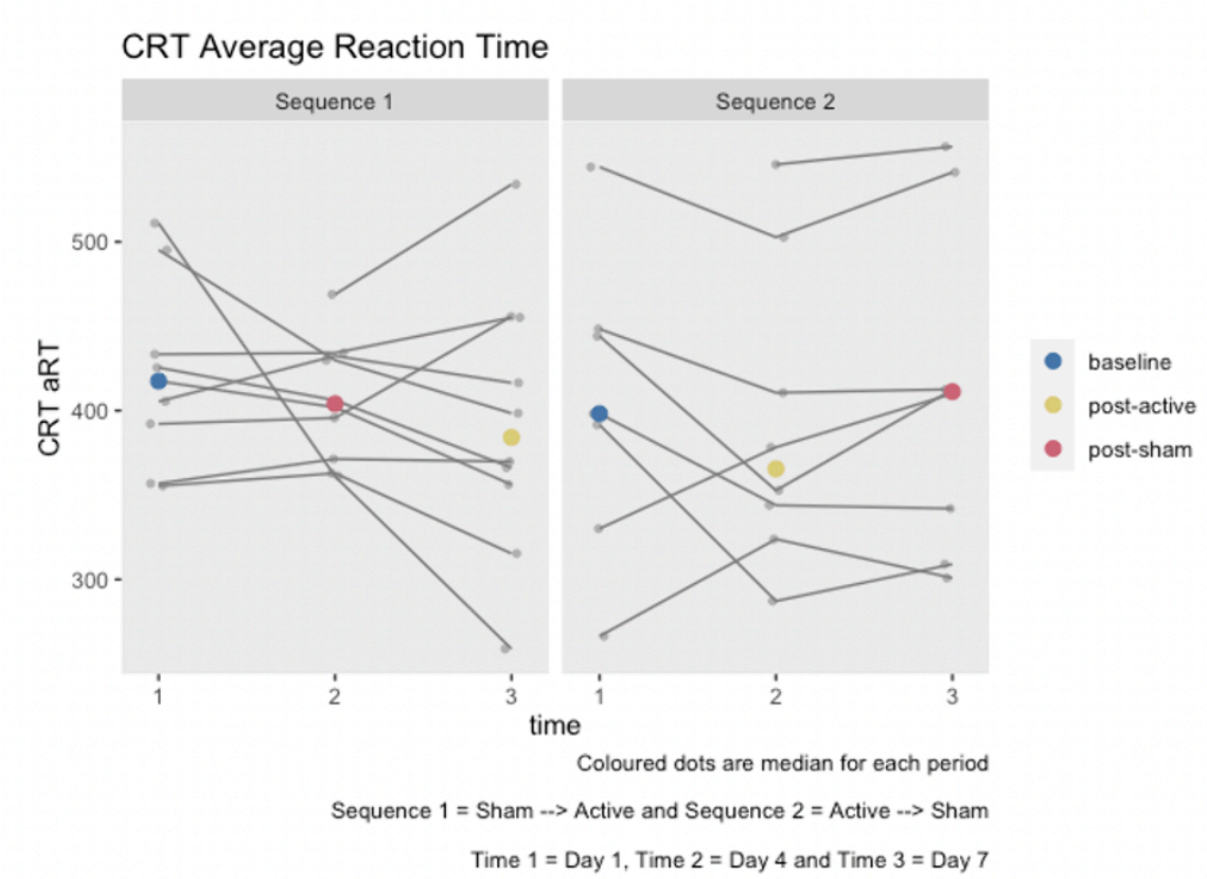
Table showing the data used for the paired samples t-test using THINC-it to compare post-active taVNS (trans-auricular vagus nerve stimulation) and post-sham with baseline

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	PDQ-5 Baseline	9.89	18	4.296	1.013
	PDQ-5 A	9.56	18	3.761	.886
Pair 2	PDQ-5 Baseline	9.89	18	4.296	1.013
	PDQ-5 S	9.50	18	4.369	1.030
Pair 3	CRT Baseline (ms)	441.3400	18	106.97599	25.21448
	CRT A (ms)	392.8528	18	80.73784	19.03009
Pair 4	CRT Baseline (ms)	441.3400	18	106.97599	25.21448
	CRT S (ms)	408.2761	18	67.15020	15.82745
Pair 5	N-back Baseline (ms)	1034.9572	18	258.95745	61.03686
	N-back A (ms)	804.0589	18	138.31736	32.60171
Pair 6	N-back Baseline (ms)	1034.9572	18	258.95745	61.03686
	N-back S (ms)	842.9639	18	144.89978	34.15321
Pair 7	DSST Baseline (ms)	1765.8622	18	293.42578	69.16112
	DSST A (ms)	1578.6317	18	275.85805	65.02036
Pair 8	DSST Baseline (ms)	1765.8622	18	293.42578	69.16112
	DSST-S (ms)	1603.5633	18	187.17965	44.11867
Pair 9	TMT-B baseline (ms)	23649.22	18	9947.557	2344.662
	TMT-B A (ms)	18137.39	18	5030.631	1185.731
Pair 10	TMT-B baseline (ms)	23649.22	18	9947.557	2344.662
	TMT-S (ms)	17651.33	18	5430.867	1280.068

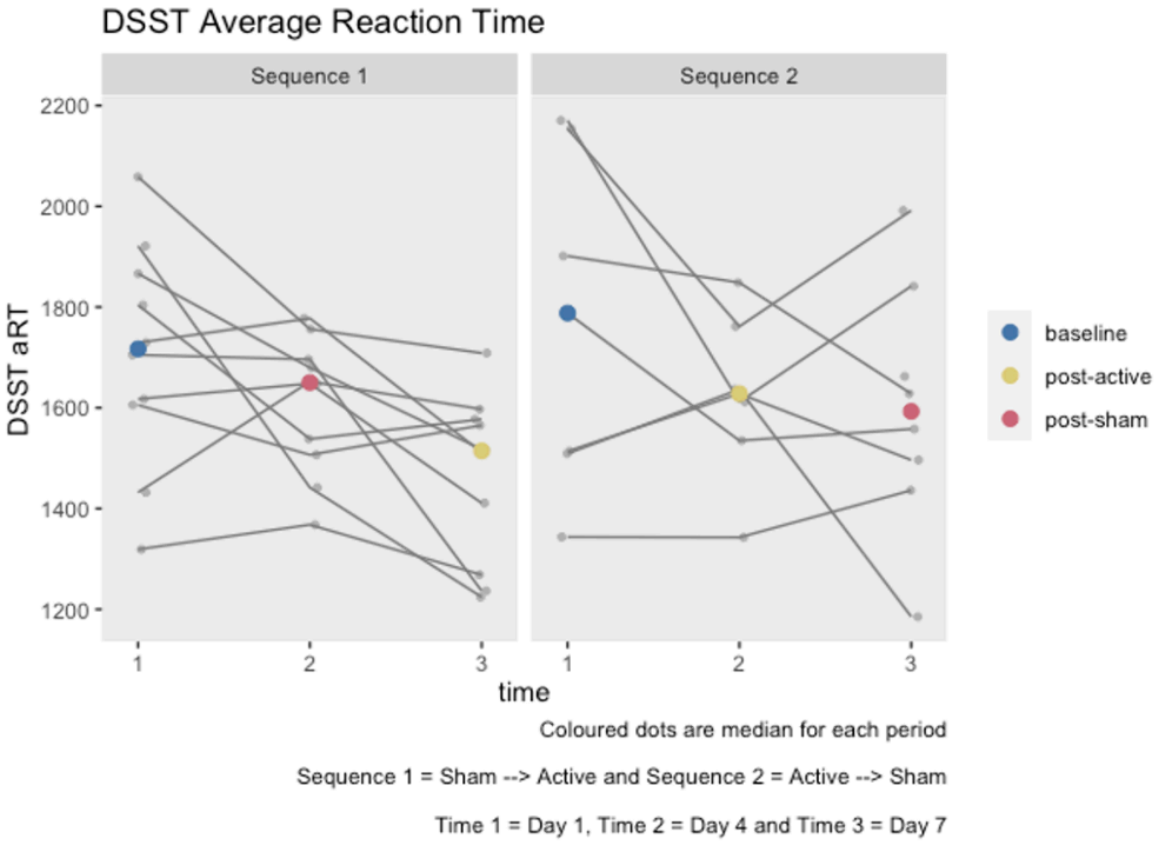
Paired Samples Test of THINC-it data comparing post-active taVNS (trans-auricular vagus nerve stimulation) and post-sham with baseline

		Paired Differences							Significance	
					95% Confidence Interval					
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper	t	df	One-Sided p	Two-Sided p
Pair 1	PDQ-5 Baseline - PDQ-5 A	.333	1.782	.420	-.553	1.220	.793	17	.219	.438
Pair 2	PDQ-5 Baseline - PDQ-5 S	.389	1.720	.405	-.466	1.244	.959	17	.175	.351
Pair 3	CRT Baseline (ms) - CRT A (ms)	48.48722	82.20882	19.37681	7.60574	89.36871	2.502	17	.011	.023
Pair 4	CRT Baseline (ms) - CRT S (ms)	33.06389	66.90759	15.77027	-.20847	66.33625	2.097	17	.026	.051
Pair 5	N-back Baseline (ms) - N-back A (ms)	230.89833	188.96323	44.53906	136.92913	324.86753	5.184	17	<.001	<.001
Pair 6	N-back Baseline (ms) - N-back S (ms)	191.99333	214.04601	50.45113	85.55076	298.43591	3.806	17	<.001	.001
Pair 7	DSST Baseline (ms) - DSST A (ms)	187.23056	249.77667	58.87293	63.01954	311.44157	3.180	17	.003	.005
Pair 8	DSST Baseline (ms) - DSST-S (ms)	162.29889	225.05300	53.04550	50.38266	274.21511	3.060	17	.004	.007
Pair 9	TMT-B baseline (ms) - TMT-B A (ms)	5511.833	9768.585	2302.478	654.030	10369.637	2.394	17	.014	.028
Pair 10	TMT-B baseline (ms) - TMT-S (ms)	5997.889	8718.456	2054.960	1662.303	10333.475	2.919	17	.005	.010

Below are the mixed effects model tables and graph for elements of THINC-it


CRT Average Reaction Time
Sequence 1
Sequence 2
CRT aRT
500
400
300
1
2
3
time
baseline
post-active
post-sham
Coloured dots are median for each period
Sequence 1 = Sham --> Active and Sequence 2 = Active --> Sham
Time 1 = Day 1, Time 2 = Day 4 and Time 3 = Day 7

	CRT average reaction time		
Predictors	*Estimates*	*CI*	*p*
(Intercept)	428.30	325.56 – 531.05	**<0.001**
rxlab [post-active]	-33.58	-63.05 – -4.11	**0.026**
rxlab [post-sham]	-18.16	-47.63 – 11.32	0.221
grp	-1.30	-67.55 – 64.96	0.969
Random Effects			
σ^2	1772.86		
$\tau_{00\ id}$	4192.31		
ICC	0.70		
N_{id}	18		
Observations	52		
Marginal R^2 / Conditional R^2	0.031 / 0.712		

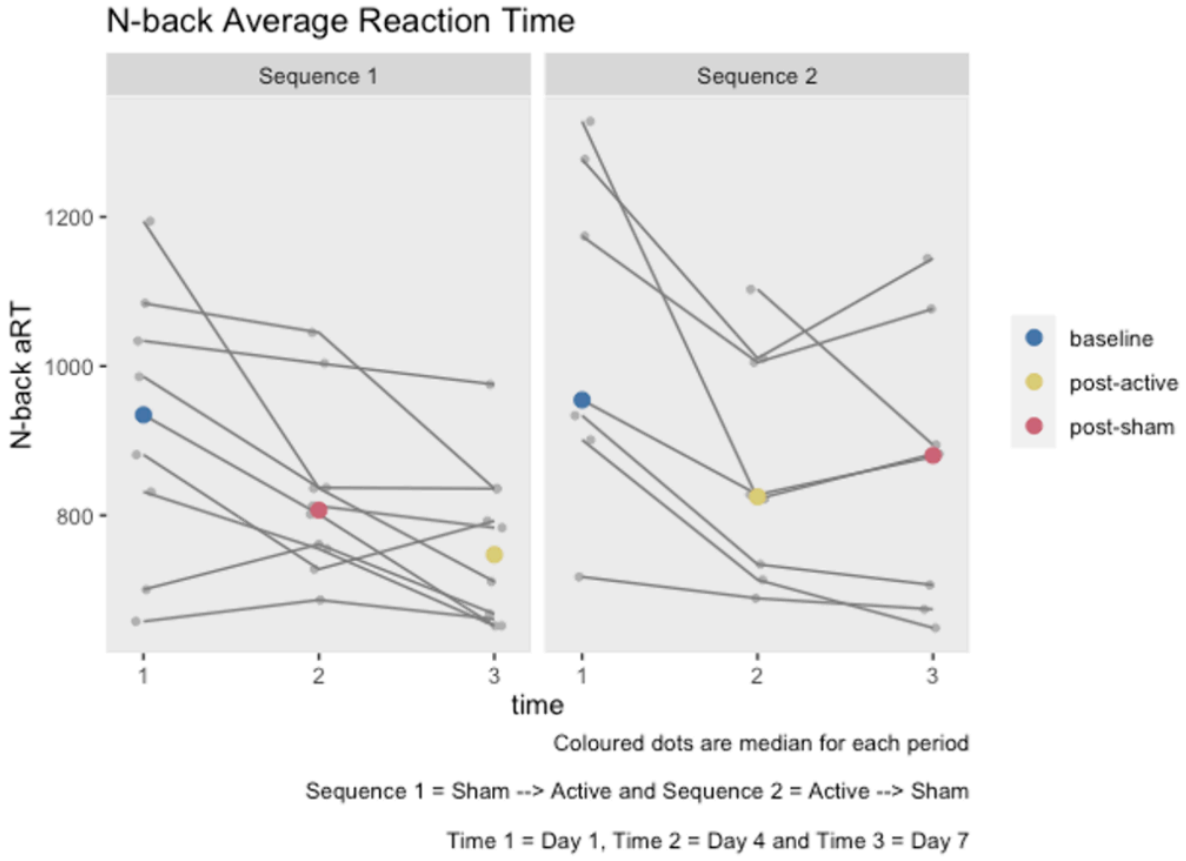


Coloured dots are median for each period

Sequence 1 = Sham --> Active and Sequence 2 = Active --> Sham

Time 1 = Day 1, Time 2 = Day 4 and Time 3 = Day 7

	DSST_aRT		
Predictors	*Estimates*	*CI*	*p*
(Intercept)	1631.33	1371.77 – 1890.90	**<0.001**
rxlab [post-active]	-203.32	-309.26 – -97.39	**<0.001**
rxlab [post-sham]	-131.00	-236.21 – -25.79	**0.016**
grp	71.47	-95.32 – 238.25	0.393
Random Effects			
σ^2	23543.10		
$\tau_{00\ id}$	21890.58		
ICC	0.48		
N_{id}	18		
Observations	52		
Marginal R^2 / Conditional R^2	0.155 / 0.562		

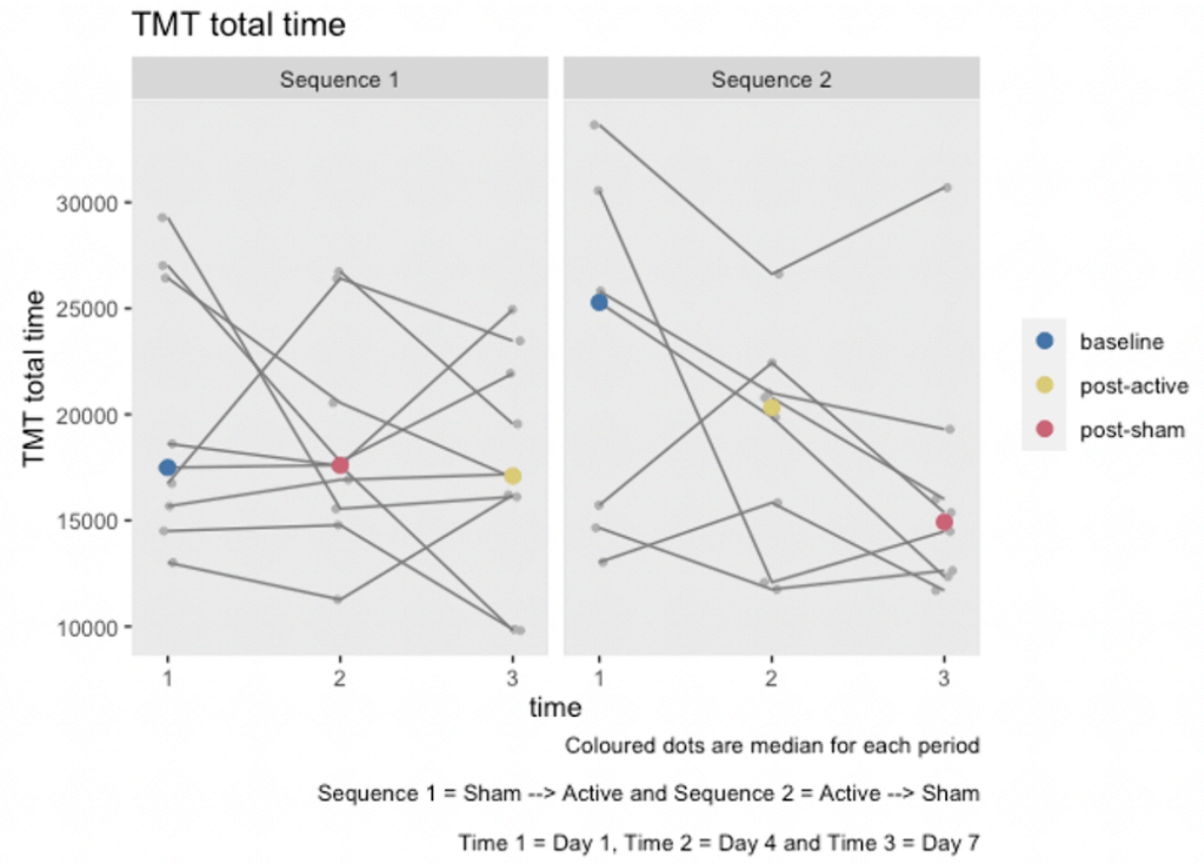


Coloured dots are median for each period

Sequence 1 = Sham --> Active and Sequence 2 = Active --> Sham

Time 1 = Day 1, Time 2 = Day 4 and Time 3 = Day 7

	Nback_aRT		
Predictors	*Estimates*	*CI*	*p*
(Intercept)	852.23	643.52 – 1060.93	**<0.001**
rxlab [post-active]	-177.99	-241.27 – -114.72	**<0.001**
rxlab [post-sham]	-139.09	-202.37 – -75.81	**<0.001**
grp	89.88	-44.46 – 224.22	0.185
Random Effects			
σ^2	8177.12		
$\tau_{00\ id}$	16924.33		
ICC	0.67		
$N_{\ id}$	18		
Observations	52		
Marginal R^2 / Conditional R^2	0.235 / 0.751		



		TMT_time	
Predictors	*Estimates*	*CI*	*p*
(Intercept)	20597.26	13527.57 – 27666.94	**<0.001**
rxlab [post-active]	-3170.77	-6308.05 – -33.48	**0.048**
rxlab [post-sham]	-3656.82	-6794.11 – -519.54	**0.023**
grp	492.16	-3969.38 – 4953.71	0.825
Random Effects			
σ^2	20223576.41		
$\tau_{00\ id}$	14755854.05		
ICC	0.42		
N_{id}	18		
Observations	52		
Marginal R^2 / Conditional R^2	0.070 / 0.462		

References: 1. Jacobs HIL, Riphagen JM, Razat CM, Wiese S, Sack AT. Transcutaneous vagus nerve stimulation boosts associative memory in older individuals. Neurobiology of Aging. 2015 May;36(5):1860–7. 2. Ridgewell C, Heaton KJ, Hildebrandt A, Couse J, Leeder T, Neumeier WH. The effects of transcutaneous auricular vagal nerve stimulation on cognition in healthy individuals: A meta-analysis. Neuropsychology. 2021 May;35(4):352–65.

Acknowledgements: This project has recieved funding from the RCPsych Academic Faculty and the Mental Health Foundation, and has been supported by the NIHR Newcastle Biomedical Research Centre.

Learning Objectives: 1. The need for a treatment option that directly targets the cognitive deficiencies associated with treatment resistant depression. 2. Demonstrating the feasibility of trans-auricle Vagal nerve stimulation as an easy to use, at home, non-invasive therapy. 3. Demonstrating the positive impact vagal nerve stimulation can have on attention and working memory in healthy individuals, leading into the potential for this helping patients with treatment resistant depression.

Financial Disclosures: No Significant relationship.

Disclosure: No significant relationships.

O149

Oral Presentations
TOPICS IN NON-INVASIVE STIMULATION
16-05-2024 10:30 - 11:20

EFFECTS OF ALPHA-TACS ON BRAIN PROCESSING OF AFFECTIVE INFORMATION AND AT REST IN FIBROMYALGIA PATIENTS

Maria Helena Coura, UGRD[1], Matheus Carvalho, UGRD[1], Yossi Zana, PhD[2], Abrahao Fontes Baptista, PhD[2], Pedro Montoya, PhD[2,3]
[1]Universidade Nove de Julho, São Paulo, Brazil, [2]Federal University of ABC, São Bernardo do Campo, Brazil, [3]University of Balearic Islands, Palma, Spain

Introduction: Fibromyalgia is a devastating chronic disease without evidence of physical alterations, which presents mainly with pain and fatigue as main symptoms, but which includes affective and cognitive alterations. Furthermore, the last decade has shown that maladaptive brain plasticity represents the relevant neurophysiological mechanism that explains the maintenance of chronic pain. Several studies have further shown that neuromodulation could be effective in improving clinical symptoms in fibromyalgia. However, it is still unclear whether non-invasive brain stimulation could reverse brain plasticity in these patients.

Materials / Methods: In the present study, we examined the effects of alpha-tACS on brain processing at rest and in response to affective stimuli. For this purpose, we assigned fibromyalgia patients to an active (n = 20) or sham (n = 20) tACS condition. The active tACS session was performed with stimulation in C3 and in F4, with an intensity of 2 mA and a frequency of 10 Hz for twenty minutes. In the sham condition, a tACS session was simulated by turning off the current after 30 seconds of stimulation. Before tACS, resting EEG and event-related potentials (ERP) elicited by affective faces were recorded from 32 electrodes. Pre-post differences in global power spectrum (theta, alpha, beta, gamma), alpha peak frequency, topographic power distribution over several brain regions of interest, brain connectivity and network characterization (degree, coefficient of global clustering, global efficiency and small world) at rest, as well as amplitudes of several ERP components will be calculated.

Results: To follow later. Preliminary results (15 active tACS vs 15 sham tACS) already indicated significant pre-post differences in the ERP amplitudes of the late-latency components elicited by affective faces, but only in fibromyalgia patients who received active tACS. Definitive results about resting EEG and the whole sample of patients will follow later.

Discussion: These preliminary findings seem to indicate that tACS could selectively modify some parameters of brain activity, particularly those involved during the processing of affective information.

Conclusions: Neuromodulation appears to cause functional brain changes that could help reverse plasticity related to chronic pain.

Acknowledgements: The financial support of São Paulo Research Foundation (FAPESP, processes: 2022/05234-9 and 2022/12916-9) (Brazil) and Spanish Ministry of Science and Innovation (PID2022-140561NB-I00) for this project are gratefully acknowledged.

Learning Objectives: - To know that fibromyalgia shows altered brain processing of affective processing, probably reflecting the maladaptive brain plasticity associated with chronic pain. - To learn that tACS at 10 Hz may cause changes in several parameters of brain activity in patients with fibromyalgia both at rest and in response to affective processing. - To show that neuromodulation might cause changes in patients' clinical symptoms through a reversal of brain plasticity.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

O150

Oral Presentations
TOPICS IN NON-INVASIVE STIMULATION
16-05-2024 10:30 - 11:20

NONINVASIVE TRANSCRANIAL ULTRASOUND DELIVERED AT PHYSIOLOGICALLY RELEVANT PULSE REPETITION FREQUENCIES DIFFERENTIALLY ACTIVE NEURONS

Emma Bortz, PhD candidate[1], Jack Sherman, PhD candidate[2], Erynne San Antonio, PhD candidate[1], Xue Han, PhD[1]
[1]Boston University, Biomedical Engineering, Boston, United States of America, [2]Boston University, Pharmacology & Experimental Therapeutics, Boston, United States of America

Introduction: Transcranial low-intensity ultrasound (US) holds promise for noninvasive neuromodulation. It operates on mechanosensitive cellular pathways, yet most studies employ supra-physiological kilohertz pulse repetition frequencies (PRFs), despite physiological neuronal activity being limited to a couple hundred hertz.

Materials / Methods: We performed large-scale cellular calcium imaging from individual motor cortex neurons expressing the genetically encoded calcium sensor GCaMP7f, in awake head-fixed mice freely locomoting (Fig. 1). We analyzed transient calcium events that capture periods of heightened neural activity, before versus during US
stimulation.

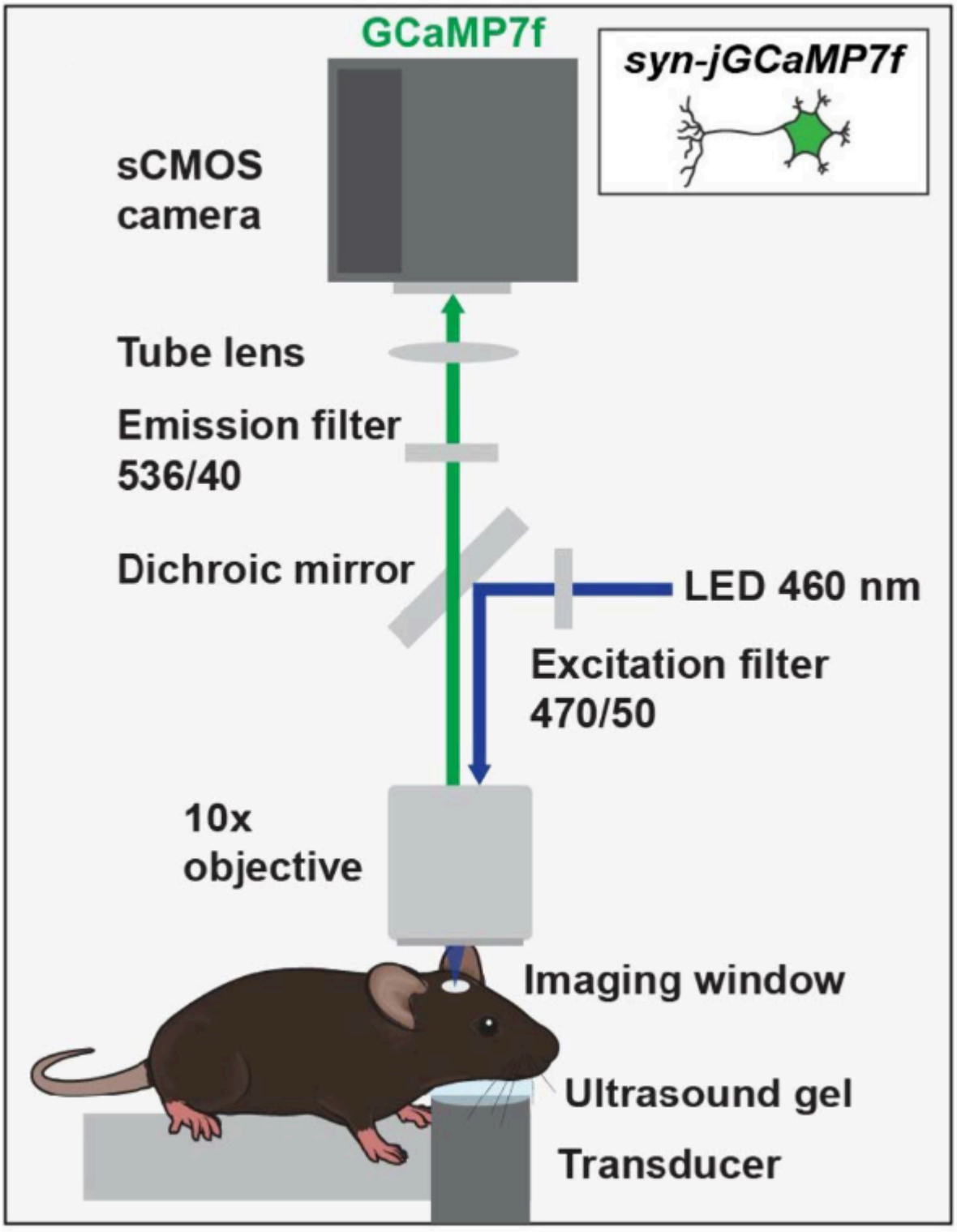


Figure 1: Experimental setup for transcranial ultrasound stimulation on a head-fixed mouse during imaging.

Results: US pulsed at physiologically relevant frequencies of 10 Hz, 40 Hz and 140 Hz effectively activated about 16-18% of neurons in awake mice, and many neurons were preferentially activated by a single PRF. US evoked neuron responses are similar between cortical neurons with versus without parvalbumin expression (Fig.
2).

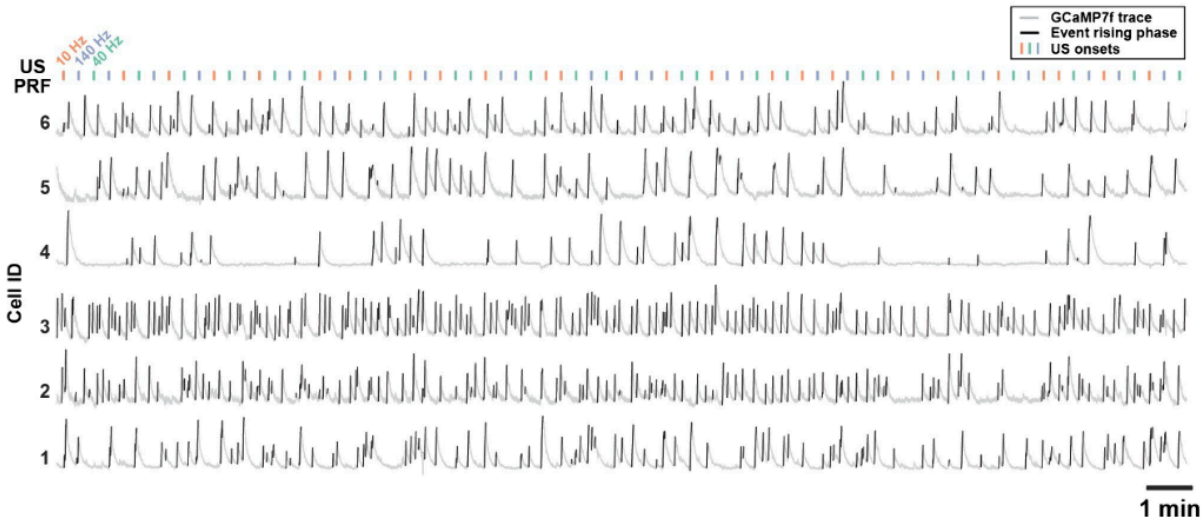


Figure 2: Direct comparison of the effect of different US PRF. Example calcium fluorescence traces over full recording for example neurons. Gray lines represent GCaMP7f fluorescence and black lines represent calcium event rising phases. Colored lines above depict US at randomly alternating PRFs. Scale bar is 1 minute.

Discussion: US-mediated neural responses have been shown to depend on brain regions[1] and cell types[2]. Our results further highlighted the heterogeneity of US evoked response across individual neurons, demonstrating that neurons were preferentially activated by certain PRFs. Thus, combining PRFs can activate a larger population of neurons, enhancing neuromodulation efficacy. The distinct responses of individual neurons and their preferential sensitivity to PRFs may be influenced by mechanosensitive channel expression and downstream cellular signaling pathways.

Conclusions: Transcranial low-intensity US delivered at physiologically relevant PRFs preferentially activate different neuron populations regardless of parvalbumin expression, and combining PRFs could activate a large fraction of neurons.

Supplemental Data:

References: [1] Tseng, H. *et al.* Region-specific effects of ultrasound on individual neurons in the awake mammalian brain. *iScience* **24**, 102955 (2021). [2] Murphy, K. R. *et al.* A tool for monitoring cell type–specific focused ultrasound neuromodulation and control of chronic epilepsy. *Proc Natl Acad Sci U S A* **119**, e2206828119 (2022).

Acknowledgements: X.H. acknowledges funding from NIH (1R01NS109794 and 1R01NS115797), and NSF grant # 1848029. E.B. acknowledges NSF grant # DGE-1840990, J.S. acknowledges funding from NIH 5T32GM008541-23, and E.S. acknowledges funding from NIH T32GM145455.

Learning Objectives: 1. Examine the effect of US delivered at physiological PRFs on individual neurons in awake mice, free of anesthesia effect. 2. Gain insights into the heterogeneity of US-mediated single cell response of classically defined excitatory versus inhibition neuron subtypes. 3. Understand the potential of transcranial low-intensity ultrasound for noninvasive neuromodulation.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O151

Oral Presentations
TOPICS IN NON-INVASIVE STIMULATION
16-05-2024 10:30 - 11:20

THE SYNERGISTIC EFFECT OF HIGH-FREQUENCY RTMS WITH ATYPICAL ANTIPSYCHOTICS ON THE ALLEVIATION OF NEGATIVE SYMPTOMS OF SCHIZOPHRENIA- A COMPARITIVE STUDY

K Srinivas, MD[1,2], Chilukuri Raviteja, MD[3,4], Kolluri Maithri, MD[5,6], P Spandana, MBBS[7], Bandita Sharma, BA Psychology[8], Vatte Vishwak Reddy, BChir[9], Sravanthi Penubarthi, BChir[9], Pustakaala Dharaneedhar, BChir[10], Vinya Konijeti, BChir[11], Anna Sai Krishna Yadav, BChir[12], Aditi Yk, BChir[13]
[1]KAMINENI INSTITUTE OF MEDICAL SCIENCES, Psychiatry, HYDERABAD, India, [2]CONSULTANT, KARLA NEUROMODULATION, Psychiatry, HYDERABAD, India, [3]TRR INSTITUTE OF MEDICAL SCIENCES, Hyderabad, , India, [4]KARLA NEUROMODULATION, Psychiatry, hyderabad, India, [5]MALLA REDDY COLLEGE FOR WOMEN, , HYDERABAD, India, [6]KARLA NEUROMODULATION, Psychiatry, HYDERABAD, India, [7]HARVARD MEDICAL SCHOOL, , BOSTON, United States of America, [8]KARLA NEUROMODULATION, Psychiatry, Hyderabad, India, [9]KAMINENI INSTITUTE OF MEDICAL SCIENCES, Psychiatry, HYD, India, [10]KAMINENI INSTITUTE OF MEDICAL SCIENCES, Psychiatry, HYD, Israel, [11]HYDERABAD, Dept. Of Psychiatry, KIMS, India, [12]TRR INSTITUTE OF MEDICAL SCIENCES, HYDERABAD, India, [13]UNIVERSITY OF NOTTIGHAM, Clinical Psychologist, NOTTIGHAM, United Kingdom

Introduction: Schizophrenia is a chronic disease which is characterized by heterogeneous domains of symptoms – cognitive, negative and positive symptoms. Positive symptoms like delusions, hallucinations and disorganized behavior have been well treated with 1st and 2nd generation antipsychotics. However, the functional outcome is mainly dependent on negative symptoms.[1] Primary negative symptoms are an intrinsic aspect of schizophrenia. Secondary negative symptoms are attributable to factors like unrelieved positive symptoms, adverse effects of antipsychotic drugs and social factors.[2]

Materials / Methods: This study explores efficacy of high frequency (20 Hz) rTMS on negative symptoms of schizophrenia.

A total of 60 participants diagnosed with schizophrenia, experiencing persistent negative symptoms, were recruited for this study. They were given rTMS (20 Hz) stimulations over left dorsolateral prefrontal cortex for 3 weeks, 3 sessions per week with each session lasting 20 minutes while being maintained on their former antipsychotic treatment. Scale for the Assessment of Negative Symptoms (SANS) was administered at baseline and post-treatment to evaluate changes in negative symptoms. Additionally, other clinical and psychosocial measures were collected to assess overall symptomatology, functional outcomes, and adverse effects.

Results: Preliminary Results
There were no significant group differences ($p > 0.05$) in sociodemographic data (age, age of onset, gender, body mass index, duration of illness, education status and marital status), as shown in Table 1
Table. 1

Descriptive Statistics		
	Mean	Std. Deviation
Age (years)	35.08	11.256
Age at onset (years)	27.33	5.769
Duration of illness (years)	7.75	7.191
Body Mass Index	22.848	2.6498
SANS Before	87.23	5.595
SANS After	55.07	7.18

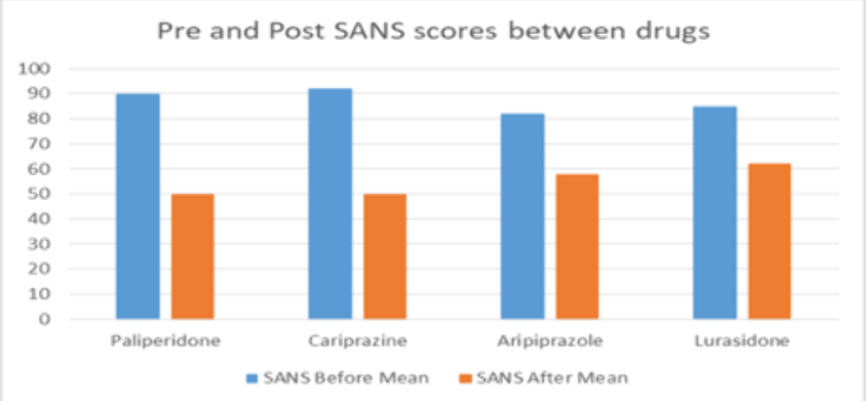
Education level		
	Frequency	Percent
Illiterate	7	11.7
10th Standard	18	30
College	35	58.3
Marital Status		
Unmarried	25	41.7
Married	30	50
Divorced/Separated	5	8.3

At baseline, patients in the 4 antipsychotic groups did not have any significant differences in total SANS score or on any of the sub scales.
Mean scores and SD of the rating scales are presented in Table 2.
Table. 2

	SANS Before		SANS After	
	Mean	Standard Deviation	Mean	Standard Deviation
Paliperidone	90	3	50	5
Cariprazine	92	4	50	5
Aripiprazole	82	4	58	4
Lurasidone	85	5	62	5

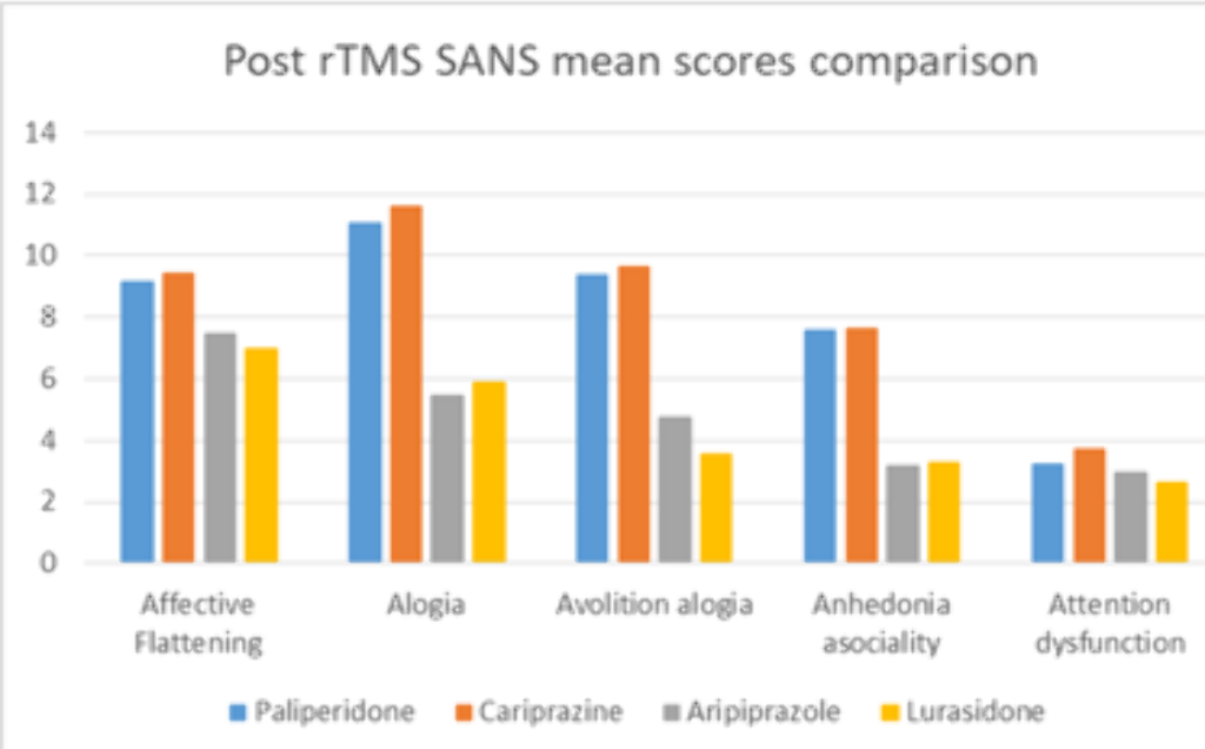
Table 3

	Paliperidone			Cariprazine			Aripiprazole			Lurasidone		
	Mean	SD	t	Mean	SD	t	Mean	SD	t	Mean	SD	t
Affective Flattening	9.200	3.649	9.765	9.467	2.200	16.669	7.467	3.204	9.025	7.000	1.604	16.907
Alogia	11.067	1.624	26.389	11.600	1.682	26.713	5.467	1.598	13.252	5.933	2.154	10.670
Avolition alogia	9.400	1.957	18.606	9.667	2.225	16.823	4.800	1.265	14.697	3.600	1.404	9.930
Anhedonia asociality	7.600	1.682	17.502	7.667	1.952	15.213	3.200	1.424	8.702	3.333	.900	14.349
Attention dysfunction	3.267	.961	13.163	3.733	.961	15.044	3.000	.756	15.370	2.667	.816	12.649



The obtained t-statistic of 24.617 suggests a significant difference in Total SANS scores before and after treatment. This indicates that the treatment had a statistically significant effect on reducing negative symptoms, as measured by the Total SANS scale.

A further comparison of SANS scores between the medications used showed that paliperidone and cariprazine were similarly efficacious, both being better than aripiprazole and lurasidone ($p<0.001$) as shown in table 3



Discussion: Studies have shown improvement in positive and negative symptoms of schizophrenia with repetitive trans cranial magnetic stimulation (rTMS). [3]. More recently, High frequency rTMS has been shown to negative symptoms of chronic schizophrenia.[4] Li et al reported improvement with 8 weeks rTMS treatment but showed delayed effects [5] Several factors account for outcomes, like patient factors, pharmacotherapy, choice of drug, dose range, Also intensity, placement, duration, frequency of sessions of rTMS and placebo effects of treatment [6,7, 8, 9]. Current study evaluated efficacy of combination of Rtms with latest antipsychotics in improving negative symptoms of schizophrenia and we found that all four newer antipsychotics were effective in reducing negative symptoms of schizophrenia when combined with high frequency rTMS. Also, paliperidone and caripraine were better than aripiprazole and lurasidone. There was also a significantly better improvement in the domains of

Conclusions: Significant reduction of SANS total score and specifically in the avolition (22%) and alogia (19%) domains.

It is noteworthy that individuals who were using paliperidone and cariprazine showed significantly better outcomes in terms of negative symptom reduction as measured by the SANS.

Supplemental Data:

References:

1. Fervaha, G., Foussias, G., Agid, O., & Remington, G. (2014). Impact of primary negative symptoms on functional outcomes in schizophrenia. European Psychiatry, 29(7), 449-455. doi:10.1016/j.eurpsy.2014.01.007

2. Möller, H. (2007). Clinical evaluation of negative symptoms in schizophrenia. European Psychiatry, 22(6), 380-386. doi:10.1016/j.eurpsy.2007.03.010

3. Goyal N, Nizamie SH, Desarkar P. Efficacy of adjuvant high frequency repetitive transcranial magnetic stimulation on negative and positive symptoms of schizophrenia: preliminary results of a double-blind sham-controlled study. J Neuropsychiatry Clin Neurosci. 2007; 19(4): 464-467.

4. Wang J, Zhou Y, Gan H, Pang J, Li H, Wang J, Li C. Efficacy Towards Negative Symptoms and Safety of Repetitive Transcranial Magnetic Stimulation Treatment for Patients with Schizophrenia: A Systematic Review. Shanghai Arch Psychiatry. 2017 Apr 25;29(2):61-76. doi: 10.11919/j.issn.1002-0829.217024. PMID: 28765677; PMCID: PMC5518263.

5. Li Z, Du XD, Zhang LL, Yang JG, Yang L, Yin M, et al. [A control study of high-frequency repetitive transcranial magnetic stimulation in chronic schizophrenia characterized by negative symptoms]. Lin Chuang Xin Shen Ji Bing Za Zhi. 2016; 22(5): 28-31.

6. Hasan A, Guse B, Cordes J, Wölwer W, Winterer G, Gaebel W, Langguth B, Landgrebe M, Eichhammer P, Frank E, Hajak G, Ohmann C, Verde PE, Rietschel M, Ahmed R, Honer WG, Malchow B, Karch S, Schneider-Axmann T, Falkai P, Wobrock T. Cognitive Effects of High-Frequency rTMS in Schizophrenia Patients With Predominant Negative Symptoms: Results From a Multicenter Randomized Sham-Controlled Trial. Schizophr Bull. 2016 May;42(3):608-18. doi: 10.1093/schbul/sbv142. Epub 2015 Oct 3. PMID: 26433217; PMCID: PMC4838079.

7. He H, Lu J, Yang L, Zheng J, Gao F, Zhai Y, Feng J, Fan Y, Ma X. Repetitive transcranial magnetic stimulation for treating the symptoms of schizophrenia: A PRISMA compliant meta-analysis. Clin Neurophysiol. 2017 May;128(5):716-724. doi: 10.1016/j.clinph.2017.02.007. Epub 2017 Feb 22. PMID: 28315614

8. Pappa S, Kalniunas A, Maret J. Cariprazine for negative symptoms in early psychosis: a pilot study with a 6-month follow-up. Front Psychiatry. 2023 Jun 22;14:1183912. doi: 10.3389/fpsyt.2023.1183912. PMID: 37426095; PMCID: PMC10323827.

9. Kumar N, Vishnubhatla S, Wadhawan AN, Minhas S, Gupta P. A randomized, double blind, sham-controlled trial of repetitive transcranial magnetic stimulation (rTMS) in the treatment of negative symptoms in schizophrenia. Brain Stimul. 2020 May-Jun;13(3):840-849. doi: 10.1016/j.brs.2020.02.016. Epub 2020 Feb 29. PMID: 32289715.

Acknowledgements: N/A

Learning Objectives: In this study we aim to evaluate the efficacy of rTMS [20hz] on left dorsolateral prefrontal cortex, 3 weeks, 3 sessions per week, 20 minutes per session, along with newer 2nd generation antipsychotics with D3 receptors antagonism and partia 5HT receptors antagonism in reducing negative symptoms of schizophrenia.

Financial Disclosures: no significant relationships

Disclosure: No significant relationships.

O152

Oral Presentations
TOPICS IN NON-INVASIVE STIMULATION
16-05-2024 10:30 - 11:20

PSYCHIATRIC PERSPECTIVE OF TMS *ON SUICIDAL IDEATION: A RETROSPECTIVE CASE SERIES STUDY

Mario Ferraz Filho, BSc (Hons), Ivete Ferrraz, MSc, Amanda Ferraris, MD
Neuromood - TMS, Neuromodulation, Curitiba, Brazil

Introduction: 1. INTRODUCTION: Suicide is a complex and global phenomenon that affects a heterogeneous population, resulting in severe social harm. In each completed case, it inflicts deep psychological distress on the quality of life of sixty individuals, making it the third leading cause of death among young people aged 15-19 years. Suicidal behavior can occur as an isolated symptom, not necessarily being associated with the expression of other psychiatric disorders. It may also be linked to early-life stressful events that cause neurobiological changes in brain development, such as excessive concentrations of 5HT 1A in the hippocampus, which can reduce brain neurotrophic factor, crucial for brain function. Neuromodulation techniques like ECT, tDCS, and TMS have been used for the treatment of self-destructive symptoms and suicidal ideation by acting on synaptic neuroplasticity and neurogenesis, with TMS standing out in the literature for its greater efficacy in psychiatric symptoms and its use as a complementary therapy in combination with medication. Its excitatory application (frequency of 5Hz+) over the left dorsolateral prefrontal cortex (DLPFC) has proven to be a promising alternative.

Materials / Methods: 4. MATERIALS AND METHODS
Descriptive observational study, which has been collecedt a series of 7 cases of patients with suicidal symptoms who underwent treatment with Transcranial Magnetic Stimulation at the Medical Clinic of Dr. Ivete Contieri Ferraz, between the years 2017 and 2020. Clinical session records were reviewed and digitized for subsequent analysis. The evaluation will be conducted through individual chart analysis for each patient, with a focus on response time in the 13Hz protocol, i.e., the reduction and remission of suicidal symptoms (thoughts of death, parasuicidal behaviors, and suicide attempts). Inclusion criteria: The inclusion criteria are patients who underwent TMS treatment for symptoms of suicidal ideation and behaviors with no response to other therapeutic approaches, with the chosen protocol being the excitatory 13Hz in left DLPFC. Exclusion criteria: Patients who, despite having suicidal ideation symptoms, did not initially follow the 13Hz excitatory protocol were excluded.

Results: Late-breaking research.

Discussion: 2. OBJECTIVES
Primary: To describe the effectiveness of transcranial magnetic stimulation in the 13Hz stimulation protocol in reducing suicidal symptoms in 7 patients.
Secondary: To individually analyze response time and converging factors. 3. JUSTIFICATION
To introduce new therapy possibilities for the treatment of suicide-related symptoms with the intention of reducing the impact of such deaths on society.

Conclusions: Late-break-research

Supplemental Data:

References: [1] ARBABI, Mohammad et al. High frequency TMS for the management of Borderline Personality Disorder: a case report. Asian journal of psychiatry, v. 6, n. 6, p. 614-617, 2013. [2] BACHMANN, Silke. Epidemiology of suicide and the psychiatric perspective. International journal of environmental research and public health, v. 15, n. 7, p. 1425, 2018. [3] BEWERNICK, Bettina; SCHLAEPFER, Thomas E. Update on neuromodulation for treatment-resistant depression. F1000Research, v. 4, 2015. [4] BOZZAY, Melanie L. et al. Transcranial magnetic stimulation to reduce suicidality–A review and naturalistic outcomes. Journal of psychiatric research, 2020. [5]

BOZZAY, Melanie L. et al. Combined transcranial magnetic stimulation and brief cognitive behavioral therapy for suicide: study protocol for a randomized controlled trial in veterans. Trials, v. 21, n. 1, p. 1-12, 2020. [6] COSTANZA, Alessandra et al. Neurobiology of suicide: do biomarkers exist?. International journal of legal medicine, v. 128, n. 1, p. 73-82, 2014. [7] CROARKIN, Paul E. et al. High-frequency repetitive TMS for suicidal ideation in adolescents with depression. Journal of affective disorders, v. 239, p. 282-290, 2018. [8] DE VIDOVICH, Giulia Zelda et al. Repetitive TMS on left cerebellum affects impulsivity in borderline personality disorder: A pilot study. Frontiers in human neuroscience, v. 10, p. 582, 2016..

Acknowledgements:

Learning Objectives: Primary: To describe the effectiveness of transcranial magnetic stimulation in the 13Hz stimulatory protocol in reducing suicidal symptoms in 7 patients Secondary: Individually analyze response time and converging factors.

Financial Disclosures: No significant relationships'

Disclosure: No significant relationships.

O153

Oral Presentations
NEUROMODULATION FOR CARDIOVASCULAR DISORDERS
16-05-2024 10:30 - 11:20

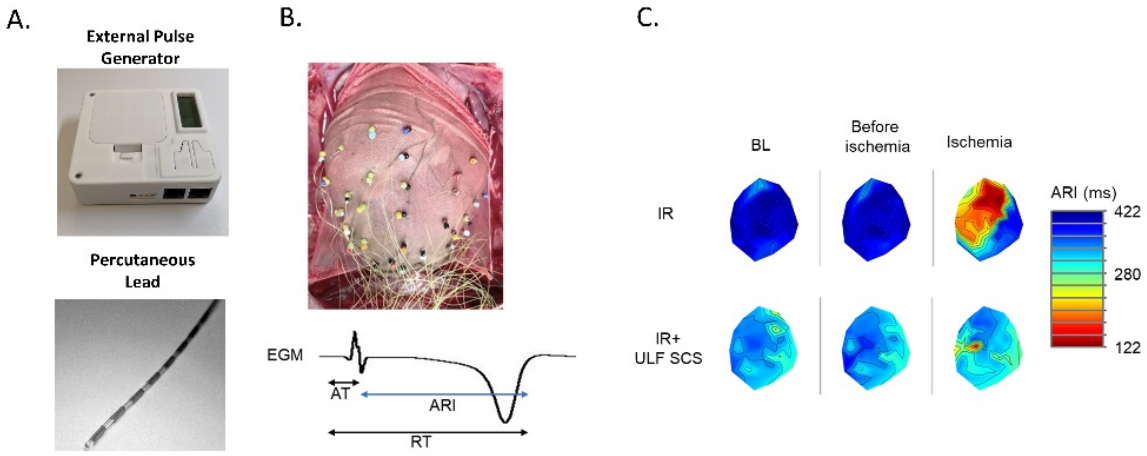
THORACIC ULTRA LOW-FREQUENCY SPINAL CORD STIMULATION REDUCES ISCHEMIA REPERFUSION-INDUCED CARDIAC ARRHYTHMIAS

Yuki Kuwabara, MD[1], Benjamin Wong, BSc (Hons)[1], Tom Flores, PhD[2], Erick Carranza, BSc (Hons)[2], Adrian Zalewski, MD[1], Aman Mahajan, MD, PhD[1], Siamak Salavatian, MEng. PhD[1]
[1]University of Pittsburgh, Anesthesiology, Pittsburgh, United States of America, [2]Presidio Medical, Inc., San Francisco, United States of America

Introduction: Myocardial ischemia-reperfusion (IR) injury is associated with sympathetic overactivity and a heightened risk of ventricular tachyarrhythmias (VTs).[1] The spinal cord as a major nexus point for control of sympathetic reflexes to the heart is an attractive target for neuromodulation therapy to mitigate sympathoexcitation.[2-5] Ultra-low frequency spinal cord stimulation (ULFSCS) is shown to have a promising effect in directly inhibiting spinal neural activity. In this pilot study, we evaluated the efficacy of ULFSCS in mitigating IR-induced sympathoexcitation and VTs.

Materials / Methods: Six Yorkshire pigs (45-55 kgs), were used for the ULFSCS group. The data from these 6 ULFSCS animals were compared to 7 sham Yorkshire pigs from a subset of Yorkshire pigs in published data by our group [6] subjected to identical protocols and equipment, excluding the ULFSCS therapy. Animals were sedated, and mechanically ventilated under anesthesia and underwent laminectomy to expose the spinal T1-T4 section to perform ULFSCS (Fig.1, Presidio Medical Inc) and a sternotomy to expose the heart for performing myocardial ischemia intervention. Local electrocardiograms (EGMs) were recorded (Fig2) to measure the activation recovery interval (ARI), dispersion of repolarization (DOR), and Tpeak-Tend/QTc ratio. ARI shortens during sympathoexcitation, and DOR augmentation is a major sign of potential reentrant VTs. Myocardial ischemia (1hr) reperfusion (1hr) injury was induced by left anterior descending (LAD) coronary artery ligation.

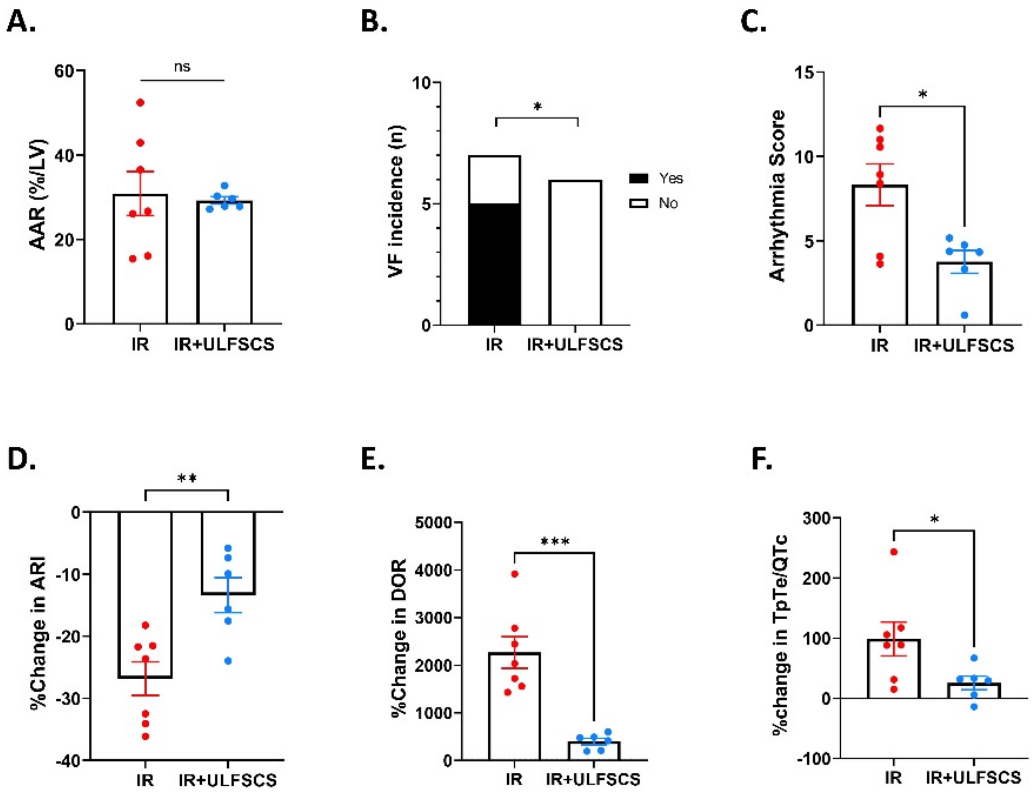
Figure 1



Results: ARI shortening was significantly mitigated with ULFSCS (IR: -27 ± 2.7 %, ULFSCS: -13 ± 2.8 %. P = 0.0057). Both DOR (IR: 2268 ± 330 %, ULFSCS: 397 ± 67 %. P = 0.0003) and TpTe/QTc interval were reduced with ULFSCS (IR: 99 ± 28, ULFSCS: 26 ± 11. P = 0.0445. There was no ventricular fibrillation (VF) incidence in animals with ULFSCS during IR injury while five animals out of seven had VF in the animals without ULFSCS (IR-only animals) (P = 0.021). In addition, the arrhythmia score during IR injury was lower in the ULFSCS animals compared to the IR animals (IR: 8.3 ± 1.2, ULFSCS: 3.8 ± 0.68. P =

0.0104).

Figure 2



Discussion: ULFSCS decreased sympathoexcitation (by mitigating the ARI shortening) and suppressed the arrhythmogenicity (by decreasing DOR and TpTe/Qc), which resulted in no ULFSCS animals experiencing VFs during the IR injury. Further studies are needed to investigate the mechanism of action of the thoracic ULFSCS in providing cardioprotective effects.

Conclusions: In this preliminary study, thoracic ULFSCS mitigated cardiac sympathoexcitation and decreased arrhythmogenicity and VT episodes during IR injury.

Supplemental Data:

References: 1 Luqman, N., Sung, R. J., Wang, C.-L. & Kuo, C.-T. Myocardial ischemia and ventricular fibrillation: pathophysiology and clinical implications. *International journal of cardiology* **119**, 283-290 (2007). 2 Howard-Quijano, K. *et al.* GABAergic Signaling during Spinal Cord Stimulation Reduces Cardiac Arrhythmias in a Porcine Model. *Anesthesiology* **138**, 372-387, doi:10.1097/ALN.0000000000004516 (2023). 3 Howard-Quijano, K. *et al.* Spinal Cord Stimulation Reduces Ventricular Arrhythmias by Attenuating Reactive Gliosis and Activation of Spinal Interneurons. *JACC Clin Electrophysiol* **7**, 1211-1225, doi:10.1016/j.jacep.2021.05.016 (2021). 4 Omura, Y. *et al.* Spinal Anesthesia Reduces Myocardial Ischemia-triggered Ventricular Arrhythmias by Suppressing Spinal Cord Neuronal Network Interactions in Pigs. *Anesthesiology* **134**, 405-420, doi:10.1097/ALN.0000000000003662 (2021). 5 Salavatian, S. *et al.* Spinal neuromodulation mitigates myocardial ischemia-induced sympathoexcitation by suppressing the intermediolateral nucleus hyperactivity and spinal neural synchrony. *Front Neurosci* **17**, 1180294, doi:10.3389/fnins.2023.1180294 (2023). 6 Kuwabara, Y. *et al.* Thoracic dorsal root ganglion stimulation reduces acute myocardial ischemia induced ventricular arrhythmias. *Front Neurosci* **17**, 1091230, doi:10.3389/fnins.2023.1091230 (2023).

Acknowledgements: The support of Presidio Medical, Inc. for this project is gratefully acknowledged

Learning Objectives: Objective 1: Learning the role of spinal cord in causing the sympathoexcitation during myocardial ischemia reperfusion (IR) injury. Objective 2: Learning the impact of IR injury on the activation recovery interval, dispersion of repolarization, TpTe interval and arrhythmogenecity Objective 3: Learning the cardioprotective effect of ultra low frequency spinal cord stimulation in the setting of IR injury

Financial Disclosures: This study was sponsored by the Presidio Medical Inc. Tom Flores (compensation >$100K) and Erick Carrnaza (compensation $5-20K) are Presidio Medical Inc. employee.

Disclosure: No significant relationships.

O154

Oral Presentations
NEUROMODULATION FOR CARDIOVASCULAR DISORDERS
16-05-2024 10:30 - 11:20

REGULATION OF CARDIAC NEUROTRANSMITTERS BY AXONAL MODULATION

Corey Smith, PhD[1], Tina Vrabec, PhD[2], Shane Bender, BSc (Hons)[3], Shyue-An Chan, PhD[1], Jeffrey Ardell, PhD[4]
[1]Case Western Reserve University, Physiology And Biophysics, Cleveland, United States of America, [2]Case Western Reserve University, Physical Medicine And Rehabilitation, Metrohealth Medical Center, Cleveland, United States of America, [3]Case Western Reserve University, Biomedical Engineering, Cleveland, United States of America, [4]UCLA, Medicine/cardiology, Los Angeles, United States of America

Introduction: Sympathetic control of regional cardiac function occurs through postganglionic sympathetic innervation from stellate ganglia. Norepinephrine (NE) is the primary neurotransmitter released from postganglionic sympathetic efferent nerves and increases cardiac mechanical and electrical function. Neuropeptide Y (NPY) is an abundant cardiac co-transmitter released from the same efferent nerves under intense activation. NPY plays a vital role in homeostatic processes including angiogenesis, vasoconstriction, and cardiac remodeling. Chronic elevated sympathetic stress, resulting in increased NE and NPY release, has been implicated in the pathogenesis of several cardiovascular disorders including hypertension, myocardial infarction, heart failure, and arrhythmias, which may result in sudden cardiac death (SCD). The ability to measure and regulate neurotransmitters and neuropeptides in vivo that are relevant to the assessment and progression of disease is of great interest to the scientific and medical communities. The current methods to measure these neurotransmitters can take several days or weeks to obtain and are incompatible with real time regulation through feedback control of neuronal activity, as they can be limited in resolution both spatially and temporally (e.g., fluid compartment microdialysis of interstitial fluid analyzed by enzyme-linked immunosorbent assay [ELISA], high-performance liquid chromatography [HPLC], or mass spectrometry); thus, their guidance of timely diagnosis and treatment is disrupted.

Materials / Methods: In the present study, a novel adaptation of an electrochemical detection of NE levels at high spatial and temporal resolution in vivo is presented (Fast scanning cyclic voltammetry; FSCV). NPY levels are detected in vivo through the use of a capacitive immunoprobe biosensor. We instituted graded block of sympathetic drive to the heart by using DC block protocols delivered to stellate ganglia through a separated interface nerve electrode (SINE), which our group has shown to increase both safety and run time.

Results: In the infarcted porcine heart, programmed ventricular pacing is associated with reflex increases in NE and NPY release, both of which contribute to arrhythmias, including the potential for SCD. Our data demonstrate that partial DC block of sympathetic fibers to the heart mitigate both NE and NPY release. NE release was decreased as a function of block level while NPY release was prevented at all levels of DC block.

Discussion: Programmed ventricular pacing evokes transmitter (NE, NPY) release from sympathetic nerves that contributes to arrythmia formation in the infarcted heart. Site specific axonal modulation of the stellate ganglia mitigates this arrhythmic potential.

Conclusions: Future applications include development of dynamic regulation of cardiac neurotransmitters in real-time.

Supplemental Data:

References: None.

Acknowledgements: The support of the National Institutes of Health for this project is gratefully acknowledged.

Learning Objectives: 1. What are the hemodynamic consequences of ectopic programmed pacing in the heart? 2. What are the neuronal transmitter systems responsible for neuro-regulation of hemodynamic responses to ectopic programmed pacing. 3. How does neuronal block mitigate the hemodynamic consequences of ectopic programmed pacing in the heart.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

O155

Oral Presentations
NEUROMODULATION FOR CARDIOVASCULAR DISORDERS
16-05-2024 10:30 - 11:20

CLOSED-LOOP SCS FOR THE TREATMENT OF CHRONIC PAIN ASSOCIATED WITH RAYNAUD'S PHENOMENON

Jarek Maciaczyk, MD, PhD[1], Gregor Bara, MD[1], Birte Dietz, PhD[2], Dave Mugan, BSc (Hons)[3], Pantelis Karakostas, MD[1], Valentin Schäfer, MD[1]
[1]Universitätsklinikum Bonn, Bonn, Germany, [2]Saluda Medical, Cologne, Germany, [3]Saluda Medical, Harrogate, United Kingdom

Introduction: Raynaud's phenomenon (RP) is an episodically occurring vasospasm of the peripheral arteries that causes cyanosis, erythema, pain, paresthesia, and sometimes ulceration of the fingers and/or toes[1]. There are few reports, mostly case series, on the utility of spinal cord stimulation (SCS) to treat RP[2]–[9]. However, there is a lack of objective evidence on the physiological effects (e.g., vasodilation) of SCS in this condition.
Here we present the objective results of the effects on peripheral blood flow and the subjective changes resulting in the frequency and severity of Raynaud's attacks, from our pilot study.

Materials / Methods: This is a prospective, single-center pilot study to evaluate the effectiveness of ECAP-controlled closed-loop-SCS in treating RP. Patient outcomes such as Raynaud Severity/ Condition Score, Cochin Hand Function Scale, SHAQ RP VAS, EQ-5D-5L, PGIC and objective peripheral
circulation assessments were collected. To assess the effect on the vascular system, high-resolution Doppler ultrasonography was performed in each patient at the study intervals (baseline, trial-end, 1-month, 3-months, and 6-months) using a 24MHz hockey stick on a high-performance ultrasound machine (GE LOGIQe10 (2021) by an experienced vascular ultrasonographer.

Results: Mean baseline (n=10) severity of attacks was 6.7±1.160 which decreased to 3.250±1.581 6-months after implantation (n=8; Fig.1A). Mean baseline (±SD; n=9) weekly attack frequency was 21.78±17.81 and decreased to 12.63±13.07 6-months after implantation (n=8; Fig.1B). Mean baseline (n=10) Raynaud's condition score was 6.5±2.068279 and decreased to 2.625±1.846812 6-months after implantation (n=8). Seven participants experienced a clinically meaningful change (MID) in symptom severity as informed by the Raynaud's condition score (-1.4) at 3-months (Fig.1C; [10]).
Mean baseline (±SD; n=10) arterial occlusion in warmed fingers were 8.7±4.347 and decreased to 1.833±3.601 6-months after implantation (n=6; Fig.1D). Pain reduction greater than 30% was achieved in more than 50% of patients at each follow-up visit. A clinically meaningful improvement from baseline was observed at all time points except the 3-months' time point in patient-reported outcomes using the EQ-5D-5L
(Table1).

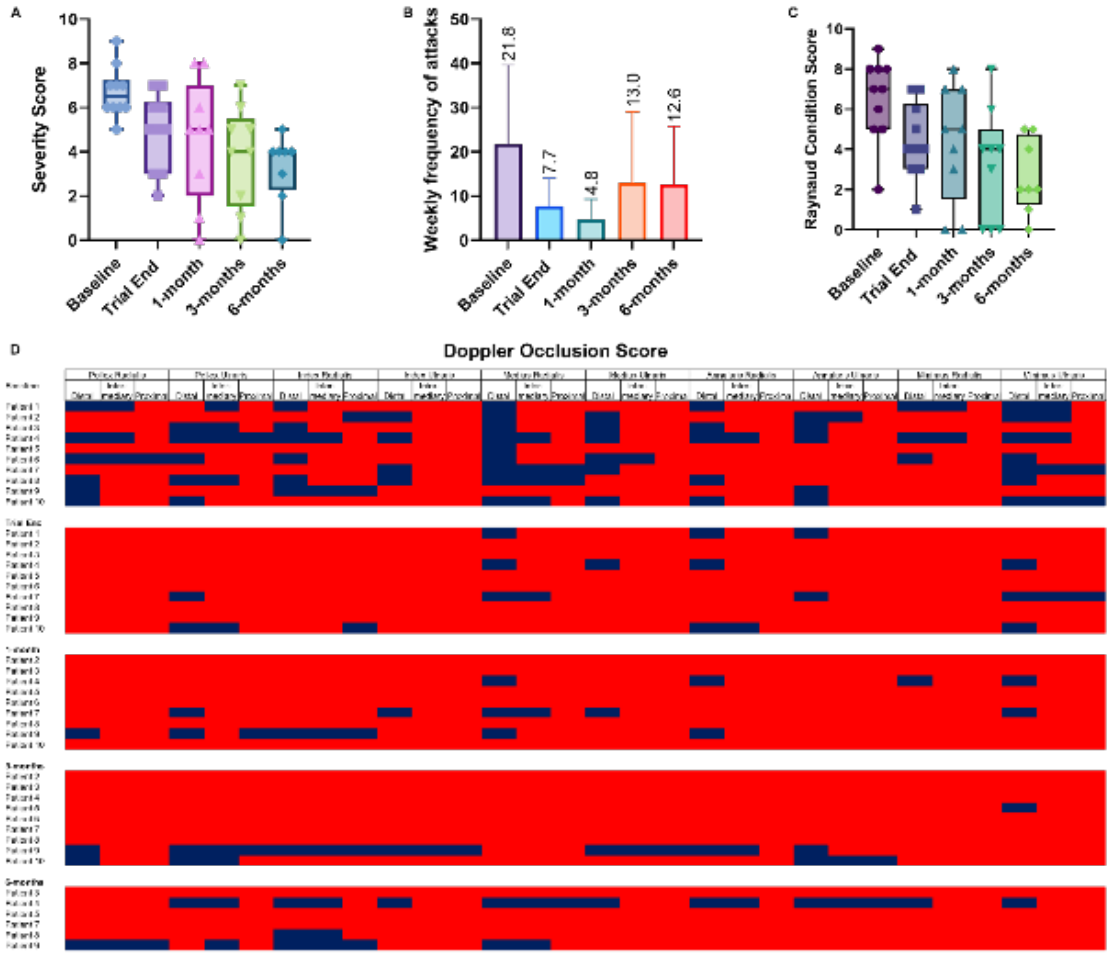


Figure 1: Patient reported outcomes and detailed analysis of peripheral blood flow assessments. Frequency of attacks, Severity and Raynaud condition score. (A) Mean baseline (n = 10) severity of attacks was 6.7 ± 1.160 which decreased to 4.9 ± 1.729 after the test phase (n = 10, Trial End), 4.556 ± 0.9296 1-month after implantation (n = 9), 3.778 ± 2.333 3-months after implantation (n = 9) and to 3.250 ± 1.581 6-months after implantation (n = 8). (B) Mean baseline (± SD; n = 9) weekly attack frequency was 21.78 ± 17.81 and decreased to 7.667 ± 6.364 after the test phase (n = 9; Trial End). 4.778 ± 4.549 1-month after implantation (n = 9). 13.0 ± 16.05 3-months after implantation (n = 9) and to 12.63 ± 13.07 6-months after implantation (n = 8). (C) Mean baseline (n = 10) Raynaud's condition score was 6.5 ± 2.068279 and decreased to 4.4 ± 1.897367 after the test phase (n = 10. Trial End). 4.333333 ± 2.915476 1-month after implantation (n = 9), 3.222222 ± 2.818589 3-months after implantation (n = 9) and to 2.625 ± 1.846812 6-months after implantation (n = 8). (D) This section offers a detailed visualization of the arteries in different states. Normal arteries are depicted in red, while occluded arteries are represented in blue. These assessments were conducted at various time points on hands that were previously warmed in a hand bath. Ultrasound examinations were performed on the distal, intermediate, and proximal sections of the artery. Each patient underwent a total of 30 examinations on the most severely affected hand. It is worth noting that the number of patients decreased at the 6-month mark as some patients had their devices switched off. These detailed peripheral blood flow assessments provide valuable insights into the changes in arterial status and the potential effects of SCS on peripheral circulation in patients with Raynaud's phenomenon.

Table 1: Patient reported Outcomes. Data are mean or n/N (%). EQ-5D = European Quality of Life Five-Dimensional, MID = Minimal Important Difference, VAS = Visual Analog Scale, PGIC = Patient Global Impression of Change, SHAQ RP = Scleroderma Health Assessment Questionnaire Raynaud Phenomenon

	Trial End	1-month	3-months	6-months
VAS percentage change from baseline	36%	45%	38%	69%*
VAS responder rates				
30% reduction	56%	56%	50%	100%
50% reduction	33%	56%	50%	71%
80% reduction	22%	33%	25%	43%
EQ-5D-5L index change from baseline (MID = 0.083)	0.13	0.15	0.07	0.15
Cochin Hand Function Scale change from baseline (Score from 0 – 90)	-6.30	-14.61	-15.94	-16.13
SHAQ RP change from baseline	-0.16	-0.23	-0.35	-0.22
PGIC		2.44	2.78	2.25

Discussion: ECAP-controlled closed-loop SCS resulted in a significant improvement in the severity of RP attacks and Raynaud's condition score, as well as an objective reduction in peripheral occlusion and ulceration. While one of the combined primary endpoints was successfully achieved in terms of severity at the 3-months follow-up, it's worth noting that the primary endpoint related to frequency improvement was not met during the same timeframe.

Conclusions: In conclusion, ECAP-controlled closed-loop-SCS alleviates RP symptoms and improves peripheral blood flow.

Supplemental Data:

References: 1. Herrick, A.L. (2012). The pathogenesis, diagnosis and treatment of Raynaud phenomenon. Nat. Rev. Rheumatol. 8, 469–479. https://doi.org/10.1038/nrrheum.2012.96. 2. Barba, A., Escribano, J., and García-Alfageme, A. (1992). The treatment of vasospastic disease by chronic spinal cord stimulation. A case report. Angiologia 44, 136–138. 3. Benyamin, R., Kramer, J., and Vallejo, R. (2007). A Case of Spinal Cord Stimulation in Raynaud's Phenomenon: Can Subthreshold Sensory Stimulation Have an Effect? Pain Physician, 6. 4. Chapman, K.B., Kloosterman, J., Schor, J.A., Girardi, G.E., van Helmond, N., and Yousef, T.A. (2021). Objective improvements in peripheral arterial disease from dorsal root ganglion stimulation: a case series. Ann. Vasc. Surg. 74, 519-e7. 5. Devulder, J., De Colvenaer, L., Rolly, G., Caemaert, J., Calliauw, L., and Martens, F. (1990). Spinal cord stimulation in chronic pain therapy. Clin. J. Pain 6, 51–56. 6. ERTILAV, E., and AYDIN, O.N. (2020). Spinal cord stimulator for the treatment of ischemic pain-Burger's Disease and Raynaud's disease: A report of 2 cases and literature. 7. Francaviglia, N., Silvestro, C., Maiello, M., Bragazzi, R., and Bernucci, C. (1994). Spinal cord stimulation for the treatment of progressive systemic sclerosis and Raynaud's syndrome. Br. J. Neurosurg. 8, 567–571. 8. Giglio, M., Preziosa, A., Rekatsina, M., Viswanath, O., Urits, I., Varrassi, G., Paladini, A., and Puntillo, F. (2021). Successful spinal cord stimulation for necrotizing Raynaud's phenomenon in COVID-19 affected patient: the nightmare comes back. Cureus 13. 9. Issa, M.A. (2012). Cervical Spinal Cord Stimulation with 5-ColumnPaddle

Lead In Raynaud's Disease. Pain Physician 4;15, 303–309. 10.36076/ppj.2012/15/303. 10. Ito, H., Tanei, T., Sugawara, K., Sando, Y., and Hori, N. (2022). Spinal cord stimulation for the treatment of pain and toe ulceration associated with systemic sclerosis: a case report. FUKUSHIMA J. Med. Sci. 68, 37–41. 10.5387/fms.2021-33. 11. Münster, T., Tiebel, N., Seyer, H., and Maihöfner, C. (2012). Modulation of Somatosensory Profiles by Spinal Cord Stimulation in Primary Raynaud′s Syndrome: SCS Influences QST in Primary Raynaud′s Syndrome. Pain Pract. 12, 469–475. 10.1111/j.1533-2500.2012.00531.x. 12. Neuhauser, B., Perkmann, R., Klinger, P.J., Giacomuzzi, S., Kofler, A., and Fraedrich, G. (2001). Clinical and Objective Data of Spinal Cord Stimulation for the Treatment of Severe Raynaud's Phenomenon. EJVES Extra 1, 3–4. 10.1053/ejvx.2000.0002. 13. Niclauss, L., Roumy, A., and Gersbach, P. (2013). Spinal Cord Stimulation in Thromboangiitis Obliterans and Secondary Raynaud's-Syndrome. EJVES Extra 26, e9–e11. 10.1016/j.ejvsextra.2013.03.007. 14. Provenzano, D.A., Nicholson, L., Jarzabek, G., Lutton, E., Catalane, D.B., and Mackin, E. (2011). Spinal Cord Stimulation Utilization to Treat the Microcirculatory Vascular Insufficiency and Ulcers Associated with Scleroderma: A Case Report and Review of the Literature. Pain Med. 12, 1331–1335. 10.1111/j.1526-4637.2011.01214.x. 15. Robaina, F.J., Dominguez, M., Díaz, M., Rodriguez, J.L., and de Vera, J.A. (1989). Spinal cord stimulation for relief of chronic pain in vasospastic disorders of the upper limbs. Neurosurgery 24, 63–67. 16. Sciacca, V., Petrakis, I., and Borzomati, V. (1998). Spinal cord stimulation in vibration white finger. VASA Z. Gefasskrankheiten 27, 247–249. 17. Sibell, D.M., and Stacey, B.R. (2005). Successful Use of Spinal Cord Stimulation in the Treatment of Severe Raynaud's Disease of the Hands. CASE Rep. 102, 5. 18. Ting, J.C., Fukshansky, M., and Burton, A.W. (2007). Treatment of Refractory Ischemic Pain from Chemotherapy-Induced Raynaud?s Syndrome With Spinal Cord Stimulation. Pain Pract. 7, 143–146. 10.1111/j.1533-2500.2007.00122.x. 19. Wolter, T., and Kieselbach, K. (2011). Spinal Cord Stimulation for Raynaud's Syndrome: Long-Term Alleviation of Bilateral Pain With a Single Cervical Lead: SPINAL CORD STIMULATION FOR RAYNAUD'S SYNDROME. Neuromodulation Technol. Neural Interface 14, 229–234. 10.1111/j.1525-1403.2011.00332.x. 20. Khanna, P.P., Maranian, P., Gregory, J., and Khanna, D. (2010). The minimally important difference and patient acceptable symptom state for the Raynaud's condition score in patients with Raynaud's phenomenon in a large randomised controlled clinical trial. Ann. Rheum. Dis. 69, 588–591. 10.1136/ard.2009.107706.

Acknowledgements:

Learning Objectives: Pathological arterial occlusions in patients with Raynaud's Phenomenon can be treated with ECAP-controlled closed-loop-SCS. Raynaud symptoms can be treated with ECAP-controlled closed-loop-SCS. Overall assessment of an SCS therapy for chronic pain in Raynaud's Phenomenon requires the implementation of objective and multiple patient-related outcomes measures.

Financial Disclosures: Jarek Maciaczyk: speaker fees: Boston Scientific, Saluda, Nevro; Advisory Board: Boston Scientific, Saluda, Nevro; Research Grant: Mainstay, Saluda Gregor Bara: no significant relationship Birte Dietz: Senior Medical Science Liason at Saluda Medical Dave Mugan: VP Scietific Affairs atof Saluda Medical Pantelis Karakostas: no significsnt relationship VSS: speaker fees: AbbVie, Boehringer Ingelheim, BMS, Chugai, Celgene, Hexal, Janssen, Lilly, Medac, Novartis, Onkowissen, Pfizer, Roche, Royal College of Physicians, Rheumaakademie, Sanofi, Takeda, UCB; Advisory board member: AbbVie, Amgen, BMS, Boehringer Ingelheim, Celgene, Chugai, Gilead, Hexal, Lilly, Medac, Novartis, Pfizer, Roche, Sanofi; research support: Boehringer Ingelheim, Celgene, Hexal, Universität Bonn, Lilly, Novartis, Roche, Alexion

Disclosure: No significant relationships.

O156

Oral Presentations
NEUROMODULATION FOR CARDIOVASCULAR DISORDERS
16-05-2024 10:30 - 11:20

SPINAL CORD STIMULATION IN NON-RECONSTRUCTABLE CRITICAL LIMB ISCHEMIA: A SINGLE-SITE LONG-TERM REVIEW OF 10-YEAR EXPERIENCE

Naoufel Ouerchefani, MD
Foch hospital, Neurosurgery, Suresnes, France

Introduction: Spinal cord stimulation (SCS) is a therapeutic option for patients with critical limb ischemia (CLI) and significant ischemic rest pain. SCS is used when vascular reconstruction is not possible or has failed in order to minimize or delay the need for major limb amputation. Here we report long-term real-world outcomes in 49 PAD patients who received SCS treatment for non-reconstructable CLI between 2012 and 2023.

Materials / Methods: This is a consecutive, observational, single-center case-series based an on-going, real-world evaluation of SCS outcomes for chronic pain (Clinicaltrials.gov: NCT01550575). All evaluated patients were implanted with an SCS device and documented data from their medical records were used to assess their condition at baseline and post-implant follow-up visits. Data collection includes diagnosis and medical history, pain scores, walking distance before claudication, evaluation of ulcers and amputation procedures. All data were collected by site personnel, as per standard practice and without sponsor involvement.

Results: To date, we reviewed 49 CLI cases implanted with SCS. At baseline, majority of patients were in Fontaine stage III (56%) or IV (40%), and 13 patients had 1 to 3 foot ulcers with an average size of 2.8 cm². The average follow-up is 2.5 years after the implant of non-rechargeable systems. At last-follow-up, pain scores were reduced by 4.6-point and walking distance before claudication increased from 71.5 to 263 meters. The frequency and size of foot ulcers remained stable in 9/12 patients with 2.7 cm² average size. Post-implant, surgical amputations were conducted in 9 patients (18%), on average 574 days (19-month) after implant, and were all below-the-knee procedures. 4 amputations were done within the first 6-months after implant, and 5 took place between 1- and 3.4-years after SCS implant. Stage III patients tended to have better outcomes when compared to stage IV (better pain relief and longer walking distance) and lower risk for amputation (out of the 9 patients amputated, 67% were in Fontaine stage IV at baseline).

Discussion: Spinal cord stimulation in under-utilized for CLI patients, and we hope our experience will support multidisciplinary discussions across specialties so that more patients can get access to SCS in the future.

Conclusions: Our results confirm recent findings from the literature[1] supporting SCS in CLI patients, with significant ischemic pain reduction and improved function. We may suggest the hypothesis that earlier SCS intervention may optimize the outcomes and delay and/or reduce the risk for a major limb amputation.

Supplemental Data:

References: 1. Piedade GS, Vesper J, Reichstein D, Dauphin AK, Damirchi S. Spinal cord stimulation in non-reconstructable critical limb ischemia: a retrospective study of 71 cases. Acta Neurochir (Wien). 2023 Apr;165(4):967-973. doi: 10.1007/s00701-022-05448-8. Epub 2023 Jan 4. PMID: 36598544; PMCID: PMC10068652.

Acknowledgements:

Learning Objectives: 1. Impact of SCS on pain, function and limb salvage in CLI 2. Long term outcomes of SCS in CLI patients 3. Patient outcomes in relation to Fontaine stage

Financial Disclosures: Naoufel Ouerchefani reports paid consulting activities for Boston Scientific, Abbott and Medtronic.

Disclosure: I am an employee of Boston Scientific, sponsor of the Patient Retrospective Outcomes (PRO) Study and part of the Clinical Research Team.

O157

Oral Presentations
NEUROMODULATION FOR CARDIOVASCULAR DISORDERS
16-05-2024 10:30 - 11:20

OPEN LABEL STUDY PHASE I FOR SAFETY IN CERVICAL LATERAL CORD MAGNETIC STIMULATION IN FOUR CASES OF SPASTIC CEREBRAL PALSY. PRELIMINARY RESULTS

Juan Carlos M. Andreani, MD[1], Franco Moscovicz, MD[2], Fernando Montani, PhD[3]
[1]Ministery of Public Health- Pcia de Buenos Aires - Argentina, Provincial Program Of Neuromodulation, Avellaneda, Argentina, [2]Conicet, Infibioc- Fctad De Farmacia Y Bioquímica - Universidad De Buenos Aires, Buenos Aires, Argentina, [3]Conicet, Iflp-conicet Universidad Nacional De La Plata, La Plata, Argentina

Introduction: Lateral cord magnetic stimulation (LCS) is a new tool proposed to treat spastic cerebral palsy (SCP) based on animal research (1,2) and we are focusing on its clinical application through Cervical Magnetic Stimulation (3). This presentation aims to show preliminary results on safety and secondary outcomes (Ashworth and Duffy scales).

Materials / Methods: 2 males and 2 females, with unilateral refractory Spastic Cerebral Palsy, mean age 32, 6 +- 5,6 years old were enrolled according to inclusion and exclusion criteria (Table 1). Lateral Cervical Magnetic Stimulation (LCMs) was applied at the affected side, at 80% of the motor threshold of the cervical musculature, with 10 trains of 100 pulses at 10Hz, completing 1,000 pulses in total. Each train lasted 10 seconds with an interval of 50 seconds, during 30 minutes. Applications were repeated twice a week during 2 months.
Ashworth and Duffy Scales were pre-interventional and weekly measured and adverse events were recorded during weekly assesments.

Results: Adverse events were dizziness (1 episode, Patient 1), and mild cephalagia, 2 episodes (Patient 3). Ashworth Scale improved from a mean 3.1+- 0.7 to 2.5 +- 0.5 and Duffy Scale dropped from 8.1+- 1.2 to 5.2 +- 0.9

Discussion: The rationale of this clinical trial is that the author has demonstrated the decrease in the threshold of excitability of the nociceptive response by electrical stimulation of the lateral spinal cord in an animal model, thus its beneficial action on abnormal muscle tone and also improvements in motor function. . and speech functions (4,5) are predictable.
Spastic Cerebral Palsy has been chosen as a therapeutic target population due to its chronic and irreversible manifestations that, until now, have few therapeutic options.
It is ancient knowledge that electrical currents can alter the functions of the Nervous System (6). In recent decades there has been an improvement in these stimulation techniques, with Transcranial Magnetic Stimulation (TMS) applied through a coil that receives an alternating electric current (7). This therapy, developed in the eighties, is capable of modulating brain activity, through the stimulation of different areas of the Nervous System, with minimal side effects.
The objective of this presentation is to show preliminary results of safety measures, tolerance and results on outcome measures.

Conclusions: Preliminary results show this method well tolerated with good results on speech performance and Spasticity.

Supplemental Data:

TABLE 1

INCLUSION AND EXCLUSION CRITERIA

INCLUSION CRITERIA

- Age 18 years or older.
- Spastic Cerebral Palsy with stable condition diagnosed in the chilhood through Hammersmith Infant Neurological Examination and/ or Prechtl Qualitative Assessment of General Movements
- Motor disability unilateral or predominantly unilateral.
- Clinically evident speech disorders. Duffy Scale 5 or lower
- Normally or slightly subnormal intellectual coefficient (Weschler's test – WAIS – IV = or > 80, and /or Minimental test = or > 24)
- Absence of psychiatric disorders
- Absence of congenital genetic or metabolic disease
- Absence of treatment any type of previous treatment with Magnetic Stimulation

EXCLUSION CRITERIA

- Cardiac or severe respiratory disorders.
- Steady abnormal postures (except possible orthopedic surgical correction)
- Recurrent chronic bronchial or pulmonary infections.
- Psychiatric disorders
- Chronic recurrent urinary infections
- Severe osteoporosis in affected limbs
- Chronic skin ulcers
- Drug addiction.
- History of seizure disorder
- Personal history, or in close relatives, of medical legal complaint

TABLE 2

ADVERSE EVENTS

Patient 1 Dizzines 1 episode, cephalalgia 3 episodes

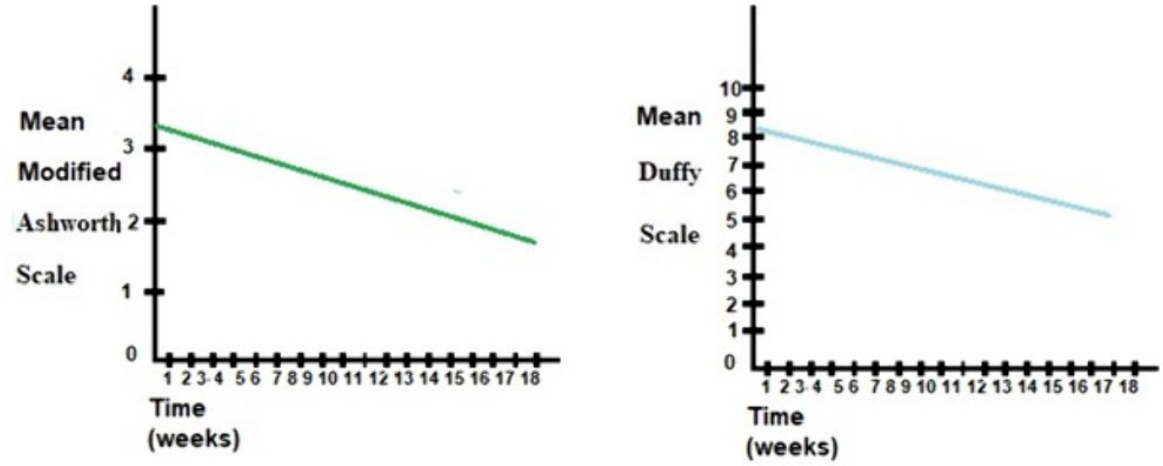
Patient 2 None

Patient 3 Dizzines 1 episode

Patient 4 None

TABLE 3 _____

Modified Ashworth Scale improved from a mean 3.3+- 0.9 to 2.4 +- 0.5 and Duffy Scale dropped from 8.3+- 1.4 to 5.5 +- 1.4 to 5.5 +- 1



References: 1) Andreani JCM, Guma C. Lateral Cord Stimulation (LCS) to relieve spasticity experimental protocol and results. Proceedings of the 10th Conference of the International Federation of Electrical Stimulation (IFESS) Montreal-Canada, July 4-8th 2005. pp 153-5. 2) Andreani JCM, Guma C. Surgically Brain Damaged Pig as a model to investigate FES's applications on spasticity of cerebral and related diseases. Proceedings of the 10th Conference of the International Federation of Electrical Stimulation (IFESS) Montreal-Canada, July 4-8th 2005. pp 156-8. 3) Nakagawa K, Nakazawa K. Static Magnetic Field Stimulation Applied Over the Cervical Spinal Cord Can Decrease Corticospinal Excitability in Finger Muscle. Clin Neurophysiol Pract. 2018 Feb 23;3:49-53. 4) Andreani JCM, Guma C. New animal model to mimic spastic cerebral palsy: the brain damaged pig preparation. Neuromodulation Vol 11 N3 ; pp 196-201. 5) Andreani JCM, Guma C. Lateral cord stimulation decreases spastic electromyographic spreading. Responses in a brain-damaged pig preparation. Neuromodulation Vol 11 N3; pp 202-207. 6) Khedr EM, Kotb H, Kamel NF, Ahmed MA,

Sadek R, Rothwell JC. Longlasting antalgic effects of daily sessions of repetitive transcranial magnetic stimulation in central and peripheral neuropathic pain. J Neurol Neurosurg Psychiatry 2005;76:833–838. 7) Korzhova J, Sinitsyn D, Chervyakov A et al. Transcranial and spinal cord magnetic stimulation in treatment of spasticity: a literature review and meta-analysis. Eur J Phys Rehabil Med 2018;54:75-84

Acknowledgements: The authors thank Professor Osvaldo Rosso of Conicet (La Plata - Argentina) for the assistance provided in the calibration and adaptation of the magnetic parameters used, and to the authorities of the CENIT foundation of Buenos Aires - Argentina for free loan of the magnetic stimulation equipment and to the authorities of the Ministry of Health of the province of Buenos Aires for providing us with transportation to transport the participants from their homes or chronic hospitalization centers, to the place of application, and their corresponding returns.

Learning Objectives: 1) To show the progress in the application of Lateral Cord Stimulation for the refractory Spasticity 22) Highlight the preliminary results on the safety and feasibility of magnetic spinal Lateral Cord stimulation (msLCS)

Financial Disclosures: The authors have no conflict of interest

Disclosure: No significant relationships.

Poster Abstracts

159

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

COMBINATION OF RTMS AND LORETA FOR MANAGING HUNTINGTON'S DISEASE: A CASE REPORT

Seyed Masoud Arzaghi, MD
Tehran University of Medical Sciences, Tehran, Iran

Introduction: Huntington disease (HD) is a progressive brain disorder that causes uncontrolled movements, emotional problems, and loss of thinking ability. Other less well-known, but prevalent and often debilitating features of HD include unintended weight loss, sleep, and circadian rhythm disturbances, and autonomic nervous system dysfunction.We report on the use of repetitive transcranial magnetic stimulation (rTMS) with a combination of LORETA in a 73 -year-old man with old onset HD.

Materials / Methods: Before age 65, he was a high functioning individual. Over about five years, he started to show progressively movement disorders. He was referred for a neurological evaluation of choreoathetosis movements and was diagnosed with late-onset HD, confirmed by genetic testing. In the following step, an electroencephalogram (EEG) of the brain was acquired from him and then functional localization of the patient brain was done by LORETA software and according to the obtained result, the proper rTMS protocol was prepared specifically for the patient. The prescribed protocol includes inhibitory rTMS. Pharmacologic prescriptions including Tetrabenazine, Citalopram, Haloperidol, Clonazepam, Pregabalin were also involved in the treatment procedures. Before starting the therapy, the patient and his family described increased difficulty performing daily tasks and getting in and out of a seated position, feeling exhausted, slow, and stiff upon awakening and throughout the day, and difficulty using his hands to eat. The patient was administered to inhibitory rTMS over the right M1, left M1, and left SMA at 3 Hz with 40%, 70%, and 30% of the motor threshold respectively per session. This protocol has been applied for 12 sessions (three times in a week). The second round of rTMS was prescribed similar to the first one with the addition of the left superior temporal at 3 Hz with 40% of the motor threshold. By completing 24 sessions, a maintenance procedure has been applied to the patient once a week for eight sessions.

Results: It is worth mentioning that, after four sessions of rTMS, the patient showed significant improvements in his movements and overall body condition. He reported better coordination, decreased in-voluntary movements and so better mood and regaining energy.

Discussion: Along with drug therapy, transcranial magnetic stimulation (TMS) as a non-invasive and painless method to stimulate the human brain is a safe and efficasious neuro-rehabilitation method to manage the progression of neurodegenerative diseases such as HD.

Conclusions: Given the current study, we propose that rTMS could be a safely administered rehabilitation method to managing HD patients.

Supplemental Data: -

References: none

Acknowledgements: We gretefully thanks the patient and his family to ccoperate with authors.

Learning Objectives: 1- Repetitive Transcranial Magnetic Stimulation is a successful neuro-rehabilitation method in Huntington's disease. 2- Given highly-burdened neurodegenerative diseases such as HD, administring neuromodulative modalities could safely treat Depression. 3- It sounds more speculative neuromodulatory methods are warranted given complex pharmacotherapy of neurodegenerative diseases.

Financial Disclosures: It declared that the presenting author doesn't have any commercial relationship.

Disclosure: No significant relationships.

160

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

ELUCIDATING THE MECHANISMS OF ACTION OF PULSED RADIOFREQUENCY FOR PAIN

Daniel Benzecry Almeida, MD[1,2], Joel Duarte, MD[2], Jonathan De La Cruz, MD[3]
[1]INSTITUTO DE NEUROLOGIA DE CURITIBA, Functional Neurosurgery, CURITIBA, Brazil, [2]INSTITUTO DE NEUROLOGIA DE CURITIBA, Neurosurgery, CURITIBA, Brazil, [3]University of Antioquia, Medellin, Colombia

Introduction: Pulsed Radiofrequency (PR) is a therapeutic strategy for selected patients with chronic pain, including cases such as radicular pain, facet pain syndrome and complex regional pain syndrome. Despite its current use in clinical practice, few studies have focused on the mechanisms of action of PR.

Materials / Methods: The authors reviewed all scientific data using Pubmed papers from 1980 to November 2022. A total of 11,476 journal articles were analyzed, with only 49 papers found to be dedicated to the mechanisms of action of PR. All the information was organized according to the main mechanism of analgesia.

Results: Various neuromodulatory effects have been descibed in human and animal models of PR. They include myelin desctruction followed by regeneration, mitochondrial edema and rupture, disarrangement of microtubules and microfilaments, fibroblast and macrophage activation, collagen reorganization, improvement in synaptic transmission and regulation of inflammatory response and cellular signaling.

Discussion: There is a paucity of clinical and experimental studies about the mechanisms of action of PR. Acccording to this review, PR induces multiple changes in nerve fibers and axons and perineural space, producing several effects mostly described as neuromodulatory and anti-nociceptive. PRF has been shown to be nondestructive based on the following findings that have thus far emerged from the relevant research: (a) PRF is effective in temperatures below the heat-lesion threshold; (b) there is no significant sensory loss; and (c) a typical PRF procedure does not promote pain, even when touching sensory structures.

Conclusions: Despite the few numbers of studies, PR seems to induce a significant analgesic effect in selected human and animal models of pain, due to multiple mechanisms of action. Further studies are mandatory.

Supplemental Data:

References: Podhajsky RJ, Sekiguchi Y, Kikuchi S, Myers RR: The histologic effects of pulsed and continuous radiofrequency lesions at 42 degrees C to rat dorsal root ganglion and sciatic nerve. Spine (Phila Pa 1976). 2005, 30:1008-13. 10.1097/01.brs.0000161005.31398.58 Facchini G, Spinnato P, Guglielmi G, Albisinni U, Bazzocchi A: A comprehensive review of pulsed radiofrequency in the treatment of pain associated with different spinal conditions. Br J Radiol. 2017, 90:20150406. 10.1259/bjr.20150406 Li X, Ni J, Yng L, et al.: A prospective study of Gasserian ganglion pulsed radiofrequency combined with continuous radiofrequency for the treatment of trigeminal neuralgia. J Clin Neurosci. 2012, 19:824-8. Sluijter ME, Imani F: Evolution and mode of action of pulsed radiofrequency. Anesth Pain Med. 2013, 2:139-41. 10.5812/aapm.10213 Chua NH, Vissers KC, Sluijter ME: Pulsed radiofrequency treatment in interventional pain management: mechanisms and potential indications-a review. Acta Neurochir (Wien). 2011, 153:763-71. 10.1007/s00701-010-0881-5 Hailong J, Hao R, Zipu J, Nan J, Fang L: Pulsed radiofrequency improves neuropathic pain in chronic constriction injury rats through the upregulation of the transcription and translation levels of glial cell line-derived neurotrophic factor. Pain Physician. 2018, 21:33-40. Hamann W, Abou-Sherif S, Thompson S, Hall S: Pulsed radiofrequency applied to dorsal root ganglia causes a selective increase

in ATF3 in small neurons. Eur J Pain. 2006, 10:171-6. 10.1016/j.ejpain.2005.03.001 Elawamy A, Abdalla EE, Shehata GA: Effects of pulsed versus conventional versus combined radiofrequency for the treatment of trigeminal neuralgia: a prospective study. Pain Physician. 2017, 20:873-81. Abejón D, Reig E: Is pulsed radiofrequency a neuromodulation technique?. Neuromodulation. 2003, 6:1-3. 10.1046/j.1525-1403.2003.03009.x Malik K, Benzon HT: Radiofrequency applications to dorsal root ganglia: a literature review. Anesthesiology. 2008, 109:527-42. 10.1097/ALN.0b013e318182c86e

Acknowledgements: None

Learning Objectives: 1. Analyze the current literature focusing on the mechanisms of action of Pulsed Radiofrequency for Pain 2. Describe the mechanisms of action of Pulsed Radiofrequency in human and animal models 3. Encourage the search for further data about how Pulsed Radiofrequency works for patients with Chronic Pain and in which cases they could benefit

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

161

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

DEVELOPMENT OF A METHOD AND TOOL FOR UTILIZING FUNCTIONAL MRI TO IDENTIFY VAGUS NERVE STIMULATION PARAMETERS THAT MAXIMIZE THERAPEUTIC RESPONSE TO AN OPTOELECTRONIC NEUROSTIMULATOR

Alexandre Berger, MSBmE[1,2,3], Catherine Léonard, PhD[1], Aurore Nieuwenhuys, MSBmE, MSBmE[1], Jérôme Garnier, PhD[1], Gilles Vandewalle, PhD[2], Riëm El Tahry, PhD[3,4]
[1]Synergia Medical, Mont-Saint-Guibert, Belgium, [2]GIGA-Cyclotron Research Center-In vivo Imaging, University of Liège, Liège, Belgium, [3]Institute of Neuroscience (IoNS), Catholic University of Louvain, Woluwe-Saint-Lambert, Belgium, [4]Center for Refractory Epilepsy, Department of Neurology, Cliniques Universitaires Saint-Luc, Brussels, Belgium

Introduction: The use of functional MRI (fMRI) to identify the neurostimulation parameters maximizing therapeutic response is a promising tool for personalized therapy. The locus coeruleus (LC) is involved in the antiseizure effects of vagus nerve stimulation (VNS) in drug-resistant epileptic patients(1,2). However, imaging investigations about this nucleus have been limited by its small size and the need of specific MRI sequences to visualize it in vivo. Furthermore, while previous VNS devices hampered fMRI investigations due to embedded ferromagnetic materials, the development of an optoelectronic neurostimulator overcomes these limitations. The present study aimed at (i) developing and optimizing an MRI sequence to visualize the LC; (ii) developing a device – the Optical Communication Device (OCD), to communicate with the optoelectronic neurostimulator during fMRI acquisitions, (iii) defining the optimal parameters that maximize the LC activation in a pilot study in sheep implanted with an optoelectronic neurostimulator.

Materials / Methods: A SIGNA^{TM} Premier 3T MRI system (GE Healthcare, Milwaukee, WI, USA) was used for the optimization of the Magnetization-Transfer Turbo-Flash sequence for LC visualization. The MRI signal was evaluated in four landmarks, positioned in the left and right LC, the CSF and the rhomboid fossa (**Fig.1**). The sequence with the highest LC contrast compared to the neighboring structures was chosen as the reference sequence. Custom-made glass optical fibers were used to transmit near-infrared signals bidirectionally between the External Communication and Charging Device (ECCD) and the Implantable Pulse Generator (IPG). The IPG was positioned within the MRI's static field to assess system sensitivity to MRI noise. Communication testing included various thicknesses of pig skin to determine the maximum thickness for reliable communication.

Results: MT-TFL 7 gives the best discrimination between the two LC and the landmarks (**Fig.1**-**Fig.2**, details of sequences in **Tab.1**). Inside the static field of the MRI, communication with the implant passed for ~50% of the communication commands sent. Using 15m-optical fibers, communication with the IPG remained stable for up to 7.5mm-skin thickness. A sheep has been implanted with the optoelectronic neurostimulator.

Discussion: The signal loss through the skin remains acceptable. Optimization of the OCD is still undergoing for decreasing the sensitivity to the noise. A reliable visualization of the LC has been obtained with the optimized MRI sequence that will be used as part of the pilot MRI acquisitions where the stimulation parameters will be tuned to maximize LC activation with VNS.

Conclusions: This pilot study consitutes the first in vivo acquisitions optimizing VNS based on LC activation.

Supplemental Data:

Sequence	Flip angle (°)	TR (ms)	TE (ms)	Voxel size (mm^3)	Number of slices	Averages
1. MT-TFL	8	81	4	0.39 x 0.39 x 1.5	28	1
2. MT-TFL	8	54	4	0.39 x 0.39 x 1.2	28	1
3. MT-TFL	8	54	5	0.39 x 0.39 x 1.7	28	1
4. MT-TFL	12	54	5	0.39 x 0.39 x 1.7	28	1
5. MT-TFL	16	54	5	0.39 x 0.39 x 1.7	28	1
6. MT-TFL	16	68	5	0.39 x 0.39 x 1.7	28	1
7. MT-TFL	20	68	5	0.39 x 0.39 x 1.7	28	1
8. MT-TFL	16	68	10	0.39 x 0.39 x 1.7	28	1

Table 1 *– Parameters of MT-TFL sequences tested for LC sequence optimization.*

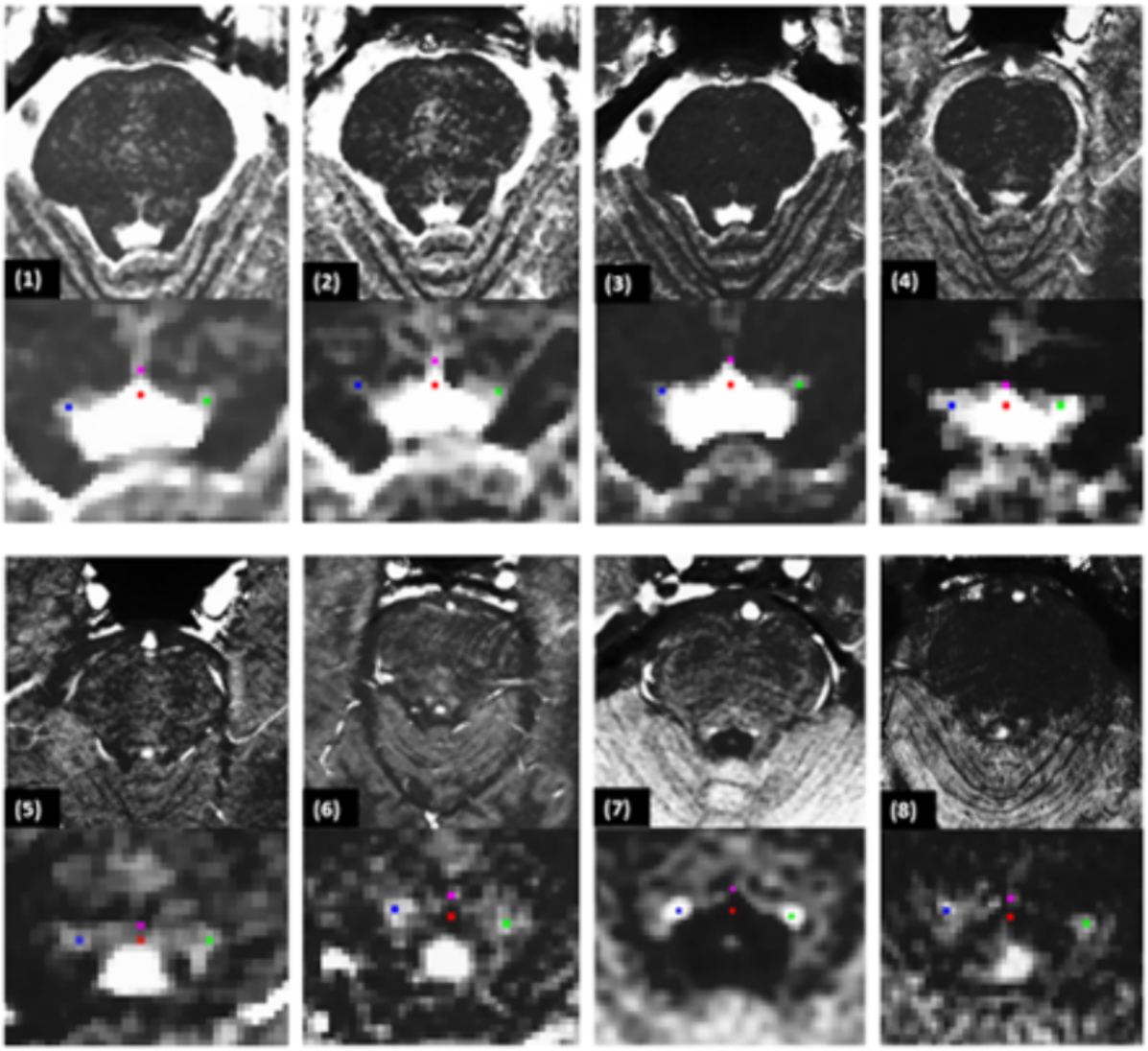


Figure 1 *– LC sequence selection - landmarks for each MT-TFL sequence : CSF (red), right LC (blue), left LC (green) and the anterior-most part of the rhomboid*

fossa (pink).

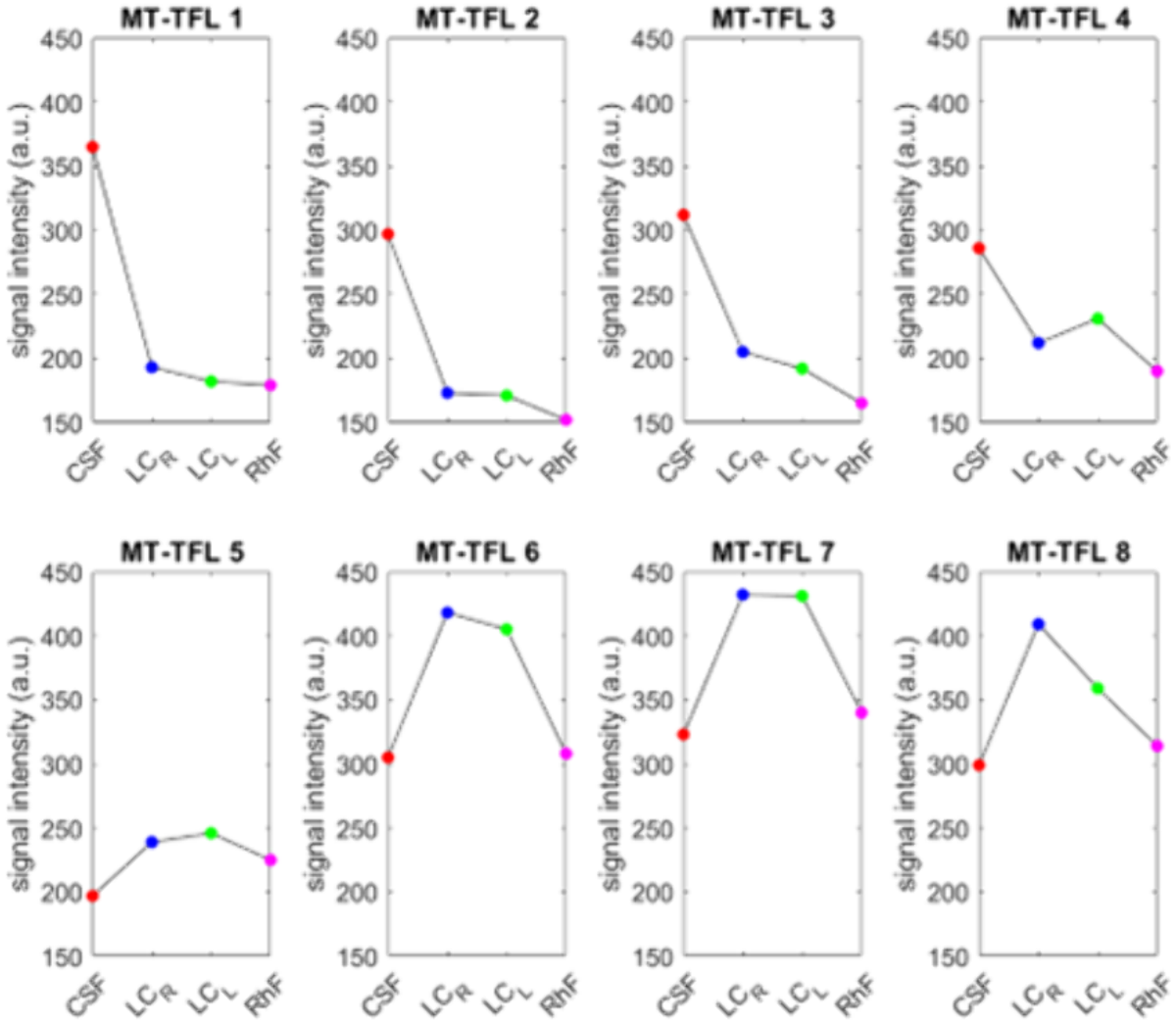


Figure 2 *– LC sequence selection - intensity in the landmarks to study the contrast between the LC and the surrounding tissues. CSF : cerebrospinal fluid, LC_R : right locus coeruleus, LC_L : left locus coeruleus, and RhF : anterior-most part of the rhomboid fossa.*

References: 1. Krahl SE, Clark KB, Smith DC, Browning RA. Locus Coeruleus Lesions Suppress the Seizure-Attenuating Effects of Vagus Nerve Stimulation. Epilepsia. 1998 Jul;39(7):709–14. 2. Dorr AE, Debonnel G. Effect of Vagus Nerve Stimulation on Serotonergic and Noradrenergic Transmission. Journal of Pharmacology and Experimental Therapeutics. 2006 Aug;318(2):890–8.

Acknowledgements: AB is supported by Synergia Medical and the Walloon Region (Industrial Doctorate program, convention n°8193).

Learning Objectives: - Extract LC activation peri-stimulation in vivo. - Develop a system to control the stimulation parameters remotely. - Acquire the first fMRI data of a sheep implanted with an optoelectronic neurostimulator. - Propose a novel personalized strategy for establishing the stimulation parameters based on the central activation of the vagal efferent network assessed using fMRI.

Financial Disclosures: This project received financial support from the Walloon Region (Belgium)

Disclosure: AB is supported by Synergia Medical and the Walloon Region (Industrial Doctorate program, convention n°8193).

162

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

VALIDATION OF THE MULTIDIMENSIONAL CLINICAL RESPONSE INDEX IN A 295-PATIENT COHORT SUFFERING FROM CHRONIC NON-SPECIFIC PAIN TREATED WITH IMPLANTED NEUROSTIMULATION

Philippe Rigoard, MD[1], Amine Ounajim, PhD[1], Lisa Goudman, PhD[2], Bertille Lorgeoux, MSc[1], Sandrine Baron, RN[1], Nivole Kevin, MSc[1], Mathilde Many, MSc[1], Lucie Lampert, MSc[1], Romain David, MD[1], Maarten Moens, MD[2], Maxime Billot, PhD[1]
[1]University Hospital Centre Poitiers, PRISMATICS Lab, Prismatics (predictive Research In Spine/neurostimulation Management And Thoracic Innovation In Cardiac Surgery), Poitiers, France, [2]Vrije Universiteit Brussel, Stimulus Research Group, Jette, Belgium

Introduction: A significant portion of patients undergoing spine surgery (10–50%) [1] experience new or persistent back and leg pain after the procedure [2], referred to as Persistent Spinal Pain Syndrome type 2 (PSPS-T2) [3]. PSPS-T2 is influenced by various factors and adversely affects patients' quality of life [4-6]. Despite constantly innovative digital technologies and Artificial Intelligence (AI), pain is still assessed by “gold-standard tools” such as the Numerical Pain Rating Scale (NRPS) score [7]. Pain intensity assessment have limitations in capturing the multidimensional nature of pain. In a previous prospective observational study including 200 PSPS-T2 patients, we internally validated the Multidimensional Clinical Response Index (MCRI) to evaluate the pain-related health status of PSPS-T2 patients, which considers pain intensity, functional capacity, psychological well-being, quality of life, and pain mapping. Our aim was to conduct external validation of the MCRI evaluation tool in chronic pain patients treated with implanted neurostimulation by comparing the MCRI to other assessments including ODI, EQ-5D, HADS, NPRS, and pain surface.

Materials / Methods: In this study, we used data from the real-life retrospective observational study: PRISMAP, which included 295 patients with up to 5 years of follow-up after undergoing neurostimulation implantation. To compare the MCRI to other assessments including ODI, EQ-5D, HADS, NPRS, and pain surface, we used Pearson’s rho correlations between the various measures, as well as by analyzing their sensitivity and specificity in detecting satisfaction with change, as measured by the PGIC, to evaluate criterion validity.

Results: The MCRI, as a single composite measure, outperformed other assessments in capturing several dimensions of pain more accurately with correlations above 0.64. Furthermore, it demonstrated the most balanced performance compared to the remaining indexes, exhibiting the highest sensitivity (84.4%) and specificity (68.9%) for identifying patient satisfaction with change (PGIC > 5).

Discussion: The MCRI tool has shown good validity results, by indicating that this novel composite index better represents the global health of chronic pain patients. The MCRI could help to refine pain assessment and therapy evaluation by informing the physician’s perception of the patient’s condition based on objective and holistic metrics, and also by providing new insights regarding the efficacy of different neurostimulation modalities, before ultimately being adapted to other therapies.

Conclusions: The MCRI as an evaluation tool seems adequate and valid for holistically evaluating pain-related health status of chronic pain patients implanted with a neurostimulation device.

Supplemental Data:

References: 1. Macrae, W.A. Chronic Post-Surgical Pain: 10 Years On. *British Journal of Anaesthesia* **2008**, *101*, 77–86, doi:10.1093/bja/aen099. 2. Chan, C.; Peng, P. Failed Back Surgery Syndrome. *Pain Med* **2011**, *12*, 577–606, doi:10.1111/j.1526-4637.2011.01089.x. 3. Christelis, N.; Simpson, B.; Russo, M.; Stanton-Hicks, M.; Barolat, G.; Thomson, S.; Schug, S.; Baron, R.; Buchser,

E.; Carr, D.B.; et al. Persistent Spinal Pain Syndrome: A Proposal for Failed Back Surgery Syndrome and ICD-11. *Pain Med* **2021**, *22*, 807–818, doi:10.1093/pm/pnab015. 4. Schug, S.A.; Lavand'homme, P.; Barke, A.; Korwisi, B.; Rief, W.; Treede, R.-D.; IASP Taskforce for the Classification of Chronic Pain The IASP Classification of Chronic Pain for ICD-11: Chronic Postsurgical or Posttraumatic Pain. *Pain* **2019**, *160*, 45–52, doi:10.1097/j.pain.0000000000001413. 5. Naiditch, N.; Billot, M.; Moens, M.; Goudman, L.; Cornet, P.; Le Breton, D.; Roulaud, M.; Ounajim, A.; Page, P.; Lorgeoux, B.; et al. Persistent Spinal Pain Syndrome Type 2 (PSPS-T2), a Social Pain? Advocacy for a Social Gradient of Health Approach to Chronic Pain. *JCM* **2021**, *10*, 2817, doi:10.3390/jcm10132817. 6. Ounajim, A.; Billot, M.; Goudman, L.; Louis, P.-Y.; Yousri, S.; Roulaud, M.; Bouche, B.; Wood, C.; Page, P.; Lorgeoux, B.; et al. Finite Mixture Models Based on Pain Intensity, Functional Dis-Ability and Psychological Distress Assessment Allow to Identify Two Distinct Classes of Persistent Spinal Pain Syndrome Type 2 Patients Related to Their Quality of Life. *Preprints 2021, 2021080527 (doi: 10.20944/preprints202108.0527.v1)*. 7. Boonstra, A.M.; Schiphorst Preuper, H.R.; Balk, G.A.; Stewart, R.E. Cut-off Points for Mild, Moderate, and Severe Pain on the Visual Analogue Scale for Pain in Patients with Chronic Musculoskeletal Pain. *Pain* **2014**, *155*, 2545–2550, doi:10.1016/j.pain.2014.09.014.

Acknowledgements:

Learning Objectives: 1/ A single composite multidimensional clinical response index (MCRI), including quality of life, psychological distress, functional disability, pain intensity and pain surface, represented the best compromise among all existing indexes to assess patient's health status of patients with implanted neurostimulation. 2/ A single composite multidimensional clinical response index (MCRI) showing the highest sensitivity/specificity related to Patient Global Impression of Change (PGIC) following neurostimulation. 3/ Multidimensional clinical response index (MCRI) is a 0-10 scale with a Minimal Clinically Important Difference (MCID) of 1.05 points, offering higher accuracy than other evaluation methods to detect pain changes.

Financial Disclosures: Outside the submitted work : Rigoard P. reports grants and personal fees from Medtronic, Abbott and Boston Scientific. Moens M. reports speaker fees from Medtronic and Nevro. The remaining authors have nothing to disclose.

Disclosure: No significant relationships.

163

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

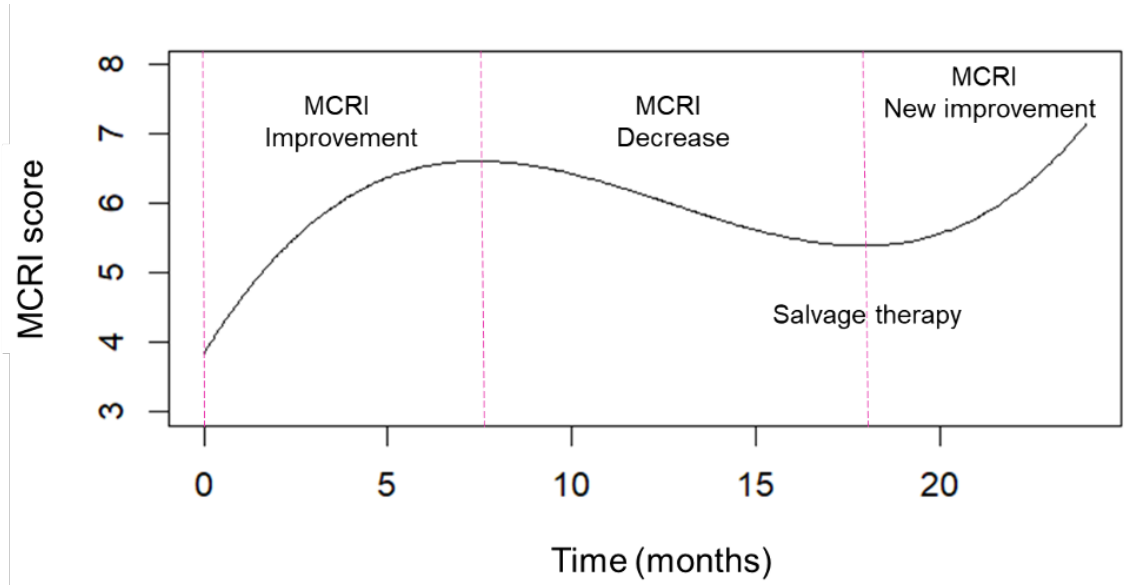
LONG-TERM TRAJECTORIES OF CHRONIC PAIN PATIENTS IMPLANTED WITH A NEUROSTIMULATION DEVICE: A LATENT CLASS TRAJECTORY ANALYSIS

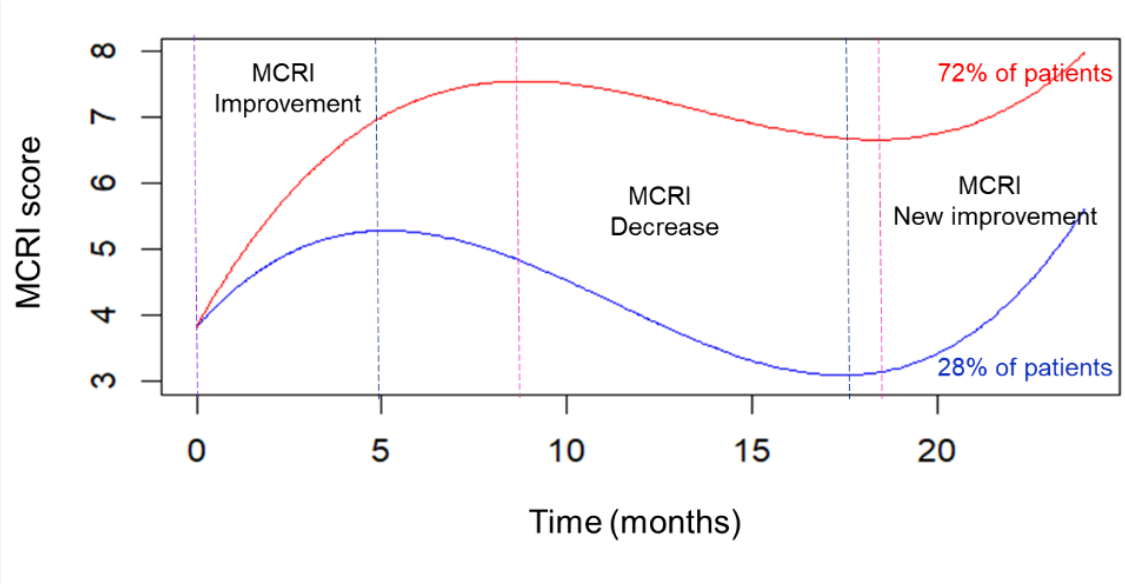
Maxime Billot, PhD[1], Amine Ounajim, PhD[1], Lisa Goudman, PhD[2], Bertille Lorgeoux, MSc[1], Sandrine Baron, RN[1], Sarah Borel, MSc[1], Manuel Roulaud, MSc[1], Nivole Kevin, MSc[1], Mathilde Many, MSc[1], Romain David, MD[1], Maarten Moens, MD[2], Philippe Rigoard, MD[1]
[1]University Hospital Centre Poitiers, PRISMATICS Lab, Prismatics (predictive Research In Spine/neurostimulation Management And Thoracic Innovation In Cardiac Surgery), Poitiers, France, [2]Laarbeeklaan 103, Stimulus Research Group, Jette, Belgium

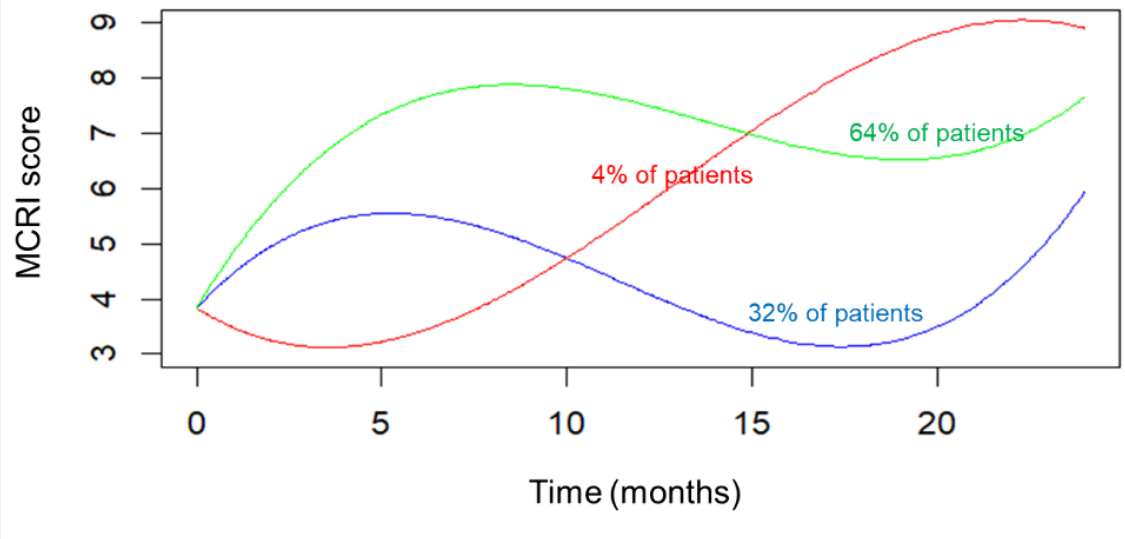
Introduction: Chronic pain is a long lasting condition that consists of pain experienced for more than 3 months. Although the complex pathway of chronic pain patients has long-term effects, assessment was currently provided at given time points with more or less short period. The consideration of distinct snapshot evaluations, which does not reflect the long lasting impact of pain on individual patients and society, may result in a significant loss of information. Latent class trajectory models were able to determine long-term patient trajectory. By using latent class trajectory models, we aimed to extract the clusters with different long-term trajectories of chronic pain patients treated with implanted neurostimulation.

Materials / Methods: Data from the PRISMAP real-life retrospective observational study, including 295 patients with a 3-year follow-up after undergoing neurostimulation implantation, was analyzed. Based on the Multidimensional Clinical Response Index (MCRI) [1], the trajectories were extracted using the clustering algorithm of latent class trajectory models [2]. Trajectories represent the evolution of the pain-related health status (MCRI), from pre-implantation visit to 3 years follow-up of patients implanted with a neurostimulation device.

Results: Among the 295 implanted patients, 174 had a 1-year follow-up, 98 had a 2-year follow-up and only 50 had a 3-year follow-up. We therefore analyzed up to 2-years follow-up data. The trajectories for 1-class (1 cluster including all patients), 2-class (two clusters) and 3-class (3 clusters) models can be found in Figure 1, Figure 2 and Figure 3 respectively. The 2-class model was the most relevant according to our data. In this model, the first cluster (72% of the sample) represents patients with an improvement in their MCRI while the second cluster (28% of the sample) represents patients with negative long-term response to implanted neurostimulation. Although we observed a decrease in MCRI with a minimal MCRI at approximately 17 months post-implantation for improved patients group, the MCRI increases once again following either reprogramming visit or a new salvage therapy (implantation of an adapter or an additional lead).


MCRI score
3
4
5
6
7
8
MCRI
Improvement
MCRI
Decrease
MCRI
New improvement
Salvage therapy
0
5
10
15
20
Time (months)


MCRI score
3
4
5
6
7
8
MCRI
Improvement
72% of patients
MCRI
Decrease
MCRI
New improvement
28% of patients
0
5
10
15
20
Time (months)


MCRI score
3
4
5
6
7
8
9
64% of patients
4% of patients
32% of patients
0
5
10
15
20
Time (months)

Discussion: Thanks to this study, we gathered new insights on the long-term evolution of patients with implanted neurostimulation.

Conclusions: Long-term, real-life trajectory analysis of implanted neurostimulation patients is crucial to get a more relevant understanding and a precise view of their pathway. This type of analyses could allow for better recommendations and patient long-term management.

Supplemental Data:

References: 1. Rigoard P, et al. A Novel Multi-Dimensional Clinical Response Index Dedicated to Improving Global Assessment of Pain in Patients with Persistent Spinal Pain Syndrome after Spinal Surgery, Based on a Real-Life Prospective Multicentric Study (PREDIBACK) and Machine Learning Techniques. J Clin Med. 2021 Oct 24;10(21):4910. 2. Proust-Lima C, Jacqmin-Gadda H. Estimation of linear mixed models with a mixture of distribution for the random effects. Comput Methods Programs Biomed. 2005 May;78(2):165-73. doi: 10.1016/j.cmpb.2004.12.004. PMID: 15848271; PMCID: PMC1913221.

Acknowledgements:

Learning Objectives: 1/ To understand how the long-term trajectories can be used to get a better understanding of patients pathway following implanted neurostimulation. 2/ To get a glimpse of the statistical methods such as latent class trajectory models for the clustering of patients trajectories. 3/ To propose a new way for evaluating implanted neurostimulation efficacy and other long-term therapies.

Financial Disclosures: Moens M. reports speaker fees from Medtronic and Nevro, and Rigoard P. reports grants and personal fees from Medtronic, Abbott and Boston Scientific. Remaining authors have nothing to disclose.

Disclosure: No significant relationships.

164

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

BEHAVIORAL ASSESSMENT OF KHZ-FREQUENCY SWEEP SPINAL CORD STIMULATION-MEDIATED PAIN RELIEF IN A RAT MODEL OF NEUROPATHY

Kerry Bradley, MSc, Dong Wang, PhD, Dongchul Lee, PhD, Kwan Yeop Lee, PhD, Zachary Kagan, PhD
Nevro Corp, Redwood City, United States of America

Introduction: 10 kHz spinal cord stimulation (SCS) has been demonstrated both preclinically and clinically to profoundly reduce neuropathic pain. Recent preclinical work has suggested that the cellular activity of dorsal horn neurons monotonically increases with kHz, where the optimal frequency between 5 kHz – 10 kHz may be cell-dependent. In this feasibility study, we aimed to observe the behavioral effects of a kHz Frequency Sweep (kSweep) SCS waveform in neuropathic rats.

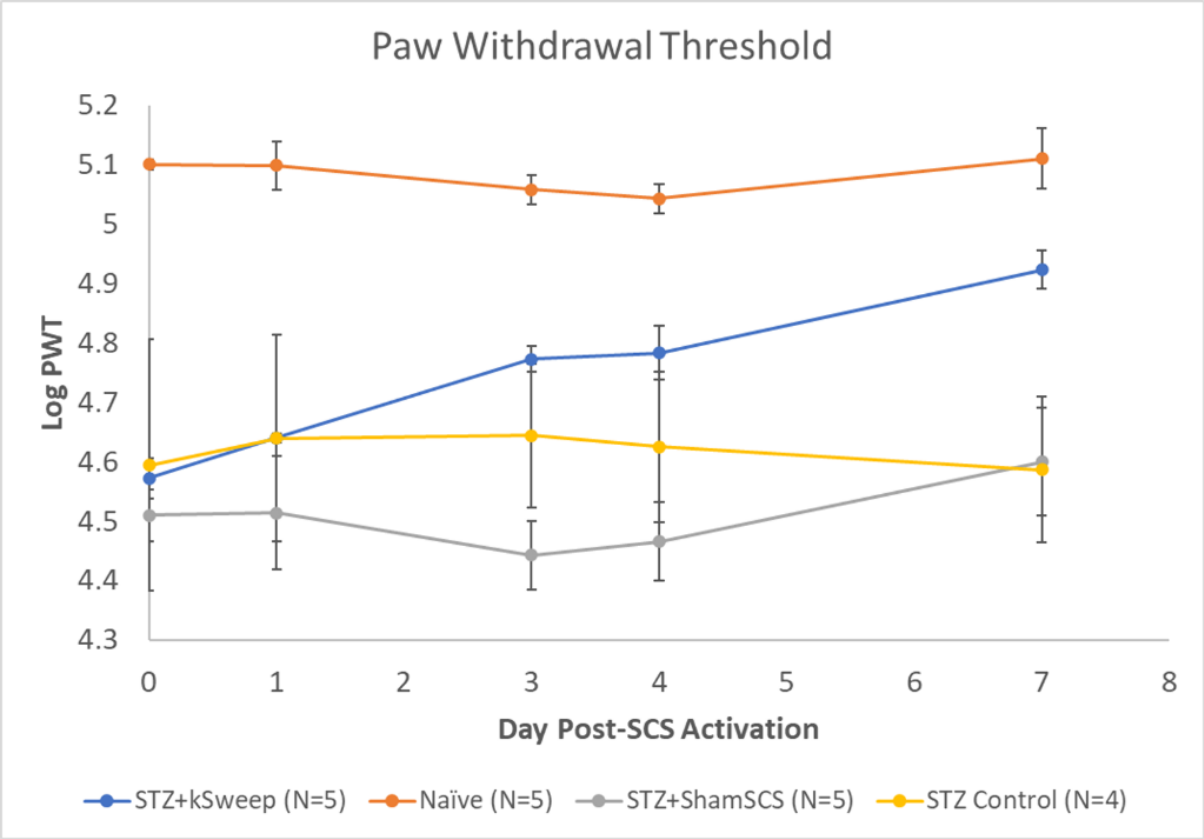
Materials / Methods: We established four testing groups: Naïve controls (N=5), streptozotocin (STZ) controls (N=4), STZ+Sham SCS (N=5) [lead implanted, 0mA], and STZ+kSweep SCS (N=5) [lead implanted, SCS amplitude = 30% motor threshold]. A single effective dose (60 mg/kg) of the cytotoxic agent STZ caused the rats to become hyperglycemic within 72 hours, which lasted for several weeks. The kSweep waveform consisted of a continuous ‘round-robin’ delivery of 20s each of 5 kHz, 6.5 kHz, 9 kHz, and 10kHz, each with pulse width = 30 us, and delivered for 24h/day. Von Frey testing was used to assess mechanical allodynia at Baseline/Day0, Day1, Day3, Day4/5, and Day7 post-stimulation activation.

Results: Mixed 2-way repeated measures ANOVA suggested statistically-significant differences between groups and over time ($p < 0.05$). Post-hoc testing revealed that kSweep SCS significantly elevated the mechanical pain withdrawal thresholds compared to STZ controls or STZ+Sham SCS animals ($p<0.05$), reaching statistical equivalence to Naïve controls ($p=0.31$).

Discussion: Compared to previous findings, these results suggest that kSweep SCS operates over similar time course with approximately similar outcomes as 10 kHz SCS, and may provide an alternative waveform for therapeutic versatility.

Conclusions: In this feasibility study, we observed that a high kHz SCS strategy, kSweep, resulted in behavioral outcomes reflective of mechanical pain reduction in a neuropathic rodent model.

Supplemental Data:



References: Kapural L, Yu C, Doust MW, Gliner BE, Vallejo R, Sitzman BT, Amirdelfan K, Morgan DM, Yearwood TL, Bundschu R, Yang T. Comparison of 10-kHz high-frequency and traditional low-frequency spinal cord stimulation for the treatment of chronic back and leg pain: 24-month results from a multicenter, randomized, controlled pivotal trial. Neurosurgery. 2016 Nov;79(5):667. Lee KY, Bae C, Lee D, Kagan Z, Bradley K, Chung JM, La JH. Low-intensity, kilohertz frequency spinal cord stimulation differently affects excitatory and inhibitory neurons in the rodent superficial dorsal horn. Neuroscience. 2020 Jan 21;428:132-9. Petersen EA, Stauss TG, Scowcroft JA, Jaasma MJ, Brooks ES, Edgar DR, White JL, Sills SM, Amirdelfan K, Guirguis MN, Xu J. Long-term efficacy of high-frequency (10 kHz) spinal cord stimulation for the treatment of painful diabetic neuropathy: 24-Month results of a randomized controlled trial. Diabetes research and clinical practice. 2023 Sep 1;203:110865.

Acknowledgements: This work was sponsored by Nevro Corp.

Learning Objectives: 1. To understand the effect of varied high kHz frequency SCS on a preclinical analog of pain relief (alleviation of mechanical hypersensitivity) 2. To observe the relative time course of pain relief with varied high kHz frequency SCS. 3. To consider the translation value of preclinical pain relief observations to clinical application of varied high kHz frequency SCS to single high kHz frequency SCS.

Financial Disclosures: Kerry Bradley, Nevro Corp, VP Scientific Affairs, Salary and stock Dongchul Lee, Nevro Corp, Director Theoretical Research, Salary and stock Dong Wang, Nevro Corp, Principal Research Scientist, Salary and stock Kwan Yeop Lee, Nevro Corp, Principal Research Scientist, Salary and stock Zachary B Kagan, Nevro Corp, Principal Research Scientist, Salary and stock

Disclosure: Kerry Bradley, Nevro corp, salary and stock

165

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

DEPTH ANALYSIS OF DORSAL HORN NEURONS ACTIVATED BY 10KHZ SPINAL CORD STIMULATION IN CALCIUM-SENSITIVE IMAGING

Dongchul Lee, PhD, Dong Wang, PhD, Kwan Yeop Lee, PhD, Zachary Kagan, PhD, Kerry Bradley, MSc
Nevro Corp, Redwood City, United States of America

Introduction: High-frequency (10 kHz) spinal cord stimulation (SCS) is an established and expanding neuromodulatory technique used for the treatment of chronic pain. The differential effects of high kHz frequencies on dorsal horn neurons have not been systematically investigated. To study the distribution of neurons activated by kilohertz SCS, we employed calcium imaging techniques to quantitatively assess the impact of electrical stimulation.

Materials / Methods: In this study, transverse spinal cord slices with a thickness of 400 μm were loaded with calcium-sensitive dyes (Cal520). Subsequently, extracellular electric fields with varying frequencies (1 kHz to 10 kHz and repeated 1kHz) and identical pulse widths (charge-balanced biphasic square pulses of 30 μs) were applied to the slices using a microelectrode in aCSF, positioned approximately 200 μm from the outer circumference of the slice to mimic an epidural placement. After a 10-second baseline, the stimulation was delivered for a duration of 10 seconds for each frequency. The fluorescence (F) changes due to the stimulation were computed by calculating the difference between the selected area of cell F during stimulation and that measured at baseline. The depth of the cells was estimated by the distance from the top of the slice (dorsal surface).

Results:

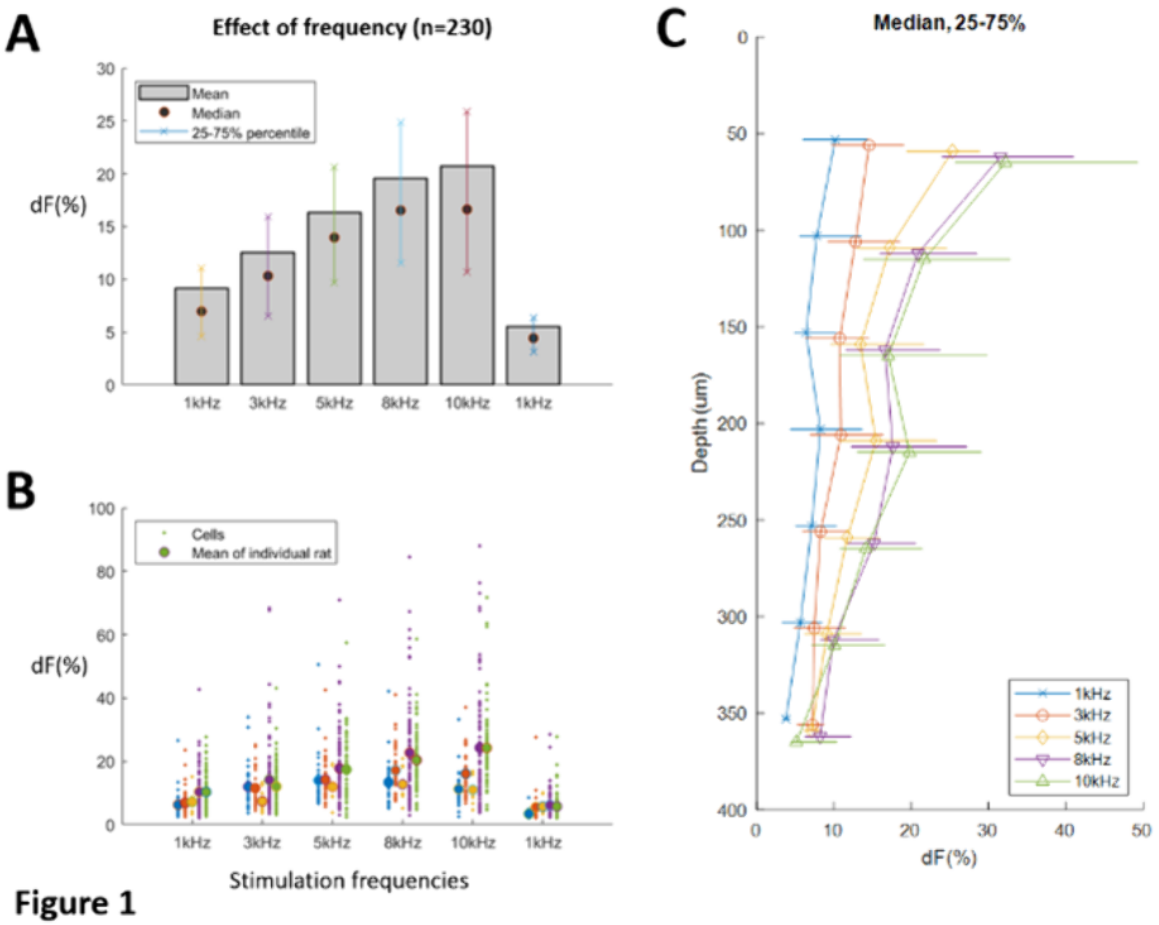


Figure 1

A total of 230 cells from 5 rats, selected based on repeatability throughout the study, were analyzed. The results showed that the mean and median values of F change (Fig1AB) were highest at 10 kHz (+21% ± 14%, +16%) compared to 8 kHz (+20% ± 12%, 16%), 5 kHz (+16% ± 10%, 14%), 3 kHz (+13% ± 9%, 10%), and 1 kHz (+9% ± 7%, 7%). Depth analysis (Fig1C) showed that superficial neurons (<100 µm) were activated more effectively than deeper neurons (up to 350 µm) due to the decay of the electric field for any frequency. The median F changes for 10 kHz vs. 1 kHz were (+26.9%, +8.9%) at <150 µm depth and (+19.8%, +8.2%) at 200 µm. Difference between 10kHz vs. 1kHz was statistically significant ($p<0.01$) up to 300 µm depth.

Discussion: We found that spinal cord neurons are activated by extracellular electric fields in the kHz range in a monotonically increasing manner.

Conclusions: For any depth ranging from 50 µm to 300 µm, higher frequencies activated neurons significantly more than lower frequencies. This effect may extend to deep dorsal horn neurons, including inhibitory interneurons and projection neurons within the spinal cord, suggesting the potential of high-frequency SCS for pain management and modulation of sensory information.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: (1) effect of 10kHz SCS (2) dorsal horn response to 10kHz (3) effect of different frequencies

Financial Disclosures: All authors are full time employees of Nevro

Disclosure: No significant relationships.

166

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

CLOSED-LOOP AMPLITUDE-MODULATED TRANSCRANIAL ALTERNATING CURRENT STIMULATION TO PROBE THE LINK BETWEEN CORTICAL SENSORIMOTOR OSCILLATIONS AND MOTOR CONTROL

Annalisa Colucci, MSc, David Haslacher, MSc, Mareike Vermehren, MSc, Niels Peekhaus, MSc, Khaled Nasr, MSc, Surjo Soekadar, MD
Charité - Universitätsmedizin Berlin, Berlin, Germany

Introduction: Sensorimotor oscillations (8-13 Hz) recordable over central scalp regions, e.g., using electroencephalography (EEG), play an important role in motor planning and execution. However, it is unclear how sensorimotor oscillations are linked to modulation of cortico-spinal excitability, particularly in motor recovery, e.g., after stroke or spinal cord lesions. Non-invasive brain stimulation (NIBS) can directly interact and modulate these brain oscillations, particularly when tuned to a specific personalized frequency and phase. However, up to now, it was unfeasible to apply such frequency- and phase-tuned alternating current stimulation due to stimulation artifacts. Here, we introduce a stimulation paradigm based on based on spatio-spectral decomposition (SSD) and real-time beamforming that allows for millisecond-precise detection of ongoing sensorimotor oscillations, removal of stimulation artefacts, and real-time adjustment of the stimulation signal's phase and amplitude.

Materials / Methods: The new paradigm was tested across five healthy volunteers who engaged in a continuous visuomotor task. Brain oscillations were recorded using 64-channel EEG. Amplitude-modulated transcranial Alternating Current Stimulation was delivered over the motor cortex targeting 6 different phases relative to the ongoing sensorimotor oscillations.

Results: We show that real-time frequency- and phase-tuned closed-loop amplitude-modulated transcranial Alternating Current Stimulation (CLAM-tACS) is feasible and safe.

Discussion: Studies that involve more participants are needed to validate these preliminary results.

Conclusions: This pilot study confirms the feasibility of using CLAM-tACS to target sensorimotor oscillations. Furthermore, it paves the way to the application of closed-loop stimulation to deepen our understanding of motor control and motor recovery.

Supplemental Data:

References:

Acknowledgements: The support of the German Research Foundation (Deutsche Forschungsgemeinschaft - DFG) for this project is gratefully acknowledged.

Learning Objectives: 1. Investigating the efficacy of Closed-loop amplitude-modulated transcranial Alternating Current Stimulation (CLAM-tACS) in modulating sensorimotor brain oscillations. I expect to corroborate further the efficacy of CLAM-tACS in modulating neural oscillations and in particular its effectiveness targeting the sensorimotor cortical oscillations and cortico-spinal neural communication. 2. Using CLAM-tACS to deepen our understanding of the sensorimotor system and investigating the causal role of mu-oscillations on motor control. I envision the use of CLAM-tACS to highlight the functional relationship between cortical mu-oscillations and motor control. I expect CLAM-tACS to induce a direct modulation of cortico-spinal neural communication and thus of motor performance and force control. 3. Paving the way to the application of CLAM-tACS to investigate motor recovery after stroke. I envision the application of CLAM-tACS to noninvasively modulate cortico-spinal neural

communication in stroke survivors, to investigate the role of mu-oscillations in motor recovery after stroke.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

167

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

A SINGLE SITE EXPERIENCE USING MULTIWAVEFORM THERAPIES WITH SPINAL CORD STIMULATION FOR CHRONIC NEUROPATHIC PAIN OVER A THIRTEEN-YEAR PEROID

Kathryn Davies, MBBS, Mark Jackson, MB ChB, Lucy Price, RN
Royal Devon and Exeter University Hospitals, Pain Medicine, EE, United Kingdom

Introduction: Previous Spinal Cord Stimulation (SCS) studies have shown that having multiple neuronal targets can optimise neural activity and improve pain relief for patients (1)(2). Multi-waveform devices that can achieve pain relief utilising both dorsal column and dorsal horn modulation may provide more sustained long-term outcomes for patients. This poster highlights the experience of a single site over nine-years using a multi-waveform SCS device.

Materials / Methods: Retrospective data from a single site was collected for patients treated with SCS between 2014 and 2023. Patients were categorised into two groups; SCS trial or direct to implant (DTI). At implant follow-up patients were asked to report on their greatest percentage change in pain relief, medication changes, and any functional improvements. Information on program use and work status was also collected, for those who reported on it. Patients achieving ≤50% pain relief at follow-up were invited for programming optimisation as per standard of care.

Results: At implant last follow-up 95% of patients are reporting ≥50% pain relief and therefore considered SCS responders. Of the patients responding to SCS therapy, 57% are achieving ≥70% pain relief. 78% of patients reported functional improvement at follow-up, with 57% having reduced opioids. Of the patients who had a DTI procedure, 86% are responding at last follow-up with an average pain reduction of 72%, 80% had improvement in function and 75% reduction in opioids.

Discussion: Data from this site demonstrate that patients using a multi-waveform device utilising surround inhibition in addition to other waveforms are achieving sustained pain relief, alongside improvements in function and medication reductions. Furthermore, the high responder rate supports the use of a DTI approach for suitable patients (3).

Conclusions: This cohort of patients demonstrate that pain relief and functional outcomes using a multi-waveform SCS device are sustained through to nine years and are in line with published research (1-2).

Supplemental Data:

References: 1. Wallace et al. COMBO RCT: Combining Mechanisms for Better Outcomes. NANS. 2022 2. Metzger et al. A Novel Fast-acting Sub-perception Spinal Cord Stimulation Therapy enables Rapid Onset of Analgesia in Patients with Chronic Pain. Expert Review of Medical Devices. 2021 3. Durate RV, Thomson S. Trial Versus No Trial of Spinal Cord Stimulation for Chronic Neuropathic Pain: Cost Analysis in United Kingdom National Health Service. Neuromodulation. 2019;22(2):208-214

Acknowledgements:

Learning Objectives: 1. More neuronal targets optimise poutcomes: multiple neuronal targets can optimise neural activity and improve pain relief for patients 2.Mode of action of multiwave form stimulation: Multi-waveform devices that can achieve pain relief utilising both dorsal column and dorsal horn modulation may provide more sustained long-term outcomes for patients. 3. sustained relief over extended period is achievable: pain relief and functional outcomes using a multi-waveform SCS device are sustained

Financial Disclosures: no significant relationships

Disclosure: No significant relationships.

168

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

A RETROSPECTIVE STUDY OF A SINGLE CENTER EXPERIENCE WITH 10 KHZ HIGH-FREQUENCY THERAPY FOR SPINAL CORD STIMULATION

Kathryn Davies, MBBS[1], Mark Jackson, MB ChB[1], Lucy Price, RN[1], Shibasis Chowdhury, PhD[2]
[1]Royal Devon and Exeter University Hospitals, Pain Medicine, EE, United Kingdom, [2]Nevro Corp, Redwood City, United States of America

Introduction: Spinal cord stimulation (SCS) is a proven treatment modality for chronic intractable pain1. High-frequency SCS, including 10 kHz therapy, provides paresthesia-independent therapy with a unique mechanism of action2. The long-term durability of outcomes with 10 kHz SCS in treating chronic neuropathic pain is supported by evidence from multicenter, prospective randomised control trials with patients followed up to 24 months 3,4. Here, we present a retrospective analysis highlighting our clinical experience with 10 kHz SCS for treating chronic intractable pain.

Materials / Methods: A clinical audit on 74 patients who received 10 kHz SCS therapy between 2016 and 2023 was performed from the clinical database. All results compared outcomes at the last follow-up to baseline, which included responder Rate (RR) defined as the percentage of patients achieving ≥50% pain relief, self-reported percentage pain relief, change in analgesic medication, and improvements in sleep and function. Of the 74 patients, 4 (5.4%) were explanted following infection. Hence, the final analysis included 70 patients.

Results: The clinical audit revealed that the average time between the implant and the last follow-up was 28.9 months (3 weeks to 80 months). Analysis of patient demography revealed that of the 70 patients, 40 were female, 29 were male (1 unknown), 53 had back and or leg pain, 4 had upper limb pain, 5 had lower limb pain, 3 had foot pain, 2 had painful diabetic neuropathy, 2 had abdominal pain and 5 had unspecified pain areas. At the latest clinical follow-up, the average percentage pain reduction was 65.7% (Figure 1), with an RR of 87% (n=60). Compared to the baseline, improvement in function and sleep was reported in 75% (44/59) and 47% (28/59) of patients, respectively, with 37% (21/57) of patients reporting decreased use of analgesic medication (Figure 2).

Discussion: This analysis provides evidence for the long-term durability of 10 kHz SCS therapy for treating chronic neuropathic pain of the trunk and limbs in a real-world healthcare setting. These findings align with reports from other studies2,3 and provide evidence for the real-world clinical use of 10 kHz SCS to treat chronic neuropathic pain conditions.

Conclusions: The evidence from our centre contributes to the body of evidence for sustained pain relief with 10kHz SCS and closely aligns with data from published literature. Further research involving a multi-centric approach to evaluate the long-term benefits of 10 kHz SCS will help explore the utility of this therapy for patients with chronic pain.

Supplemental Data:

References: Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin National Institute of Health and Care Excellence (NICE) guidance [TA159] Published: 22 October 2008 Carolis, G.D. et al. (2017) “Paresthesia-independence: An assessment of technical factors related to 10 kHz paresthesia-free spinal cord stimulation,” May 2017, 4(20;4), pp. 331–341. Available at: https://doi.org/10.36076/ppj.2017.341. Kapural, L. et al. (2016) “Comparison of 10-KHz high-frequency and traditional low-frequency spinal cord stimulation for the treatment of chronic back and Leg Pain,” Neurosurgery, 79(5), pp. 667–677. Available at: https://doi.org/10.1227/neu.0000000000001418. Amirdelfan, K. et al. (2018) “Long-term quality of life improvement for chronic intractable back and leg pain patients using spinal cord stimulation: 12-

month results from the Senza-RCT," Quality of Life Research, 27(8), pp. 2035–2044. Available at: https://doi.org/10.1007/s11136-018-1890-8.

Acknowledgements:

Learning Objectives: 1. the long term efficacy of 10kHz spinal cord stimulation - demonstrated by the results 2. diverse indications for SCS and the efficacy of 10Khz in trunkal neuropathic pain 3. SCS and 10KHz offers improved quality of life through improvement in pain, improved function, reduced medication use, improved sleep

Financial Disclosures: Dr Chowdhuryis paid employee of Nevro Corp. and is provided with restricted stock units form Nevro (<5%)

Disclosure: No significant relationships.

169

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

CHRONICALLY RECORDED IMPEDANCES AND SPINAL ECAP THRESHOLDS IN RATS IN THE SPARED NERVE INJURY MODEL

David Cedeño, PhD[1,2], Ricardo Vallejo, MD, PhD[1,2], David Platt, MSc[1,2], Joseph Williams, PhD[1], Leonid Litvak, PhD[3], David Dinsmoor, MSc[3], Malgorzata Straka, PhD[4]
[1]Illinois Wesleyan University, Blooomington, United States of America, [2]SGX Medical LLC, Bloomington, United States of America, [3]Medtronic, Neuroscience, Fridley, United States of America, [4]Medtronic, Minneapolis, United States of America

Introduction: The effect of spinal cord stimulation (SCS) on neuropathic pain is often studied preclinically using a spared nerve injury (SNI) model. While SCS amplitudes are often set clinically relative to the perception threshold (PT), amplitudes in preclinical models are programmed in reference to the visual motor threshold (vMT). Recent work explored the relationship between vMTs and spinal evoked compound action potentials (ECAPs)—a sensed measure of neural activation that closely relates to PT[1]—in rats using SCS in both anesthetized[2] and awake conditions[3] for up to one day. Here, we investigated the changes in impedances, ECAPs and vMTs following a common SNI timeline across 16 days.

Materials / Methods: We implanted nine anesthetized rats with a six-contact epidural lead, then recorded impedances, ECAP thresholds (ECAPTs), and vMTs (Fig 1). Following our traditional SNI-SCS approach, we performed anesthetized recordings from day 0 onward, along with awake recordings from day 1 onward, to evaluate effect of chronic healing (days 1 to 7), nerve injury (days 7 to 14), and continuous SCS (days 14-16) using differential target multiplexed programming (DTMP). For statistical comparisons, we fit data to a generalized linear mixed-effects (GLME) model and compared effects using estimated marginal means with a Bonferroni correction.

Results: Impedances between neighboring electrodes were stable from day 7 onward (Fig 2). We observed ECAPs in all nine rats for all conditions tested and characterized neural activation via both ECAPTs and ECAPT:vMT ratios. . ECAPT:vMTs were significantly higher post-injury (both day 14 and 16) as compared to days 0, 1 and 7 (Fig 3). No significant differences were observed after SCS (between days 14 and 16), across anesthesia states, or pulse widths. Averaging across anesthesia states and pulse widths, ECAPT:vMT increased from 35± 2% (mean ± S.E.) on implantation day to 54± 1% on day 16.

Discussion: The increase in ECAPT and ECAPT:vMTs after nerve injury may indicate a change in neural excitability or activation that is not altered after two days of continuous SCS using DTMP.

Conclusions: We present, for the first time, rat impedances and ECAPs measured in anesthetized and awake animals for up to 16 days, tracking animals pre-SNI, post SNI, and after continuous SCS. Relevant to translational preclinical research, we observed that 35% of vMT should be used to estimate PT in acute studies similar to our previous work[2]; the ratio increases to ~50% vMT in chronically implanted SNI animals, similar to prior reports suggesting PTs occur at 40-50% of MT[4,5,6].

Supplemental Data:

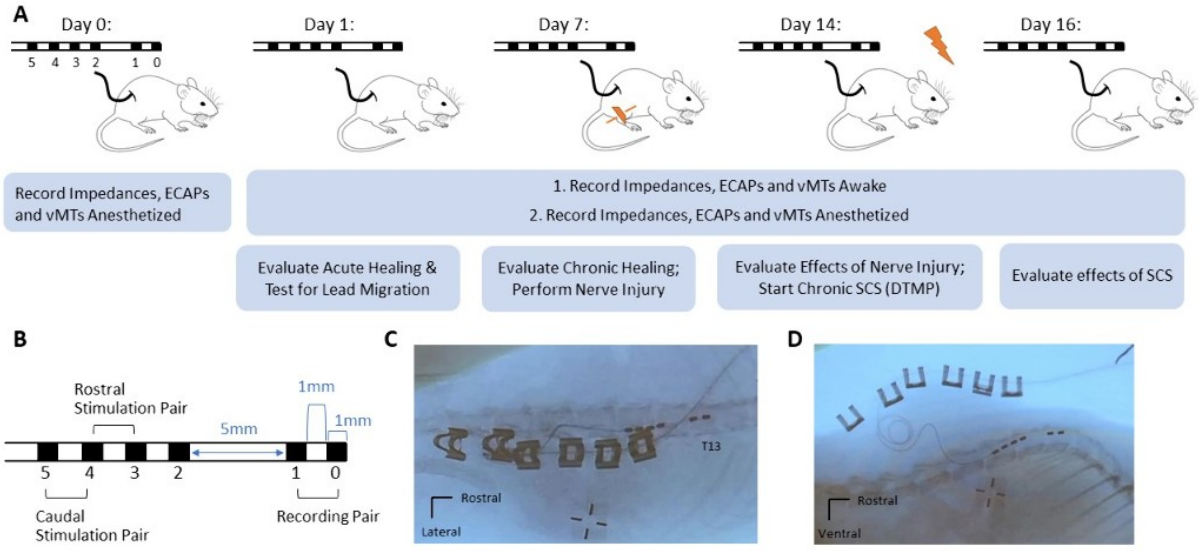


Figure 1: (**A**) A summary of the experimental paradigm. Impedances, ECAPs and vMTs were recorded in the anesthetized rat during implantation (day 0) and were recorded in both awake and anesthetized states on 1, 7, 14, and 16 days after implantation. ECAPs and vMTs were recorded in response to 50 Hz stimuli delivered on two different stimulation electrode pairs with 50, 100, 150, or 200 µs PWs and amplitudes from 0 µA to just above vMT in 5 µA steps. SNI was performed after recordings on day 7, and the effect of the SNI pain model on ECAPs was evaluated on day 14. Additionally, all animals developed the pain model based on Paw Withdrawal Thresholds (PWT) that were collected 5 days post SNI on the injured limb. PWT was 31± 4% (mean ± S.E.) compared to the contralateral limb on the same day. After recordings on day 14, continuous SCS via a DTMP paradigm was applied on contacts e2e3 and e4e5 until day 16. (**B**) The configuration of the SCS lead. ECAPs were recorded on e0e1 in response to 50Hz stimulation applied on the rostral stimulation pair e3e4 and (in separate recordings) on the caudal stimulation pair e4e5. (**C,D**) The lead was placed in T13-L2 as shown in post-mortem images of an exemplar rat.

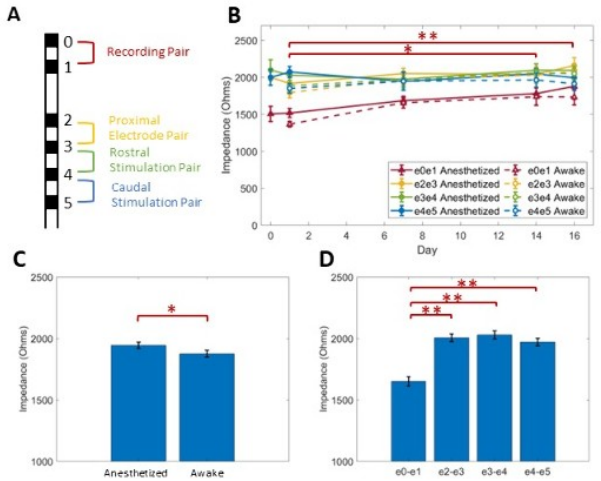


Figure 2: Impedances between neighboring contacts (**A**) were measured in awake and anesthetized states over time (**B**). Impedances were significantly lower on day 1 compared to day 14 and 16 (B), in

awake conditions compared to anesthetized (C), and on the distal recording pair (D). Data summarizes mean ± S.E, with significant comparisons: * indicates P<0.05, ** indicates P<0.001

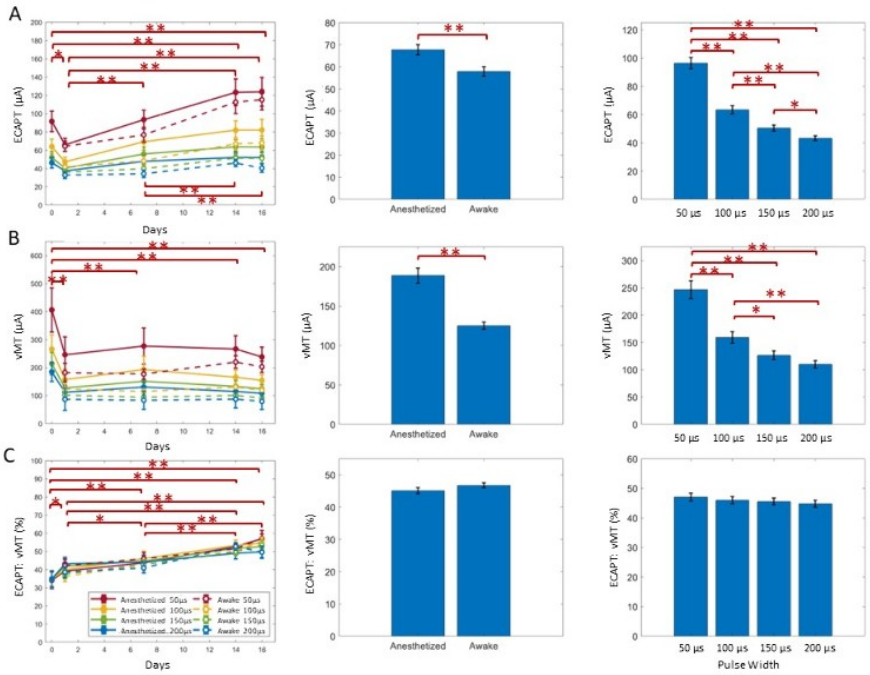


Figure 3: ECAPT (**A**) was calculated for each growth curve collected for each condition and was divided by the vMT (**B**) to create the ECAPT:vMT ratio (**C**). Comparison statistics are summarized for day (left column), anesthesia state (middle column) and pulse width (right column), where * indicates P<0.05, ** indicates P<0.001.

References: 1. Pilitsis, J. G. *et al.* The Evoked Compound Action Potential as a Predictor for Perception in Chronic Pain Patients: Tools for Automatic Spinal Cord Stimulator Programming and Control. *Front. Neurosci.* **15**, 1–11 (2021). 2. Cedeño, D. L. *et al.* Spinal Evoked Compound Action Potentials in Rats with Clinically Relevant Stimulation Modalities. *Neuromodulation* **26**, 68–77 (2023). 3. Dietz, B. E., Mugan, D., Vuong, Q. C. & Obara, I. Electrically Evoked Compound Action Potentials in Spinal Cord Stimulation: Implications for Preclinical Research Models. *Neuromodulation* **25**, 64–74 (2022). 4. Shechter, R. *et al.* Conventional and kilohertz-frequency spinal cord stimulation produces intensity- and frequency-dependent inhibition of mechanical hypersensitivity in a rat model of neuropathic pain. *Anesthesiology* **119**, 422–432 (2013). 5. Song, Z., Viisanen, H., Meyerson, B. A., Pertovaara, A. & Linderoth, B. Efficacy of Kilohertz-Frequency and Conventional Spinal Cord Stimulation in Rat Models of Different Pain Conditions. *Neuromodulation Technol. Neural Interface* **17**, 226–235 (2014). 6. Cedeño, D. L., Kelley, C. A. & Vallejo, R. Effect of stimulation intensity of a differential target multiplexed SCS program in an animal model of neuropathic pain. *Pain Pract.* **23**, 639–646 (2023).

Acknowledgements: This work was supported by Medtronic plc.

Learning Objectives: 1. ECAPs can be recorded chronically in rats. 2. Lead impedances show stability in the neural interface after 7 days post implantation. 3. Following at least 1 day post implantation, muscle activation from SCS appears consistent over 7-day healing and after SNI, in contrast to concurrent changes in neural excitability or activation

Financial Disclosures: Dr. Vallejo is a consultant for Medtronic plc. Drs. Cedeño and Vallejo are co-inventors of patents related to DTMP assigned to Medtronic. Dr. Litvak, Dr. Straka, and Mr. Dinsmoor are employees of Medtronic plc. Dr. Williams and Mr. Platt have no conflicts to disclose.

Disclosure: I am employee of Medtronic plc

170

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

POSITION-RELATED CHANGES IN THE PARESTHESIA AREA WITH CLOSED-LOOP DEVICES: ANALYSIS WITH A COMPUTER MODEL

Jose L. Dura, MSc, PhD[1], Jose De Andres, MD, PhD[2,3], Javier Saiz, MSc, PhD[1]
[1]Universitat Politecnica de Valencia, Center Of Research And Innovation In Bioengineering, Valencia, Spain, [2]General University Hospital, Anesthesia, Critical Care, And Multidisciplinary Pain Management Department, Valencia, Spain, [3]Valencia University Medical School, Anesthesia Unit, Surgical Specialties Department, VALENCIA, Spain

Introduction: The number of fibers in the dorsal columns stimulated is influenced by the distance between the active electrodes and the spinal cord, among other factors. As this distance varies with the position of the body (and with other factors as the respiration), the patient must adjust the amplitude of the neurostimulator's pulses when he changes his body position. The evaluation of these changes measuring the evoking compound action potential (EACP) allows the last generation of neurostimulator to change the amplitude, resulting in a fixed paresthesia feeling independently of the body position or other factors as coughs. The closed-loop algorithm based on ECAP maintains paresthesia's strength, but there is no information on the position of the fibers stimulated for each body position.

Materials / Methods: Using our previously published computer model, we analyzed the fibers stimulated for three body positions: prone, standing and supine, considering a different distance from the active poles to the spine for each position. The model computes the fibers that are stimulated in the dorsal column with a diameter larger than 12µm, with a guarded cathode (GC) and a double guarded cathode (DGC) polarity configuration.

Results: By assigning the same ratio (1.4) between the perception ratio and the amplitude used for the simulation, the paresthesia strength is maintained for the three body positions. Contrary to what we might think, the quantity of stimulated fibers increases when the distance between the poles and the spine increases up to 23% (from supine to prone) using the DGC polarity with two leads separated by 6 mm.

Discussion: The fact that fibers are lost between the prone and supine positions has two consequences. On one side, it can cause a loss of paresthesia area, even if the closed-loop device maintains the paresthesia sensation. On the other hand, the fact that the paresthesia area was tested during the implant in prone position can suggest that the area may decrease when the patient changes his position.

Conclusions: The use of a computer model is a powerful tool to study the effects of changes in electrical factors of anatomical characteristics, such as body position. Unfortunately, the models are only valid with tonic stimulation for the moment, as all the fiber models used nowadays are based on the generation of action potentials.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: Show the usefulness of computer models. Find results clinically usable.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

171

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

SPINAL CORD STIMULATOR COMPLICATION RATES: A SINGLE-INSTITUTION, 5-YEAR STUDY (2016-2011)

Christopher Robinson, MD, PhD[1], Aleksy Donjow, MSc[2], Carol Apai, MD[3], Anh Phung, MD[1], Qing Ruan, MD[4], Michael Glicksman, MD[5], Andrew Nguyen, BSc (Hons)[6], Jack Hamilton, BSc (Hons)[7], Sravya Madabhushi, MD[1], Johnson Ho, MD[8], Efemena Diejomaoh, MD[9], Kyle Kang, MD[3], Alexandra Fonseca, MD[10], Alan Kaye, MD[11], Erkan Kurt, MD[12], Linda Kollenburg, BSc (Hons)[12], Cyrus Yazdi, MD[1], Thomas Simopoulos, MD[1], Reda Tolba, MD[13]
[1]Harvard Medical School, Boston, United States of America, [2]Massachusetts Institute of Technology, Cambridge, United States of America, [3]Rutgers New Jersey Medical School, Newark, United States of America, [4]Weill Cornell Medicine, New York, United States of America, [5]University of Pittsburgh Medical Center, Pittsburgh, United States of America, [6]Virginia Commonwealth University School of Medicine, Richmond, United States of America, [7]University of Toronto, Mississauga, Canada, [8]Rutgers Robert Wood Johnson Medical School, Department Of Anesthesiology And Perioperative Medicine, New Brunswick, United States of America, [9]Meharry Medical College, Nashville, United States of America, [10]Brigham & Women's Hospital, Boston, United States of America, [11]Louisiana State University Health Sciences Center New Orleans, Shreveport, United States of America, [12]Radboud university medical center, Neurosurgery, Veldhoven, Netherlands, [13]Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates

Introduction: Since the initial introduction of spinal cord stimulators (SCS) into the field of neuromodulation in 1967, these devices have been utilized to treat a multitude of chronic pain disorders refractory to both conservative and surgical management.[1,2] Rooted in Melzack and Wall's seminal gate control theory of pain, neuromodulation is based on the principle that electrical stimulation of larger Aβ fibers inhibits nociceptive signals conveyed by smaller Aδ and C fibers.[3] Although efficacious when indicated, SCS is not without associated risks. These risks include biological complications, such as infection, pain, and impaired wound healing, and device complications such as lead migration, lead breakage, and battery failure.[4,5]

Materials / Methods: A retrospective chart review with pre-existing IRB approval was performed on 261 patients who underwent percutaneous SCS implant between 2016-2021 by two experienced interventional chronic pain specialists. The demographics and complications were recorded in the REDCAP database (Table 1, all tables include a detailed breakdown). Data were collected on complications covering biological- (neurological injury, dural puncture, hematoma, infection, inadequate wound healing, etc.) and device-related (implantable pulse generator dysfunction, lead fracture, lead migration, unwanted stimulation, loose connections, etc.). The data was analyzed to determine the complication rate at a single large center institution. The chart review included records starting six months prior to SCS placement and up to a minimum of one year of follow up after placement.

Results: The mean age of the patients was 58.3 +/- 13.1 years with males representing 46.4% and females 53.6% of those studied (Table 1). Respective rates for biological and device complications were 9.2% and 13.8% (Tables 2-3). Thus, 78.9% of patients experienced no complications, and no deaths were reported. Of the 261 patients, 55 patients (21.5%) experienced one or more complications. Five patients (1.9%) underwent SCS explant.

Discussion: Despite the continually-expanding body of literature on SCS, data regarding the incidence of biological and device complications varies widely.[1,6–9] Continual advancements in SCS technology over the last 50 years further underscore the necessity of periodic re-assesment of SCS complication rates.[10,11]

Conclusions: Our results are consistent with current data suggesting that although the rate of complications is high, it is still low with no serious complications or deaths reported possibly more favorable than those studies citing complication and explant rates as high as 30-40% and 6.7-23.9%, respectively. [12–18]

Supplemental Data:

References: 1. Shealy, C. N., Mortimer, J. T. & Reswick, J. B. Electrical inhibition of pain by stimulation of the dorsal columns: preliminary clinical report. *Anesth Analg* **46**, 489–91 (1967). 2. Labaran, L. *et al.* A Retrospective Database Review of the Indications, Complications, and Incidence of Subsequent Spine Surgery in 12,297 Spinal Cord Stimulator Patients. *Neuromodulation* **23**, 634–638 (2020). 3. Melzack, R. & Wall, P. D. Pain mechanisms: a new theory. *Science* **150**, 971–9 (1965). 4. Zan, E., Kurt, K. N., Yousem, D. M. & Christo, P. J. Spinal cord stimulators: typical positioning and postsurgical complications. *AJR Am J Roentgenol* **196**, 437–45 (2011). 5. Mekhail, N. A. *et al.* Retrospective review of 707 cases of spinal cord stimulation: indications and complications. *Pain Pract* **11**, 148–153 (2011). 6. Bendel, M. A. *et al.* Spinal Cord Stimulator Related Infections: Findings From a Multicenter Retrospective Analysis of 2737 Implants. *Neuromodulation* **20**, 553–557 (2017). 7. Cameron, T. Safety and efficacy of spinal cord stimulation for the treatment of chronic pain: a 20-year literature review. *J Neurosurg* **100**, 254–67 (2004). 8. Deer, T. R. & Stewart, C. D. Complications of Spinal Cord Stimulation: Identification, Treatment, and Prevention. *Pain Medicine* **9**, S93–S101 (2008). 9. Eldabe, S., Buchser, E. & Duarte, R. V. Complications of Spinal Cord Stimulation and Peripheral Nerve Stimulation Techniques: A Review of the Literature. *Pain Medicine* **17**, 325–336 (2016). 10. Lam, C. M. *et al.* Advances in Spinal Cord Stimulation. *Bioengineering (Basel)* **10**, (2023). 11. Rauck, R. L. *et al.* Long-term safety of spinal cord stimulation systems in a prospective, global registry of patients with chronic pain. *Pain Manag* **13**, 115–127 (2023). 12. Bendel, M. A. *et al.* Spinal Cord Stimulator Related Infections: Findings From a Multicenter Retrospective Analysis of 2737 Implants. *Neuromodulation* **20**, 553–557 (2017). 13. Deer, T. R. & Stewart, C. D. Complications of spinal cord stimulation: Identification, treatment, and prevention. *Pain Medicine* **9**, S93–S101 (2008). 14. Simopoulos, T. T., Sharma, S., Aner, M. & Gill, J. S. The Incidence and Management of Postdural Puncture Headache in Patients Undergoing Percutaneous Lead Placement for Spinal Cord Stimulation. *Neuromodulation* **19**, 738–743 (2016). 15. Deer, T. R. *et al.* The appropriate use of neurostimulation: avoidance and treatment of complications of neurostimulation therapies for the treatment of chronic pain. Neuromodulation Appropriateness Consensus Committee. *Neuromodulation* **17**, 571–598 (2014). 16. Bendel, M. A. *et al.* Spinal Cord Stimulator Related Infections: Findings From a Multicenter Retrospective Analysis of 2737 Implants. *Neuromodulation* **20**, 553–557 (2017). 17. Turner, J. A., Loeser, J. D. & Bell, K. G. Spinal cord stimulation for chronic low back pain: a systematic literature synthesis. *Neurosurgery* **37**, 1088–95; discussion 1095-6 (1995). 18. Kumar, K. *et al.* Spinal cord stimulation versus conventional medical management for neuropathic pain: A multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain* **132**, 179–188 (2007).

Acknowledgements:

Learning Objectives: 1. To understand the overall complication rates of SCS 2. To understand biological complication rates of SCS and causes 3. To understand device complication rates of SCS and causes

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

172

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

SINGLE-INSTITUTIONAL CROSS-SECTIONAL STUDY: A SURVEY OF PATIENTS LOST TO FOLLOW UP AFTER PERMANENT SPINAL CORD STIMULATOR IMPLANT (2016-2021)

Christopher Robinson, MD, PhD[1], Sravya Madabhushi, MD[1], Linda Kollenburg, BSc (Hons)[2], Michael Glicksman, MD[3], Alexandra Fonseca, MD[4], Aleksy Donjow, MSc[5], Erkan Kurt, MD[2], Johnson Ho, MD[6], Cyrus Yazdi, MD[1], Thomas Simopoulos, MD[1], Michael Schatman, PhD[7], Alan Kaye, MD[8]
[1]Harvard Medical School, Boston, United States of America, [2]Radboud University Medical Center, Neurosurgery, Nijmegen, Netherlands, [3]University of Pittsburgh Medical Center, Pittsburgh, United States of America, [4]Brigham & Women's Hospital, Boston, United States of America, [5]Massachusetts Institute of Technology, Cambridge, United States of America, [6]Rutgers Robert Wood Johnson Medical School, Department Of Anesthesiology And Perioperative Medicine, New Brunswick, United States of America, [7]NYU Grossman School of Medicine, Population Health, New York, United States of America, [8]Louisiana State University Health Sciences Center New Orleans, Shreveport, United States of America

Introduction: Spinal cord stimulation (SCS) therapy is often an option of last resort for patients with post-laminectomy syndrome or an alternative option for patient with complex regional pain syndrome, chronic nonsurgical low back pain, and painful diabetic peripheral neuropathy when conservative management has failed.[1,2] Despite this being a helpful option, SCS is not without complications which can often lead to SCS explant. [3–5] Furthermore, as with any technology, there can be issues that lead to patient frustration and ultimately result to noncompliance and lost to follow up. Here, we explore the reasons behind a cohort of patients who were lost to follow up after permanent SCS placement.

Materials / Methods: A cross-sectional survey was performed on 49 patients who were deemed lost to follow up after not returning to clinic after 1 month following permanent SCS implant. Patients were called and asked an institutional review board-approved questionnaire assessing reasons for not returning to clinic, pain scales such as visual analog scale, Pain and Sleep Questionnaire Three-Item Index (PSQ3) and Oswestry Disability Index (ODI). Patients who were not able to be reached after > 3 attempts or patients who opted out were considered ineligible for the study.

Results: Of the patients lost to follow up, 49% (24/49) completed (eligible) the questionnaire and required on average < 2 calls to be reached (Table 1). Of the eligible patients who still used the SCS, the following reasons were obtained for not following up: 58% (14/24) due to improvement of pain, 13% (3/24) due to little to no improvement in pain, 4% (1/24) due to other urgent health conditions, 8% (2/24) due to noncompliance and missing follow-up appointments (4/24) (Table 2). The remaining 17% (4/24) stopped using the SCS after an average of 1.5 years +/- 1 year due to inadequate pain control (3/24) and unable to recharge the device (1/24). Of these, 2 of the 4 contacted their SCS representatives to help troubleshoot prior to discontinuation. No patients were explanted.

Discussion: Here, we provide the first SCS lost to follow-up cross-sectional study and found that despite being lost to follow-up, 83% of patients continued to use their SCS with the main reason being improvement in pain (58%).

Conclusions: Future studies evaluating a larger patient population across multiple institutions would provide greater insight into the reasons for patients not returning to the clinic after SCS placement and potentially capture those who discontinue it and salvage their therapy.

Supplemental Data:

References: 1. Kumar, K. *et al.* Spinal cord stimulation versus conventional medical management for neuropathic pain: A multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain* **132**, 179–188 (2007). 2. North, R. B., Kidd, D. H., Farrokhi, F. & Piantadosi, S. A.

Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: A randomized, controlled trial. *Neurosurgery* **56**, 98–106 (2005). 3. Deer, T. R. & Stewart, C. D. Complications of spinal cord stimulation: Identification, treatment, and prevention. *Pain Medicine* vol. 9 Preprint at https://doi.org/10.1111/j.1526-4637.2008.00444.x (2008). 4. Staats, P. *et al.* Remote Management of Spinal Cord Stimulation Devices for Chronic Pain: Expert Recommendations on Best Practices for Proper Utilization and Future Considerations. *Neuromodulation* Preprint at https://doi.org/10.1016/j.neurom.2023.07.003 (2023). 5. Babu, R. *et al.* Outcomes of percutaneous and paddle lead implantation for spinal cord stimulation: A comparative analysis of complications, reoperation rates, and health-care costs. *Neuromodulation* **16**, 418–427 (2013).

Acknowledgements:

Learning Objectives: 1. To better understand the reasons for lost to follow-up. 2. To evaluate if patients continued to use their SCS after lost to follow-up. 3. To determine if efforts were made to trouble shoot SCS prior to discontinuation of use.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

173

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

REAL WORLD OUTCOME DATA FOR SINGLE CENTRE PATIENTS IMPLANTED WITH SALUDA MEDICAL SPINAL CORD STIMULATORS SINCE 2020

Jenny Jennings, BSc (Hons)[1], Elyshia Harding, CSW[1], Ganesan Baranidharan, FRCA[2]
[1]Leeds General Infirmary, Chronic Pain Service, EX, United Kingdom, [2]Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

Introduction: Evoked compound action potential (ECAP)-controlled closed-loop spinal cord stimulation (SCS) has been proven to show superior pain management compared to traditional 'open-loop' SCS by providing consistent and precise activation of the spinal cord[(1,2)]. As a large SCS implanting service (approximately 200 implants per year), we wanted to review the outcomes of our patients currently implanted with ECAP-controlled SCS (n≥40) and present a case-series from single-center using ECAP-controlled closed-loop SCS with a single percutaneous lead to treat chronic pain. Our aim is to gather outcome data for our patients pre-and post-implantation to identify those who achieve ≥50% pain relief, and for those who do not achieve ≥50% pain relief, to optimize their programming to improve the effectiveness of their device.

Materials / Methods: Pre- and post-implantation data were gathered from patients implanted with ECAP-controlled closed-loop SCS in our department since 2020. To date, data have been collected for n=8 patients with persistent spinal pain syndrome (PSPS) type 2 (5F; 3M; 55.3 years (mean)) who were implanted with a single 12-contact percutaneous lead (2 patients had two leads but only one lead was programmed) guided by intraoperative paresthesia-based testing. Data were obtained from the hospital patient record (PPM+), the NNR database and the implanted device (if patient consent was obtained). Patient confidentiality was maintained throughout the assessment. The service also conducts a telephone review to gather outcomes (whether the patient experiences pain relief of ≥50.0%) and, for patients with pain relief less than 50%, optimizing their programming in clinic and monitor them by telephone after 6 weeks

Results: To date, data have been analyzed for 8 patients. Mean (±SD) Baseline (n = 8) pain scores (NRS) were 8.8±1.0 and at 24 months (n=7) scores decreased to 2.6±1.1. Patients who reported ≥50.0% pain relief were defined as responders. Mean (±SD) Baseline (n = 8) EQ5D scores were 0.2±0.3 and at 12 months (n=5) scores increased to 0.6±0.7 with improvements of more than 5xMCID (0.074) at 12- and 24 months. Further data for patients implanted since 2020 (n≥40) are currently being
compiled.

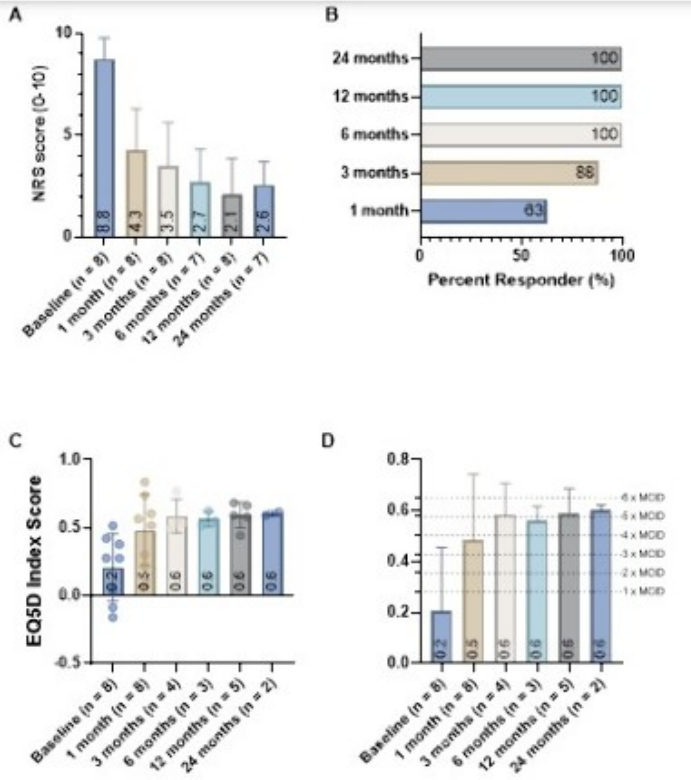


Figure 1: A, B: NRS score and Responder rate over time. Mean (±SD) Baseline (n = 8) pain scores (NRS) were 8.8±1.0 and at 24 months (n=7) scores decreased to 2.6±1.1. Patients who reported ≥50.0% pain relief were defined as responders. At 24 months, there were 100.0% responders.
B, C: EQ5D Index Score and MCID. Mean (±SD) Baseline (n=8) EQ5D scores were 0.2±0.3 and at 12 months (n=5) scores increased to 0.6±0.7. More than 5xMCID (0.074) improvement were observed at 12 months and 24 months.

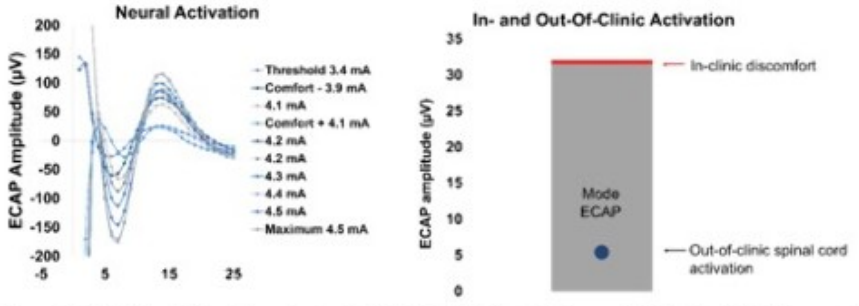


Figure 2: ECAP Amplitude. Example of an individual activation plot from an individual patient. The recorded neural signal consisted of a positive P1 peak followed by a negative N1 peak and a second positive P2 peak. The ECAP amplitude (µV) grew as current increased. In-clinic and out-of-clinic spinal cord activation.

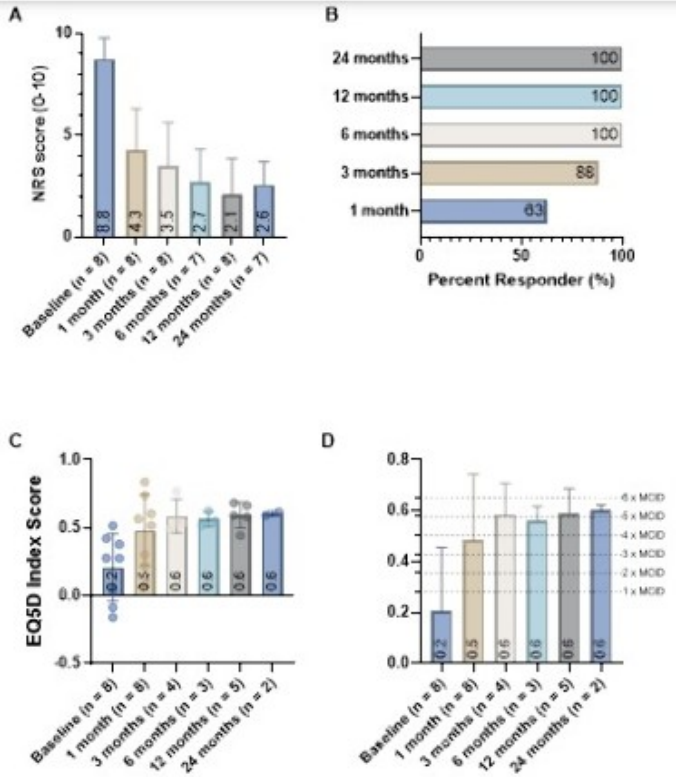


Figure 1: A, B: NRS score and Responder rate over time. Mean (±SD) Baseline (n = 8) pain scores (NRS) were 8.8±1.0 and at 24 months (n=7) scores decreased to 2.6±1.1. Patients who reported ≥50.0% pain relief were defined as responders. At 24 months, there were 100.0% responders.
B, C: EQ5D Index Score and MCID. Mean (±SD) Baseline (n=8) EQ5D scores were 0.2±0.3 and at 12 months (n=5) scores increased to 0.6±0.7. More than 5xMCID (0.074) improvement were observed at 12 months and 24 months.

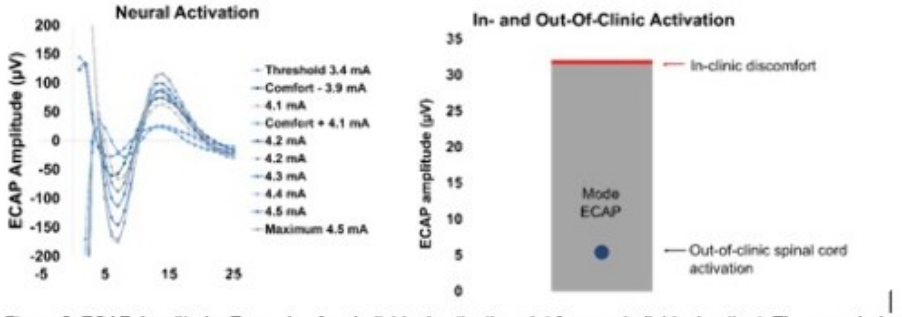


Figure 2: ECAP Amplitude. Example of an individual activation plot from an individual patient. The recorded neural signal consisted of a positive P1 peak followed by a negative N1 peak and a second positive P2 peak. The ECAP amplitude (µV) grew as current increased. In-clinic and out-of-clinic spinal cord activation.

Discussion: Neurophysiology-based programming and accurate neural activation enabled by pulse-pulse monitoring and control have been shown to provide effective, and durable pain relief[1,2]. Further data collection is required to validate these preliminary findings.

Conclusions: Initial data from this single-center case-series suggest the feasibility of using single-lead placements to treat chronic pain. The ECAP-controlled closed-loop SCS system appears to show meaningful outcomes (≥50% pain relief).

Supplemental Data:

References: 1) Mekhail N et al. Long-term safety, and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomized, controlled trial. Lancet Neurol.

2020. 2) Russo M et al. Sustained Long-Term Outcomes with Closed-Loop Spinal Cord Stimulation: 12-Month Results of the Prospective, Multicenter, Open-Label Avalon Study. Neurosurgery. 2020.

Learning Objectives: 1) To gain knowledge in outcomes of patient data 2) To gain knowlegde in the benefits of optimisation 3) To understand the Evoke compound SCS

Financial Disclosures: Boston Scientific - Consultancy Nevro - Consultancy Abbott - Consultancy

Disclosure: No significant relationships.

174

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

NICKEL ALLERGY AND SCS IMPLANTATION: A CASE SERIES

Ramkumar Kalaiyarasan, MD FRCA[1], Dr Manohar Sharma, FRCA FFPMRCA[1], Hemkumar Pushparaj, MD FFPMRCA[1], Mili Shah, MD[2], Kathryn Wilford, RN[1], Alison Cox, RN[1]
[1]The Walton Centre NHS Foundation Trust, Liverpool, United Kingdom, Department Of Pain Medicine, Liverpool, United Kingdom, [2]Royal Liverpool and Broadgreen University Hospital NHS Trust, Liverpool, United Kingdom

Introduction: Allergic reactions to medical devices are not uncommon. Many implanter colleagues do not undertake SCS in those with allergy to nickel. Previous 2 case reports in our literature search mentioned about SCS explant secondary to allergic reactions (1,2). In this case series we wanted to report 3 cases of confirmed nickel allergy with successful SCS implants.

Materials / Methods: This prospective audit has received approval from our Hospital Audit department. Patients with confirmed nickel allergy and SCS implants over the last two years in our centre were reviewed. Previously we have not offered SCS to those with confirmed allergy to nickel.

Results: Between May 2022 to March 2023, 3 patients with confirmed nickel allergy underwent SCS implantation within MDT set up. After extensive discussion and multidisciplinary team meetings involving dermatologist, SCS implants were offered after explaining possible issues with nickel allergy requiring SCS explant. 3 patients had their permanent SCS implants without any untoward events. The implants used were Boston Scientific, NEVRO and Medtronic Sacral nerve stimulation. Patients continue to be monitored for early identification of allergic reactions. None of the patients in the follow-up between 8-18 months have demonstrated any allergic reaction.

Discussion: Allergic reactions to medical devices including SCS implants can be extremely challenging to manage considering likely resemblance to infections. There are no clear guidelines on management of allergic reactions in patients with SCS implants. However, the experience and knowledge from the management of these allergic conditions with other endovascular, cardiac devices and orthopaedic implants provides some guidance, when required.

Conclusions: In carefully selected and fully informed patients with vigilance and liaison with dermatology team, patients with nickel allergy can probably undergo SCS implant without undue concern. Our case series is small, but we are still collecting longitudinal data. At least 3 other similar cases are awaiting implants after successful trial. Patient safety must be carefully evaluated and early involvement of multidisciplinary team involving pain physician, Neuromodulation specialist nurses and dermatologist is crucial when dealing with such cases. We hope to present a large series with longer follow up in due course from this prospective audit.

Supplemental Data: Not applicable

References: 1) Detailed analysis of allergic cutaneous reactions to spinal cord stimulator devices. J Pain Res. 2013 Aug 2)Skin allergic reaction to a spinal cord stimulation (SCS): an analysis of the world literature and a case report. Postepy Dermatol Alergol. 2020 Feb

Acknowledgements: Thanks to Neuromodulation team - Walton Centre

Learning Objectives: Managing patients with nickel allergy for SCS implantation

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

175

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

OPEN-SOURCE COMPUTER VISION ALGORITHM TO AUTOMATICALLY READ VAS PAIN SCORES

Koeun Lim, PhD, Sean Slee, PhD, Andrew Kibler, PhD
BIOTRONIK NRO, Inc., Clinical Technology, Lake Oswego, United States of America

Introduction: The Visual Analogue Scale (VAS) is the standard subjective metric for the assessment of chronic pain commonly used in both clinical studies and routine clinical care. However, scoring VAS assessments requires manual measurement and print scaling, leading to subjective decisions and vulnerability for error . In an ongoing long-term clinical study, over 500 VAS assessments were collected from chronic pain patients at office visits prior to and following spinal cord stimulation (SCS). A computer vision algorithm was developed and validated to address data monitoring needs, enabling improvements in efficiency and accuracy.

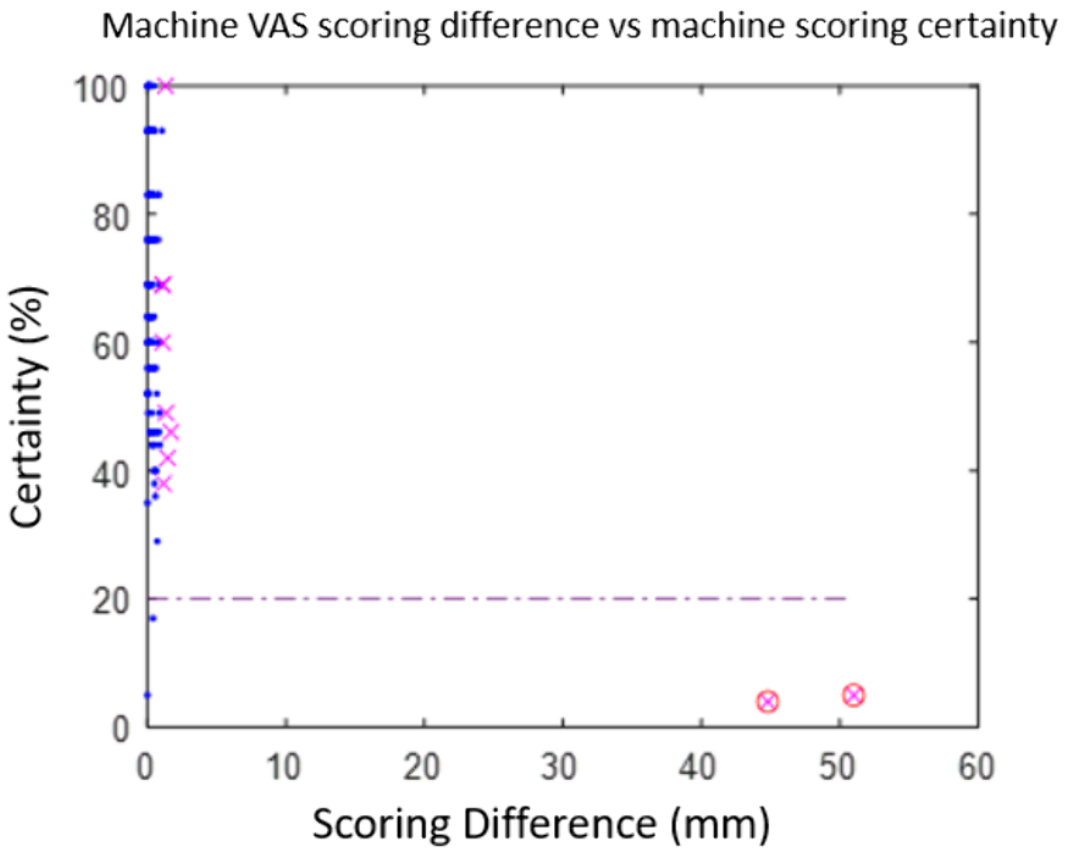
Materials / Methods: A computer vision algorithm was developed to identify visual features that can be consistently extracted from images containing VAS pain scores. Briefly, scanned PDF files containing marked VAS pain ratings were read into MATLAB where image processing was performed to facilitate feature extraction. The final algorithm outputs both VAS pain scores and certainty scores (0~100%). The algorithm was validated against a set of 150 VAS scales manually scored by 5 human experts (serving as a gold standard). The algorithm was then used to monitor clinical study data.

Results: Root mean squared error (RMSE) relative to the mean (gold standard) for the manual measurements was 0.54mm. The algorithm outperformed human experts with a RMSE of 0.47mm and a difference in mean of only 0.07mm. Detection rate of the algorithm was 98.7% such that the algorithm scored 148/150 samples. Two samples fell below 5% certainty and were not scored, leading to manual confirmation which identified incomplete and ambiguous markings. When applied to 549 VAS scales collected in a clinical study, the algorithm flagged 11% with human errors averaging a 7.1mm difference relative to the algorithm, triggering manual confirmation. Excluding these human errors, the mean difference between the human and AI measurements was 0.03mm (SD 0.56mm).

Discussion: An AI algorithm was developed to reduce human error, scaling challenges, and monitoring workload when measuring VAS in a clinical setting. The VAS pain score is a central factor determining therapy outcomes and for evaluating new innovations in pain management. Hence accurate and precise measurement of VAS pain scores is critical to inform clinical decisions and evaluate the success of an intervention.

Conclusions: The AI algorithm developed here was able to automatically scale and read scanned VAS questionnaires and demonstrated greater precision than human experts. An open-source release of this tool is expected to reduce the clinical impact of errors in VAS scoring.

Supplemental Data:



Two scores valued below 5% certainty involved additional marks on scoring chart. The algorithm identified these and flagged for review.

References: None

Acknowledgements: This work was sponsored by BIOTRONIK NRO Inc.

Learning Objectives: 1) The audience will become aware of potential issues scoring VAS metrics 2) and of common sources of error in VAS scoring 3) and of a validated, open solution to improve VAS scoring, particularly for use in clinical studies.

Financial Disclosures: The authors received salary from BIOTRONIK NRO, Inc in the execution of this work.
No financial incentives are expected from providing open-source of this work.

Disclosure: While the authors are supported by BIOTRONIK NRO, this abstract does not cover products or services, and is not about nor does it reference products or services provided by BIOTRONIK. This abstract is about improving scientific accuracy of a commonly use

176

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

ACTIVATION OF CENTRAL NEUROMODULATORY NETWORKS BY LEFT VERSUS RIGHT VAGUS NERVE STIMULATION

Nicholas Kopchenko, MSc, Catherine Thorn, PhD
University of Texas at Dallas, Neuroscience, Richardson, United States of America

Introduction: Left vagus nerve stimulation (VNS) has been FDA approved for the treatment of several neurological disorders including epilepsy, major depressive disorder, stroke, and spinal cord injury. Previous studies have shown that stimulation of the cervical vagus nerve promotes the activation of multiple neuromodulatory networks affected by these disorders.

Materials / Methods: To determine the lateralized effects of VNS on central neuromodulatory networks, we compared c-Fos expression in the locus coeruleus, raphe nuclei, dopaminergic midbrain nuclei, nucleus basalis, and hypothalamus after stimulation of the right or left vagus nerve in anesthetized rats. Adult male (n = 12) and female (n = 12) Long Evans rats were implanted with VNS cuff electrodes around either the right or left cervical vagus nerve and brief bursts of VNS (train duration = 0.5 s; amplitude = 0.8 mA; pulse frequency = 30 Hz; biphasic pulse width = 100 ms) were delivered every 15 s for 1 hour. c-Fos expression was compared within regions of interest between right VNS, left VNS, and sham stimulation treatment groups.

Results: Data is currently being collected and analyzed.

Discussion: As we continue to understand more about the nervous system we are beginning to discovering more laterlization. The bilateral projections of the vagus nerve branches and innervates several organ systems and conveys multiple modalities of information between the viscera and brain. The left and right vagus nerves innervate many of these organs differentially and may detect independent sensory stimuli.

Conclusions: Understanding the differential functional effects of right vs. left VNS on neuromodulatory signaling will inform the development of improved VNS strategies to modulate these networks to treat neurological disorders.

Supplemental Data:

References: 1. Brougher J, Aziz U, Adari N, et al. Self-Administration of Right Vagus Nerve Stimulation Activates Midbrain Dopaminergic Nuclei. *Front Neurosci*. 2021;15:782786. Published 2021 Dec 16. doi:10.3389/fnins.2021.782786 2. Han W, Tellez LA, Perkins MH, et al. A Neural Circuit for Gut-Induced Reward [published correction appears in Cell. 2018 Oct 18;175(3):887-888]. *Cell*. 2018;175(3):665-678.e23. doi:10.1016/j.cell.2018.08.049 3. Tseng CT, Brougher J, Gaulding SJ, Hassan BS, Thorn CA. Vagus nerve stimulation promotes cortical reorganization and reduces task-dependent calorie intake in male and female rats. *Brain Res*. 2020;1748:147099. doi:10.1016/j.brainres.2020.147099

Acknowledgements: The support of NIDA & UTD for this project is gratefully acknowledged.

Learning Objectives: 1. To determine if the vagus nerve has lateralized functionality. 2. To what extent does this laterization affect central neuromodulatory systems. 3. Can we use this laterlization to develop beneficial treatments for neurological disorders.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

177

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

ANATOMIC SUBSTRATES UNDERLYING OCCIPITAL AND SUPRAORBITAL NEURAL TARGETS IN THE NEUROMODULATION TREATMENT OF CHRONIC MIGRAINE

Jeffery Kramer, PhD[1], Konstantin Slavin, MD[2]
[1]Volta Research and Consulting, Research, Minneapolis, United States of America, [2]University of Illinois at Chicago, Neurosurgery, Chicago, United States of America

Introduction: Nerves in the head can be effective neuromodulation targets in the treatment of headaches. The underlying peripheral and central anatomy of the nerve fibers within the neural targets is an important component in understanding treatment mechanisms as well as potentially optimizing therapy delivery.

Materials / Methods: A review of the literature was conducted utilizing key search terms for anatomic considerations of the occipital and supraorbital nerve structures including tissue innervation distributions and central projections. Ultrastructural elements of the nerve targets were not taken into consideration and will be the subject of a separate analysis. Relevant databases (PubMed, EMBASE and Google Scholar) as well as reference back searches were used to assemble the literature base.

Results: The search protocol yielded 354 total hits with 35 individual items in the literature reviewed more in depth for key anatomical elements of the neural structures, innervation and projection patterns. Classical anatomic methodologies as well as functional anatomic techniques were utilized in animal and human studies. Rough innervation patterns of the V1 branch of the trigeminal included superficial and deep dural and perivascular structures in more anterior regions of the head. Occipital branches were also found to contain somatic input from extracranial tissues and project into the spinal cord primarily at the C2-3 level where deeper dural afferents in the occipital regions also project. Both supraorbital (V1) and occipital show functional connectivity to autonomic and pain matrix areas as well as the trigeminocervical complex in the cervical spinal cord.

Discussion: Anatomical innervation and projection patterns from the occipital and supraorbital nerves suggest both divergent and convergent pathways in the central nervous system. This anatomical representation helps explain targeting of neuromodulation therapies to different neural structures in specific headache populations. Also, it provides a foundation for combined occipital and supraorbital stimulation that may act synergistically in chronic migraine as long as consistent and efficient engagement of target nerve fibers with an electrical field can be maintained.

Conclusions: Anatomical substrates of both supraorbital (V1) and occipital nerve targets demonstrate innervation and projection patterns consistent with underlying pathophysiology observed in migraine. Independently, these neural targets show divergent patterns of innervation with functional convergence at various points in the CNS including brain nuclei and cervical spinal cord. Taken together, the combination of these targets may provide an individually tailored and dynamic approach based on variability of symptomatic presentations between different patients and over a time course of disease in individual patients.

Supplemental Data:

References:

Acknowledgements: Support by ShiraTronics is gratefully acknowledged.

Learning Objectives: 1. Describe the anatomic projections of the occipital and supraorbital nerves in both the spinal cord and the brain. Have paricipants understand these anatomical concepts. 2. Relate the anatomic connectivity to regions that have been implicated in migraine. Enable meeting atendees

to connect the neural anatomy to underlying causes of migraine. 3. Provide an anatomical framework around targeting the occipital and supraorbital nerves in combination for treatment of chronic migraine. Establish a fundamental relatiponship between the anatomy and potential therapy approaches.

Financial Disclosures: Jeff Kramer is a paid consultant for Shiratronics.

Disclosure: No significant relationships.

178

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

NEUROMODULATION BY MEDICAL YOGA THERAPY: HARNESSING PAIN RELIEF AND CORTICOMOTOR EXCITABILITY

Aasheesh Kumar, MSc[1], Akanksha Singh, MD[1], Raj Yadav, MD[1], Uma Kumar, MD[2], Srikumar Venkataraman, MD[3], Maroof Khan, PhD[4], Kishore Deepak, PhD[5], Rima Dada, MD[6], Renu Bhatia, MD[1]
[1]All India Institute of Medical Sciences, New Delhi, Physiology, Delhi, India, [2]All India Institute of Medical Sciences, New Delhi, Rheumatology, Delhi, India, [3]All India Institute of Medical Sciences, New Delhi, Physical Medicine And Rehabilitation, Delhi, India, [4]All India Institute of Medical Sciences, New Delhi, Biostatistics, Delhi, India, [5]Indian Institute of Technology, Biomedical Engineering, Delhi, India, [6]All India Institute of Medical Sciences, New Delhi, Anatomy, Delhi, India

Introduction: Fibromyalgia is an idiopathic chronic pain syndrome affecting atleast 2% of the global population; predominantly females. Besides widespread pain at tender points, symptoms like morning stiffness, brain fogging and sleep disturbances are also reported in patients. There is no permanent cure of the disease; except for the symptomatic relief by medications. Aim of our study was to investigate the role of medical yoga therapy on pain sensation and corticomotor excitability in fibromyalgia.

Materials / Methods: We assessed pain, subjectively and objectively, flexibility and corticomotor excitability of 63 fibromyalgia patients (32:31::yoga group:waitlisted control) before and after 28 days of medical yoga therapy and standard care therapy. We have used quantitative sensory testing and Transcranial Magnetic Stimulation to assess pain and corticomotor parameters respectively.

Results: Baseline demographic and clinical parameters of fibromyalgia patients of both the groups were comparable. Out of 72 FM patients 63 were able to complete the 28-day therapy. Pain and tender point counts were found significantly reduced in the patients taking medical yoga therapy only ($p<0.05$) after intervention. We have also found a significant increase in muscular activity specifically lumbar flexibility bilaterally after medical yoga therapy ($p<0.05$). We have not found any significant change in the waitlisted group. Moreover, we have found a significant improvement in corticomotor excitability of FM patients in the yoga group in some of the parameters ($p<0.05$). Cortical changes were not found in the waitlisted controls.

Discussion: In our previous study medical yoga therapy ihas been proven as an emerging lifestyle intervention to manage musculoskeletal pain conditions like chronic low back pain by reducing pain and increasing flexibilty. In fibromyalgia patients, both the peripheral and central nervous systems are found to be involved in the menifestation of pain and related symptoms.

Conclusions: Medical yoga therapy can reduce pain, improve flexibility and alter corticomotor excitability in fibromyalgia patients.

Supplemental Data:

References: •Wolfe, F., Clauw, D.J., Fitzcharles, M.A., et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care and Research.2010; 62:600–610. •Melzack R, Katz J. Measurement of pain. Surg Clin North Am 1996;79: 231-252 •Fischer AA. Pressure algometry over normal muscle. Standard values, validity and reproducibility of pressure threshold. Pain 1987;30:115-126 •Carson JW, Carson KM, Jones KD, Mist SD, Bennett RM. Follow-up of yoga of awareness for fibromyalgia: results at 3 months and replication in the wait-list group. Clin J Pain. 2012;28(9):804–813. •Curtis K, Osadchuk A, Katz J. An eight-week yoga intervention is associated with improvements in pain, psychological functioning and mindfulness, and changes in cortisol levels in women with fibromyalgia. J Pain Res. 2011;4:189–201.

Acknowledgements: We would like to acknowledge all the participants of our study for their valuable cooperation. Our sincere acknowledgement to all the members of Pain Research and TMS Laboratory and Integral Health and Wellness Clinic, Department of Physiology, AIIMS New Delhi, India.

Learning Objectives: Physiology of Yoga in Fibromyalgia. Contical Excitability of Fibromyalgia Patients. Pain Management in Fibromyalgia.

Financial Disclosures: Department of Science and Technology, Government of India: Funds for the conductance of the study. Indian Council Medical Research for providing manpower in to the presenting author.

Disclosure: No significant relationships.

179

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

MECHANISMS UNDERLYING COMBINED OCCIPITAL AND SUPRAORBITAL TRIGEMINAL (V1) NEUROMODULATION IN THE TREATMENT OF CHRONIC MIGRAINE

Robert Levy, PhD[1], Jeffery Kramer, PhD[2]
[1]Anesthesia Pain Care Consultants, Anesthesia Pain Care Consultants, Tamarac, United States of America, [2]Volta Research and Consulting, Research, Minneapolis, United States of America

Introduction: Neuromodulation of the occipital and supraorbital trigeminal (V1) nerves have been shown to produce positive clinical benefits in patients suffering from chronic migraine. There are likely a combination of mechanisms underlying this therapeutic approach.

Materials / Methods: A systematic review was conducted to explore the literature examining physiologic mechanisms underlying occipital and/or supraorbital neuromodulation. A search protocol was developed utilizing relevant terms and databases including Pubmed, EMBASE, Google Scholar and multiple related journal TOCs. Given the relatively narrow scope of the search a wide range of data dissemination vehicles were accepted including book chapters and abstracts.

Results: A total of 19 relevant publications were found for review. Both animal and human physiologic models used in the publication cohort. Techniques including neurophysiology, functional imaging, reflex testing and other invasive and non-invasive procedures were utilized. Multiple potentially relevant physiologic mechanisms were identified underlying the clinical effects of stimulation. These effects included alterations in neurophysiology of trigeminal sensory processing, neurovascular and dura interactions as well as central sensory and pain processing. These effects were seen both unilaterally and bilaterally, however there was a relatively narrow range of classic stimulation paradigms tested. Moreover, there was a lack of testing informing dose-response relationships.

Discussion: The clinical effects of combined occipital and supraorbital trigeminal (V1) nerve stimulation are likely due to a combination of physiologic mechanisms. Some of these mechanisms may be divergent based upon the specific anatomy being stimulated. For example, stimulation of the supraorbital nerve(s) may have a greater impact on the trigeminal system given its anatomical connectivity through the ophthalmic branch (V1) as opposed to stimulation of the occipital nerve(s). Functionally, this may have implications for headache pain coverage and both the physiologic changes and clinical effect for headaches with pain focused in various regions of the head. Still other mechanisms of nerve stimulation may be convergent from multiple targets based upon common anatomic and physiologic substrates such as overlapping brain regions and the Trigeminocervical complex in the cervical spinal cord.

Conclusions: Combination stimulation of both the occipital and supraorbital nerves evokes a multiplicity of physiologic changes in neural and, potentially, non-neural tissues and cells in the brain. The poly-modal action of this combined approach may provide enhanced clinical benefit in some patients while targeting some of the same underlying causes of migraine headaches.

Supplemental Data:

References:

Acknowledgements: The support of Shiratronics is gratefully acknowledged.

Learning Objectives: 1. Describe the potential underlying analgesic mechanisms of combined occipital and supraorbital nerve stimulation in chronic migraine. 2. Relate the potential MOAs in combined occipital and supraorbital stimulation to the underlying pathophysiology in chronic migraine.

Financial Disclosures: Jeff Kramer is a paid scientific consultant of Shiratronics. Level $5,001 - $20,000 USD.

Disclosure: No significant relationships.

180

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

PERCEPTION AND DOSE CONTROL WITH MULTI-RATE, CLOSED-LOOP SPINAL CORD STIMULATION

Leonid Litvak, PhD[1], Liam Matthews, BSc (Hons)[2,3], Evan Rogers, PhD[2,3], Meagan Brucker-Hahn, MSBmE[2,3], Joshua Nedrud, MSc[1], David Dinsmoor, MSc[1], Scott Lempka, Associate Professor[3,4,5]
[1]Medtronic, Neuroscience, Fridley, United States of America, [2]University of Michigan, Department Of Biomedical Engineering, Ann Arbor, United States of America, [3]University of Michigan, Biointerfaces Institute, Ann Arbor, United States of America, [4]University of Michigan, Department Of Anesthesia, Ann Arbor, United States of America, [5]University of Michigan, Biomedical Engineering, Ann Arbor, United States of America

Introduction: Tissue activation during spinal cord stimulation (SCS) varies with patient posture and activity and may lead to changes in the effective stimulation dosage, potentially contributing to suboptimal outcomes. Evoked compound action potentials (ECAPs) have been utilized in closed-loop SCS (CL-SCS) and may help mitigate inconsistent dosing by quantifying the amount of tissue activated. However, ECAPs are only elicited reliably with low-rate programs (LRPs). For high-rate programs (HRPs), novel CL-SCS algorithms utilize the ECAP elicited from the LRP to control the HRP.[1] We characterized the performance of these approaches by constructing a simple, clinically validated computational model of SCS that includes neural excitation and paresthesia intensity. Then, we utilized the model to quantify the robustness of HRP dose control with simulated postural changes.

Materials / Methods: The model simulated the SCS-induced response of 300 dorsal column (DC) fibers and a single dorsal-horn (DH) interneuron placed in an infinite homogenous medium (Fig 1). The fibers were modeled as generalized integrate-and-fire neurons with subthreshold integration, thresholds, refractory periods, and adaptation. The neural response was driven by the computed activating function.[2] The DH interneuron was characterized by shorter length, slower subthreshold integration and activation three times lower than the DC fibers[34]. The central perception model was comprised of spatial summation[5] and temporal integration;[6] with output perception intensity scaled to fit perceptual data. We modeled postural changes by changes in the electrode-to-fiber distances (D_E=3mm,4mm,5mm. We validated the model using both previously published data[7] and perception thresholds (PTs) acquired from 16 subjects using SCS rates between 2 and 1000 Hz.

Results: For both the model and clinical data, PTs were generally independent of rate below 400 Hz but declined for higher frequencies. Consistent with prior reports,[7] the model captured both the decrease in ECAP amplitude and the increase in perception intensity with higher SCS rates (Fig. 2). Stimulation at maximum sub-paresthesia HRP amplitude (99% of PT, D_{EL} = 3mm) produced subthreshold depolarization in the DH cell. In open-loop SCS, the average subthreshold neural response varied strongly with postural changes, while when the HRP was adjusted to keep the LRP-evoked ECAP constant (CL-SCS), DH subthreshold excitation was stronger and largely independent of posture (Fig. 3).

Discussion: The model describes perception intensity and ECAPS across rates. Across various postures, LRP-evoked ECAPS can be utilized to deliver higher and more consistent dose to the DH.

Conclusions: CL-SCS using an LRP-evoked ECAP can control an HRP to provide a consistent, strong subthreshold dose regardless of posture.

Supplemental Data:

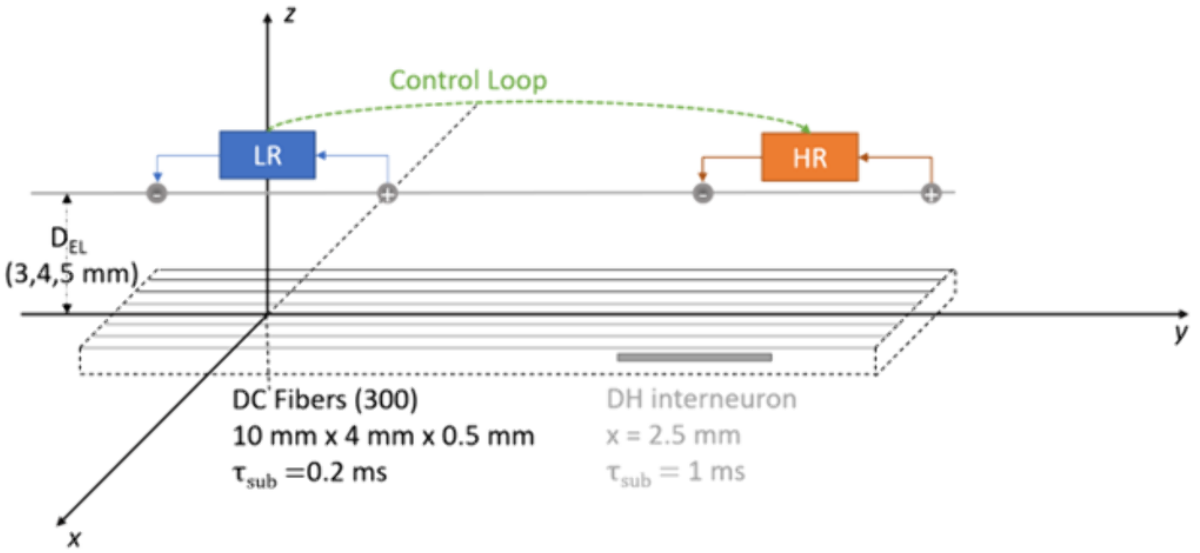


Figure 1: Model geometry.

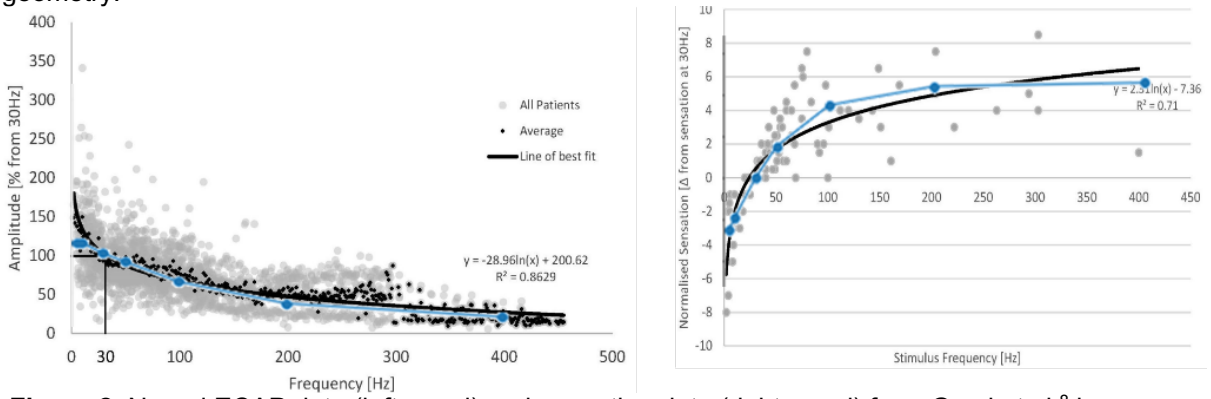


Figure 2. Neural ECAP data (left panel) and sensation data (right panel) from Gmel et al.[8] in gray and black compared to the model (blue).

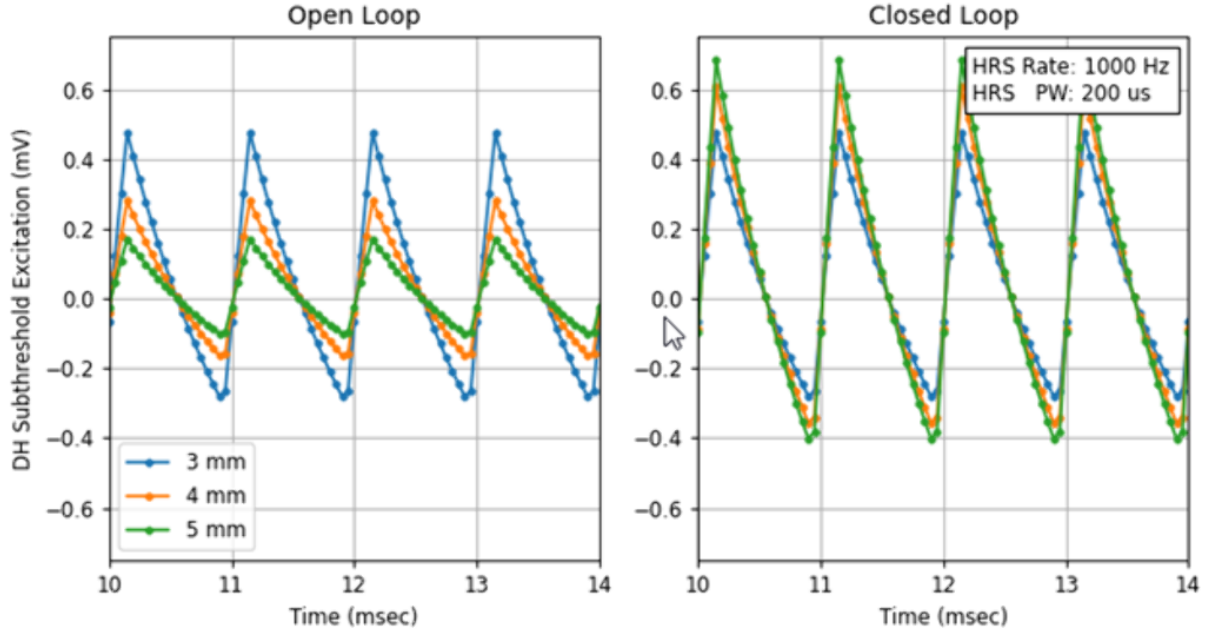


Figure 3: Subthreshold excitation in the DH interneuron model.

References: 1. Vallejo, R., Chakravarthy, K., Will, A., Trutnau, K. & Dinsmoor, D. <p>A New Direction for Closed-Loop Spinal Cord Stimulation: Combining Contemporary Therapy Paradigms with Evoked

Compound Action Potential Sensing</p>. *J. Pain Res.* **14**, 3909–3918 (2021). 2. Rattay, F. Electrical Nerve Stimulation. *Electr. Nerve Stimul.* (1990) doi:10.1007/978-3-7091-3271-5. 3. Liang, L. *et al.* A systematic review of computational models for the design of spinal cord stimulation therapies: from neural circuits to patient-specific simulations. *J. Physiol.* **0**, 1–19 (2022). 4. Rogers, E. R., Zander, H. J. & Lempka, S. F. Neural Recruitment During Conventional, Burst, and 10-kHz Spinal Cord Stimulation for Pain. *J. Pain* **23**, 434–449 (2022). 5. Graczyk, E. L. *et al.* The neural basis of perceived intensity in natural and artificial touch. *Sci. Transl. Med.* **8**, 1–11 (2016). 6. Gescheider, G. A., Berryhill, M. E., Verrillo, R. T. & Bolanowski, S. J. Vibrotactile temporal summation: Probability summation or neural integration? *Somatosens. Mot. Res.* **16**, 229–242 (1999). 7. Gmel, G. E. *et al.* The Effect of Spinal Cord Stimulation Frequency on the Neural Response and Perceived Sensation in Patients With Chronic Pain. *Front. Neurosci.* **15**, (2021). 8. Gmel, G. E. *et al.* Electrophysiological Responses in the Human S3 Nerve During Sacral Neuromodulation for Fecal Incontinence. *Front. Neurosci.* **15**, 1–10 (2021).

Acknowledgements: The support of Medtronic for this project is greatfully acknowledged.

Learning Objectives: 1. How SCS rate relates to ECAPS and paresthesia. 2. Closed loop stimulation is possible with high-rate programs. 3. How closed loop stimulation affects dose control.

Financial Disclosures: Leonid Litvak is a company employee of Medtronic (>$100K). David Dinsmoor is a company employee of Medtronic (>$100K). Joshua Nedtrud is a company employee of Medtronic (>$100K). SL has received research grants from Medtronic (>$100K).

Disclosure: No significant relationships.

181

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

THE STRESS-INDUCED ANTINOCICEPTIVE RESPONSES TO THE PERSISTENT INFLAMMATORY PAIN INVOLVE THE OREXIN RECEPTORS IN THE NUCLEUS ACCUMBENS

Seyed Mohammadmisagh Moteshakereh, MD, Mohammad Nikoohemmat, MD, Danial Farmani, MD, Abass Haghparast, BChir
Neuroscience Research Center, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran, Neuroscience, Tehran, Iran

Introduction: Stress-induced analgesia (SIA) is a well-documented physiological phenomenon where stress reduces the perception of pain. The brain's orexin peptides play a vital role in regulating various physiological functions, including wakefulness and nociception. However, the specific involvement of the orexinergic system within the nucleus accumbens (NAc) in modulating antinociception induced by forced swim stress (FSS) remains unclear.

Materials / Methods: This study involved 106 adult male Wistar rats weighing between 250–305 g. Unilateral stereotaxic surgery was performed on these rats. Different doses (1, 3, 10, and 30 nmol/0.5 µl DMSO) of antagonists for orexin-1 receptors (OX1r) and orexin-2 receptors (OX2r), specifically SB334867 and TCS OX2 29, were administered into the NAc. This administration occurred five minutes before a 6-minute exposure to FSS. To assess antinociception, the formalin test was employed, which involved injecting formalin (50 µl; 2.5%) into the hind paw plantar surface of the rats. This test elicits biphasic pain-related responses, with the first phase commencing immediately after formalin infusion and lasting 3–5 minutes. The late phase begins 15–20 minutes after formalin injection and persists for 20–40 minutes.

Results: The study found that the intra-accumbal microinjection of both SB334867 and TCS OX2 29 attenuated FSS-induced antinociception in both phases of the formalin test. Notably, TCS OX2 29 exhibited a higher potency, particularly during the early phase of the formalin test.

Discussion: These results highlight the intricate relationship between stress, the orexinergic system, and pain modulation. Stress-induced analgesia (SIA) is a phenomenon of significant interest, as it underscores the ability of stress to influence the perception of pain. Orexin peptides, known for their roles in wakefulness and nociception, emerge as key players in this intricate interplay. The findings emphasize the pivotal role of OX1 and OX2 receptors within the NAc in modulating antinociceptive responses during FSS. The enhanced effectiveness of TCS OX2 29 during the early phase of the formalin test suggests the rapid involvement of orexin receptors in the modulation of pain responses under stressful conditions.

Conclusions: In conclusion, this study offers valuable insights into the complex relationship between stress, the orexinergic system, and pain modulation. The findings support the involvement of OX1 and OX2 receptors within the NAc in the regulation of antinociceptive responses during FSS, especially in the context of persistent inflammatory pain models in rats. These results open new avenues for exploring the potential therapeutic interventions targeting orexinergic systems to alleviate pain in stress-induced scenarios.

Supplemental Data:

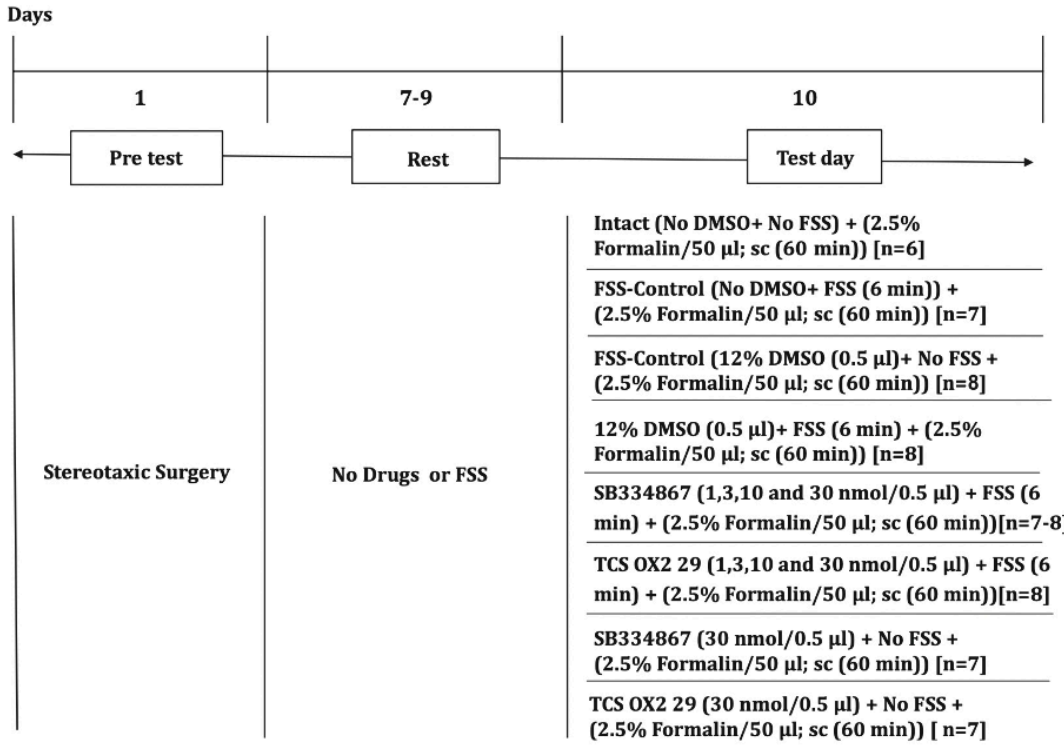
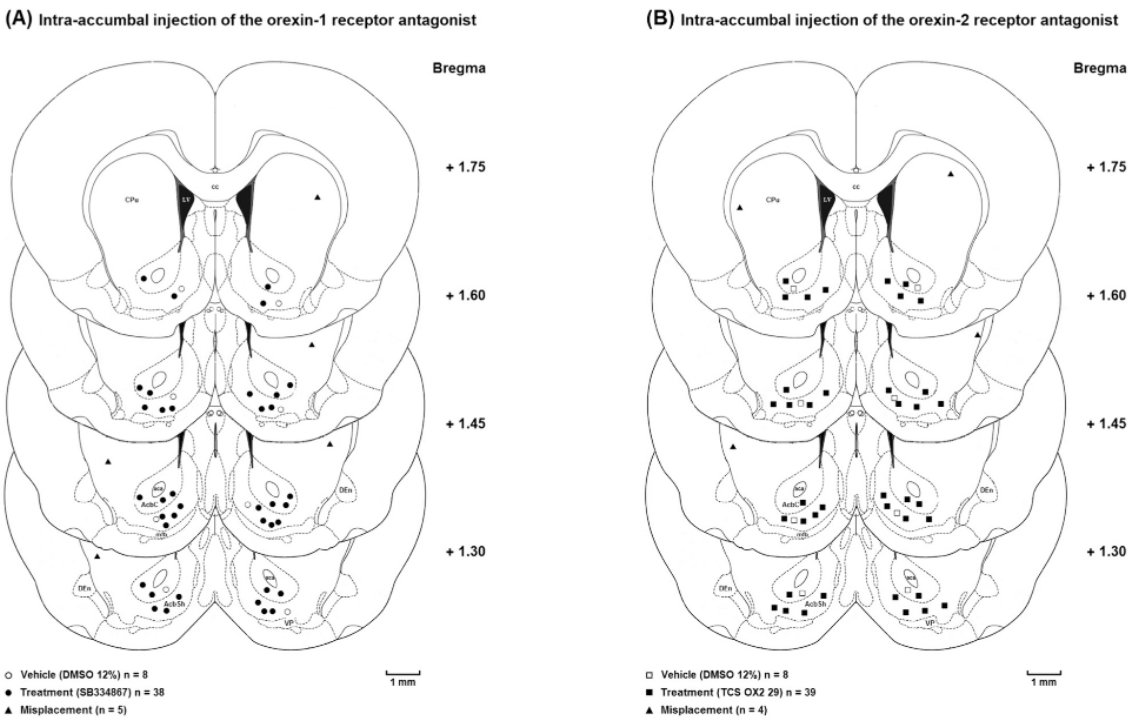
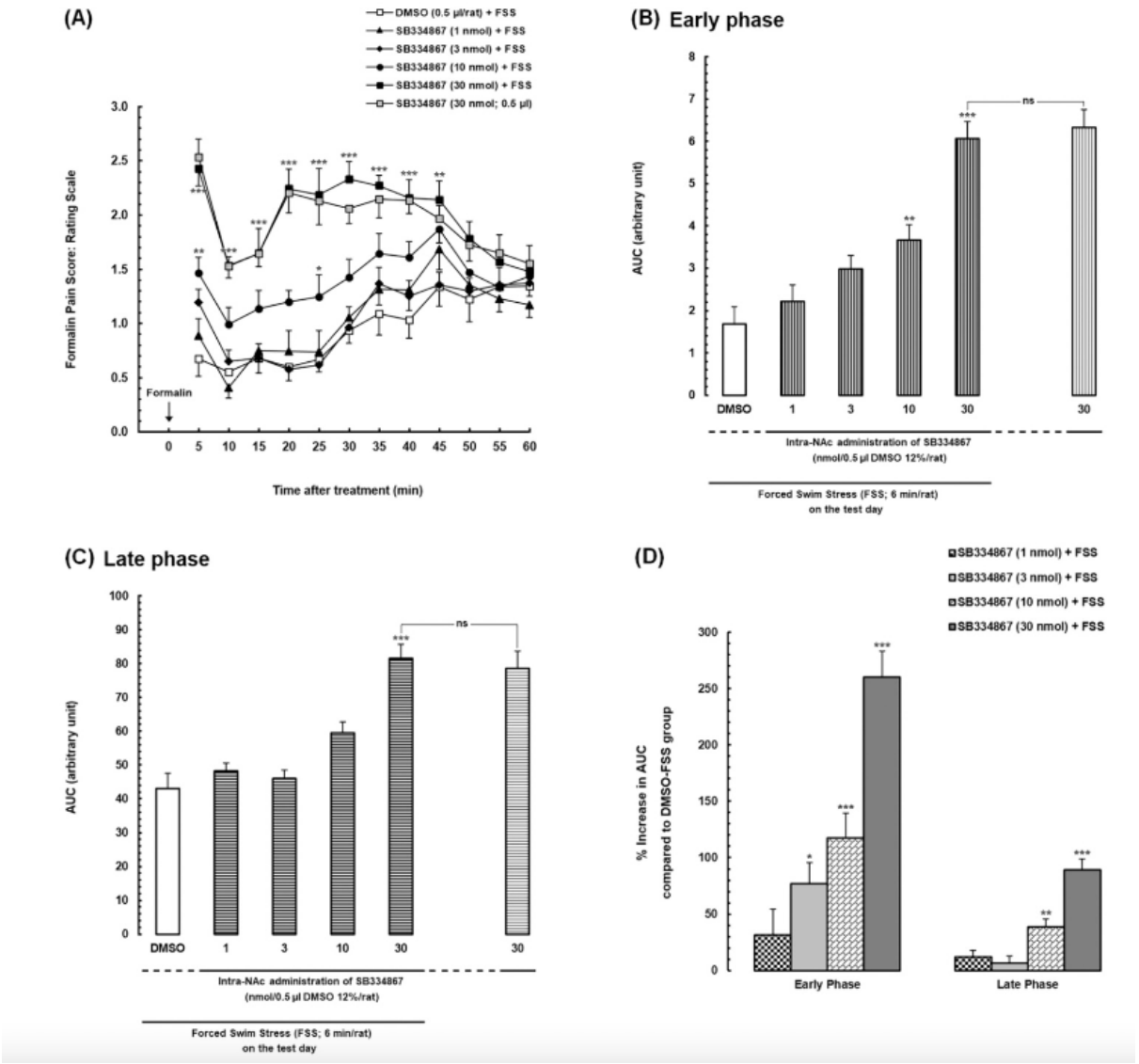
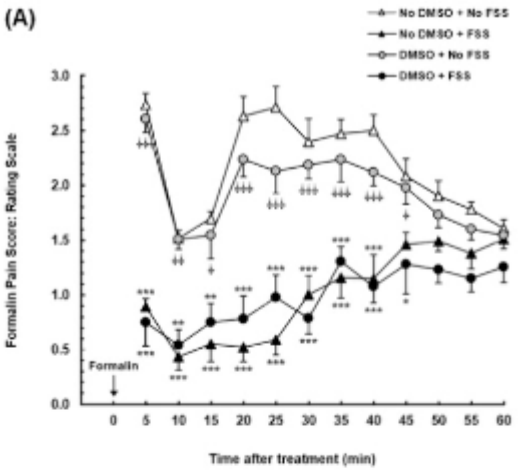
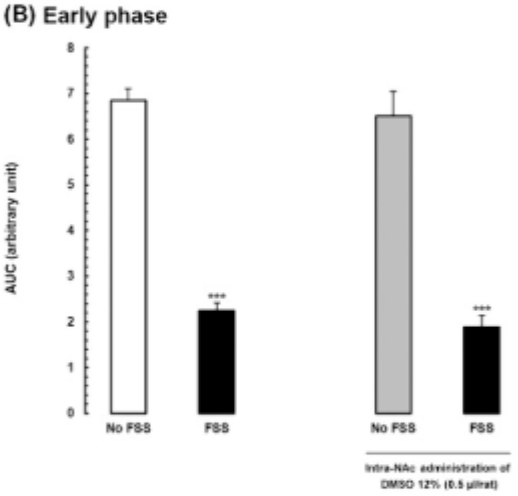


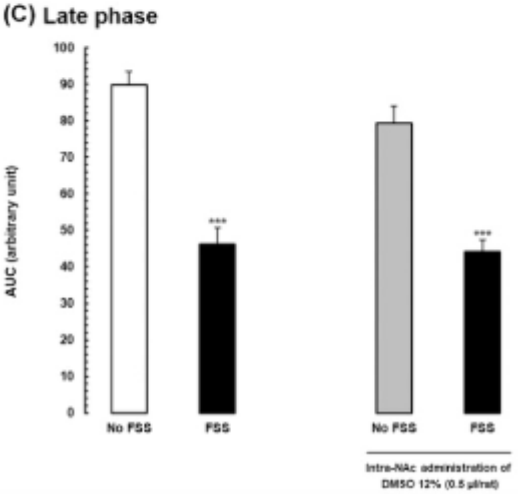
Fig. 1. Experimental diagram of the control and experimental (treatment) groups for the study.



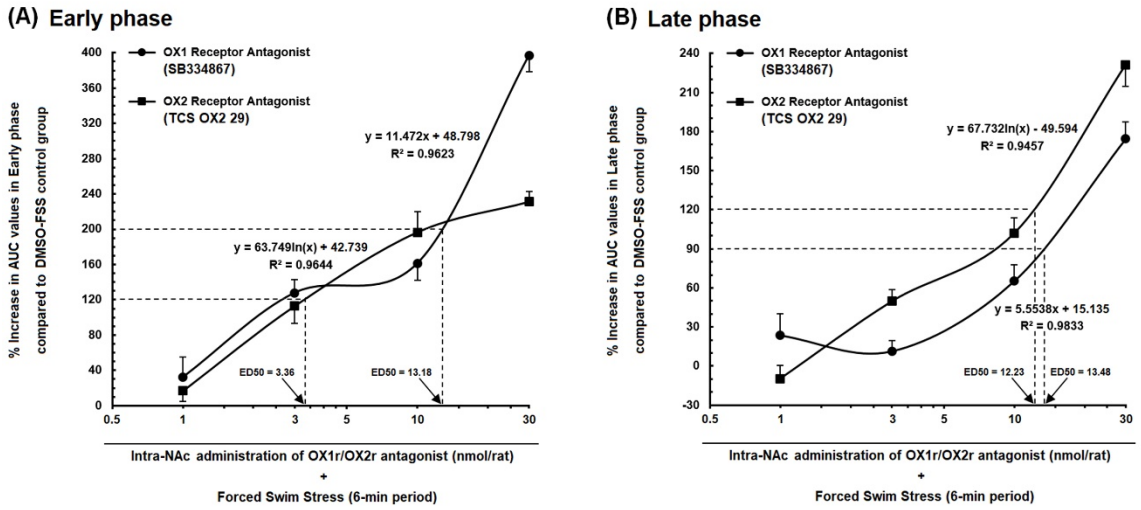

(A)
DMSO (0.5 µl/rat) + FSS
SB334867 (1 nmol) + FSS
SB334867 (3 nmol) + FSS
SB334867 (10 nmol) + FSS
SB334867 (30 nmol) + FSS
SB334867 (30 nmol; 0.5 µl)
Formalin Pain Score: Rating Scale
Formalin
Time after treatment (min)
(B) Early phase
AUC (arbitrary unit)
ns
DMSO
Intra-NAc administration of SB334867
(nmol/0.5 µl DMSO 12%/rat)
Forced Swim Stress (FSS; 6 min/rat)
on the test day
(C) Late phase
AUC (arbitrary unit)
ns
DMSO
Intra-NAc administration of SB334867
(nmol/0.5 µl DMSO 12%/rat)
Forced Swim Stress (FSS; 6 min/rat)
on the test day
(D)
SB334867 (1 nmol) + FSS
SB334867 (3 nmol) + FSS
SB334867 (10 nmol) + FSS
SB334867 (30 nmol) + FSS
% Increase in AUC
compared to DMSO-FSS group
Early Phase
Late Phase







(caption on next column)



References: "None"

Acknowledgements: The research reported in this publication was supported by Elite Researcher Grant Committee under award number 987783 from the National Institute for Medical Research Development (NIMAD), Tehran, Iran. Also, the authors would like to thank the Neuroscience Research Center, School of Medicine, Shahid Beheshti University of Medical Sci- ences for their cooperation in carrying out this study.

Learning Objectives: 1.Objective: To enhance students' critical thinking skills. Desired Result: Students will be able to analyze complex problems, evaluate different perspectives, and make well-informed decisions based on evidence and reasoning. 2.Objective: To improve students' written communication skills. Desired Result: Students will be able to effectively convey their ideas, arguments, and research findings through clear, concise, and well-structured written communication. 3.Objective: To foster students' cultural awareness and global perspective. Desired Result: Students will develop an understanding and appreciation of diverse cultures, worldviews, and global issues, enabling them to engage with global challenges and opportunities in a culturally sensitive and informed manner.

Financial Disclosures: "No significant relationships"

Disclosure: No significant relationships.

182

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

INTRA-ACCUMBAL OREXINERGIC SYSTEM CONTRIBUTES TO THE STRESS-INDUCED ANTINOCICEPTIVE BEHAVIORS IN THE ANIMAL MODEL OF ACUTE PAIN IN RATS

Mohammad Nikoohemmat, MD, Seyed Mohammadmisagh Moteshakereh, MD, Danial Farmani, MD, Abass Haghparast, BChir
Neuroscience Research Center, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran, Neuroscience, Tehran, Iran

Introduction: The intricate relationship between stress and the pain system, characterized by a reciprocal influence where stress can mitigate pain perception, is a well-documented phenomenon known as stress-induced analgesia (SIA). Orexin, a neuropeptide, is recognized for its role in modulating pain, and the impact of stress on the mesolimbic system in the context of pain modulation is well-established. However, the specific role of intra-accumbal orexin receptors in the modulation of acute pain during forced swim stress (FSS) remains a subject of uncertainty.

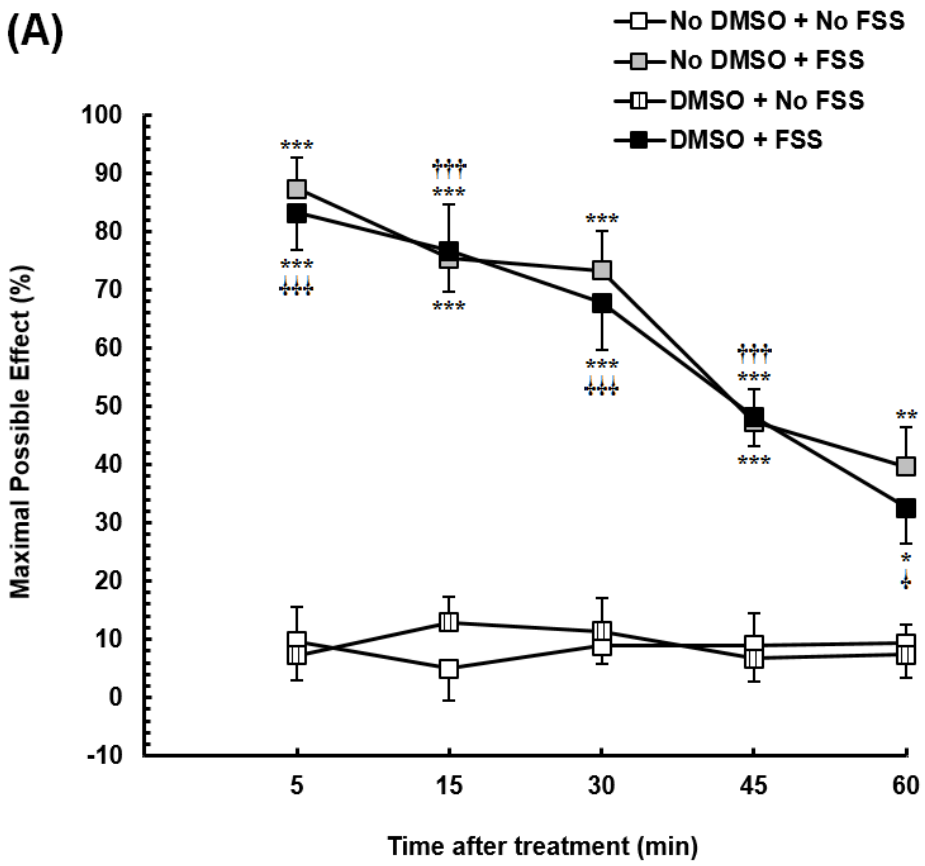
Materials / Methods: In this experimental study, 117 adult male albino Wistar rats weighing between 270 to 300 g were utilized. Unilateral implantation of cannulae above the Nucleus Accumbens (NAc) was performed. Different doses (1, 3, 10, and 30 nmol/0.5 µl DMSO) of antagonists for the orexin-1 receptor (OX1r), SB334867, and the orexin-2 receptor (OX2r), TCS OX2 29, were microinjected into the NAc. This was conducted five minutes prior to subjecting the rats to a 6-minute period of forced swim stress. Subsequently, the tail-flick test, a widely accepted model for assessing acute pain, was administered, and the nociceptive threshold (Tail-flick latency; TFL) was measured at 60-minute intervals.

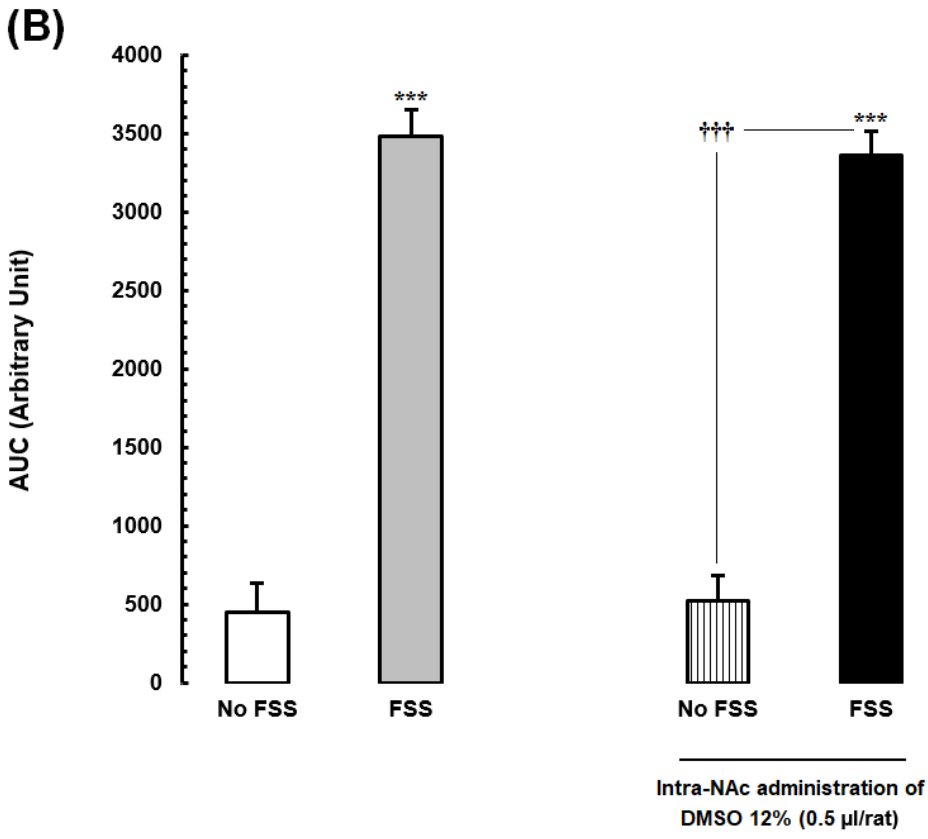
Results: The study revealed that exposure to acute stress significantly increased the Tail-flick latencies (TFLs), leading to notable antinociceptive responses. Furthermore, the intra-accumbal microinjection of SB334867 or TCS OX2 29 effectively blocked the analgesic effect of stress in the tail-flick test. Importantly, both orexin receptors, OX1r and OX2r, exhibited nearly equal modulation of stress-induced analgesia. These findings strongly suggest that OX1r and OX2r receptors within the NAc play a pivotal role in the modulation of stress-induced antinociceptive responses. The intra-accumbal microinjection of orexin receptor antagonists was found to induce antinociceptive responses during FSS-induced acute pain, emphasizing a potential role of intra-accumbal orexinergic receptors in the development of stress-induced analgesia.

Discussion: The results of this study underscore the influence of orexin receptors within the NAc in the context of stress-induced antinociception, particularly during acute pain. The ability of orexin receptor antagonists to attenuate the analgesic effect of stress holds promise for further investigation into the molecular and neural mechanisms underlying stress-induced analgesia and its potential therapeutic implications in pain management.

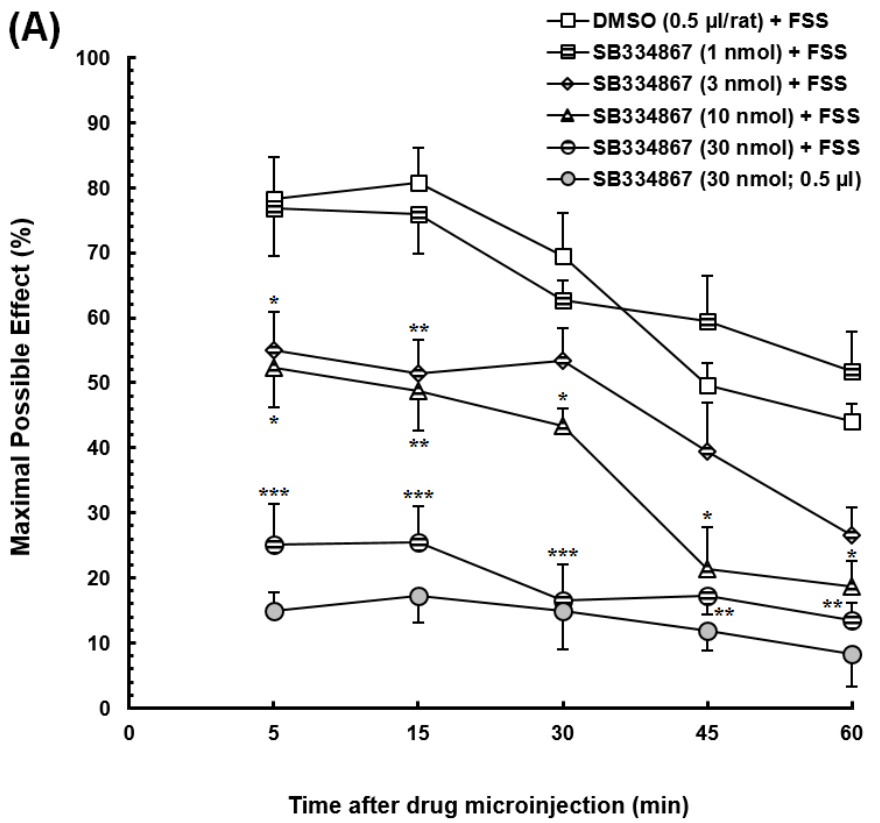
Conclusions: This study unveils how intra-accumbal orexin receptors, OX1r and OX2r, modulate stress-induced pain relief, shedding light on the intricate relationship between stress, orexin, and pain regulation. These findings advance our understanding of neural mechanisms in stress-induced analgesia, with implications for pain management and therapy.

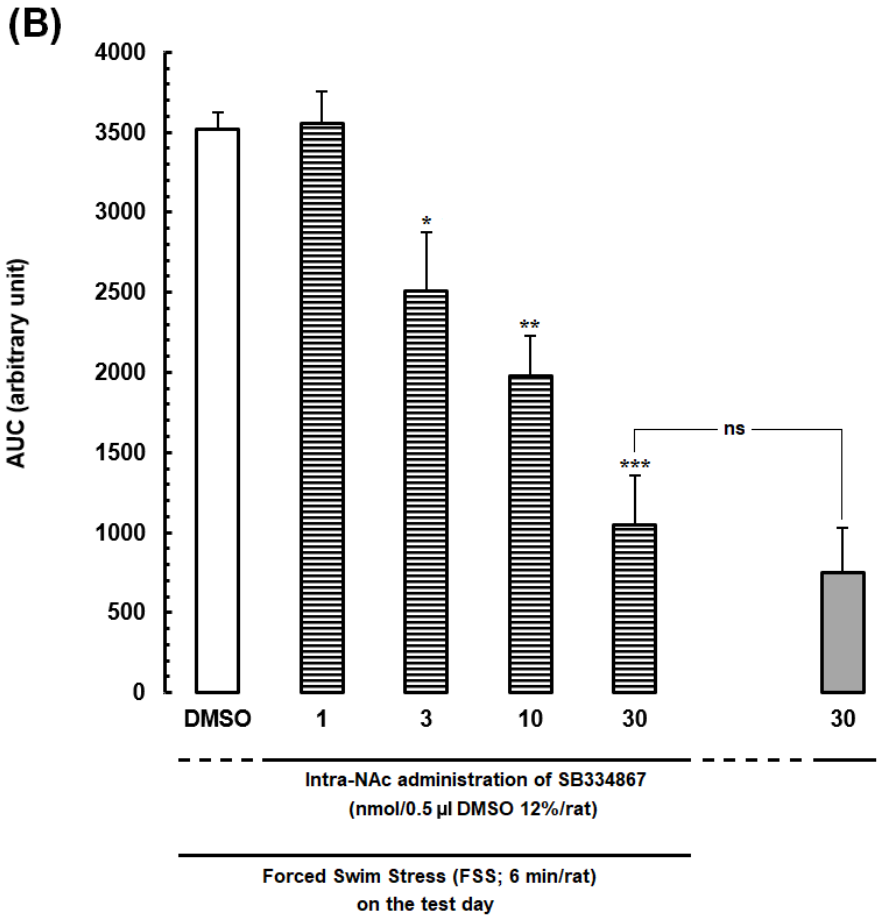
Supplemental

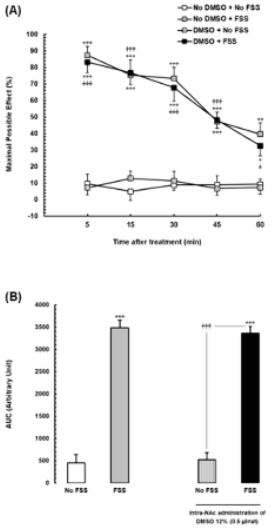

(A)
No DMSO + No FSS
No DMSO + FSS
DMSO + No FSS
DMSO + FSS
Maximal Possible Effect (%)
100
90
80
70
60
50
40
30
20
10
0
-10
5
15
30
45
60
Time after treatment (min)

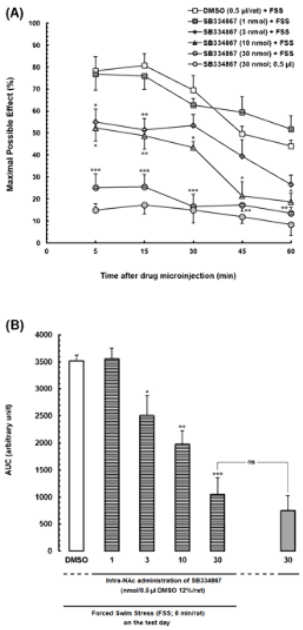

(B)
AUC (Arbitrary Unit)
4000
3500
3000
2500
2000
1500
1000
500
0
No FSS
FSS
No FSS
FSS
Intra-NAc administration of
DMSO 12% (0.5 µl/rat)

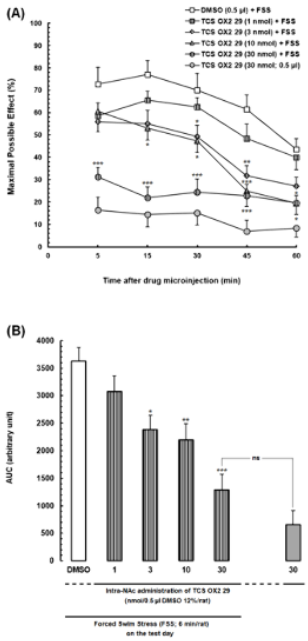
Data:

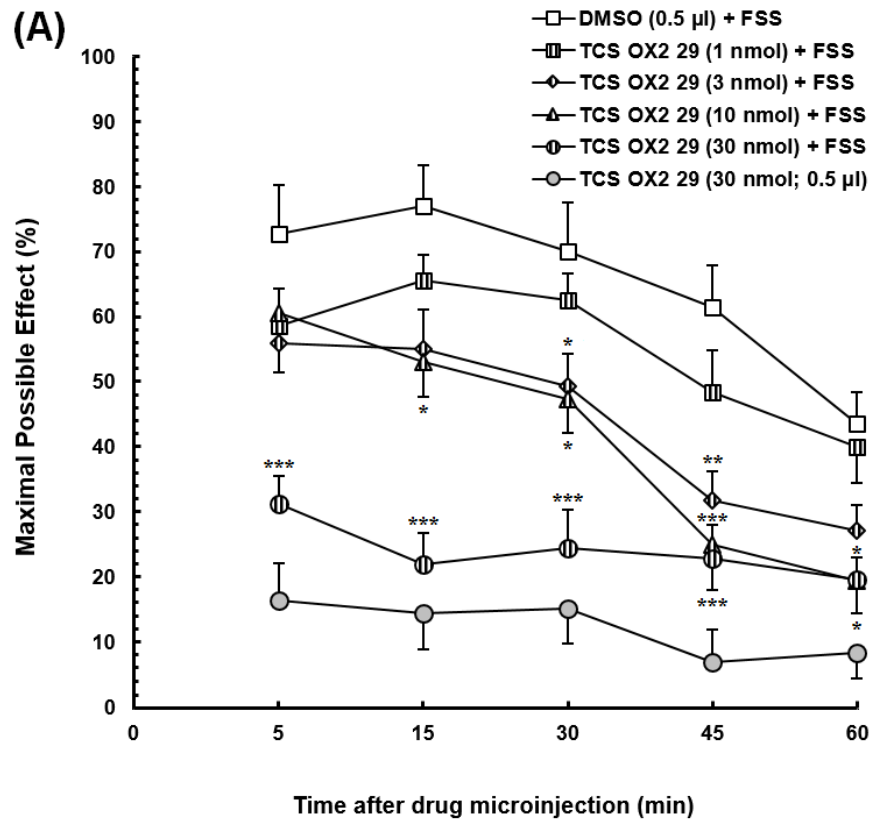

(A)
DMSO (0.5 µl/rat) + FSS
SB334867 (1 nmol) + FSS
SB334867 (3 nmol) + FSS
SB334867 (10 nmol) + FSS
SB334867 (30 nmol) + FSS
SB334867 (30 nmol; 0.5 µl)
Maximal Possible Effect (%)
Time after drug microinjection (min)

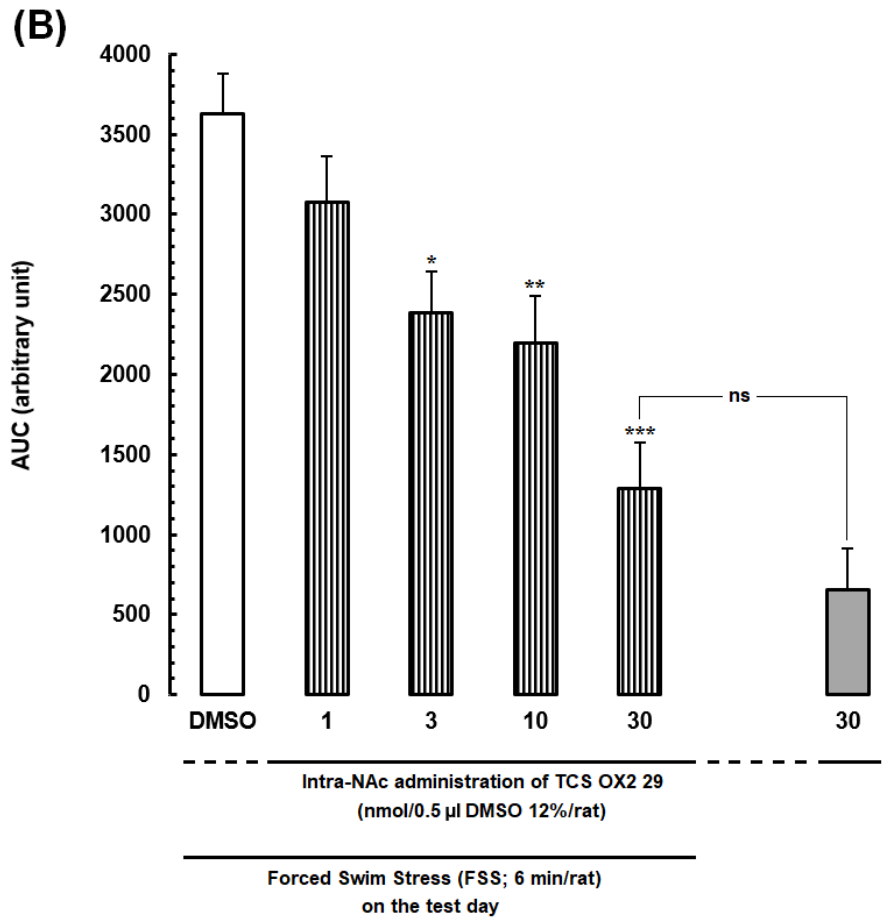

(B)
AUC (arbitrary unit)
DMSO
1
3
10
30
30
ns
Intra-NAc administration of SB334867
(nmol/0.5 µl DMSO 12%/rat)
Forced Swim Stress (FSS; 6 min/rat)
on the test day

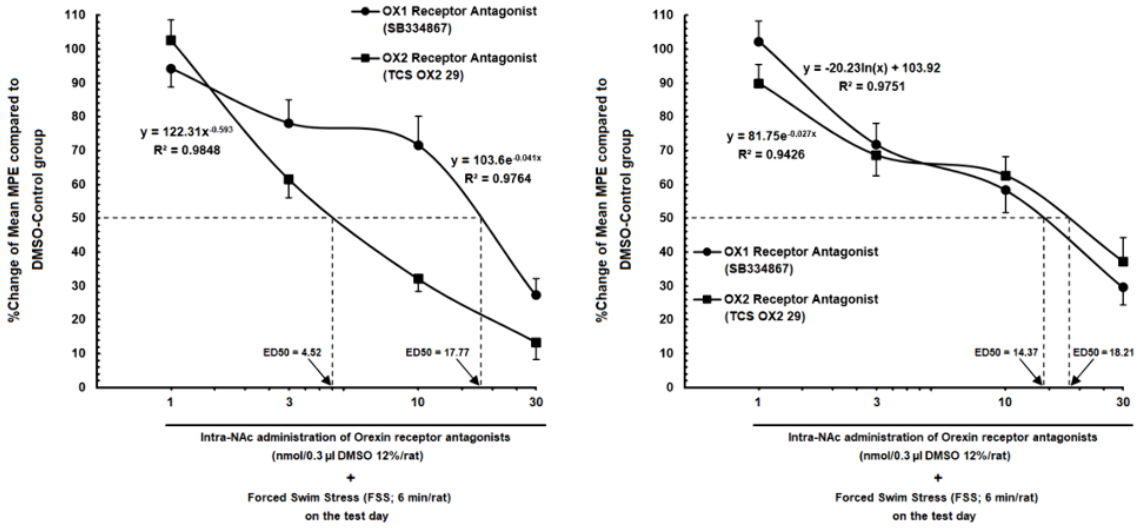

(A)
No DMSO + No FSS
No DMSO + FSS
DMSO + No FSS
DMSO + FSS
Maximal Possible Effect (%)
Time after treatment (min)
(B)
AUC (arbitrary Unit)
No FSS
FSS
No FSS
FSS
Intra-NAc administration of DMSO 12% (0.5 µl/rat)


(A)
DMSO (0.5 µl/rat) + FSS
SB334867 (1 nmol) + FSS
SB334867 (3 nmol) + FSS
SB334867 (10 nmol) + FSS
SB334867 (30 nmol) + FSS
SB334867 (30 nmol; 0.5 µl)
Maximal Possible Effect (%)
Time after drug microinjection (min)
(B)
AUC (arbitrary unit)
DMSO
1
3
10
30
30
ns
Intra-NAc administration of SB334867 (nmol/0.5 µl DMSO 12%/rat)
Forced Swim Stress (FSS; 6 min/rat) on the test day


(A)
DMSO (0.5 µl) + FSS
TCS OX2 29 (1 nmol) + FSS
TCS OX2 29 (3 nmol) + FSS
TCS OX2 29 (10 nmol) + FSS
TCS OX2 29 (30 nmol) + FSS
TCS OX2 29 (30 nmol; 0.5 µl)
Maximal Possible Effect (%)
Time after drug microinjection (min)
(B)
AUC (arbitrary unit)
DMSO
1
3
10
30
30
ns
Intra-NAc administration of TCS OX2 29 (nmol/0.5 µl DMSO 12%/rat)
Forced Swim Stress (FSS; 6 min/rat) on the test day


(A)
DMSO (0.5 µl) + FSS
TCS OX2 29 (1 nmol) + FSS
TCS OX2 29 (3 nmol) + FSS
TCS OX2 29 (10 nmol) + FSS
TCS OX2 29 (30 nmol) + FSS
TCS OX2 29 (30 nmol; 0.5 µl)
Maximal Possible Effect (%)
Time after drug microinjection (min)


(B)
AUC (arbitrary unit)
DMSO
1
3
10
30
30
ns
Intra-NAc administration of TCS OX2 29
(nmol/0.5 µl DMSO 12%/rat)
Forced Swim Stress (FSS; 6 min/rat)
on the test day



References: None

Acknowledgements: This project was supported by the Vice-Chancellor for Research & Technology of Shahid Beheshti University of Medical Sciences (00-31427-1400/11/18). Also, the authors acknowledge the Neuroscience Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran for their cooperation in carrying out this study.

Learning Objectives: 1.To enhance critical thinking skills. 2.To improve written communication skills 3.To foster cultural awareness and global perspective.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

183

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

EFFICACY OF THE "MODIFIED COLOGNE PAIN SCORE " TO THE EVALUATION OF OUTCOMES OF IMPLANTED DEVICES FOR CHRONIC PAIN MANAGEMENT

Dimitrios Peios, MD[1], Georgios Matis, MD[2], Athanasia Tsaroucha, MD[3], Christina Ble, MD[1], Ilias Kopatzidis, MD[1], Aikaterini Kyriakidou, MD[1], Athanasios Koulousakis, MD[4]
[1]St Luce's Hospital, Panorama Thessaloniki, Functional Neurosurgery, Thessaloniki, Greece, [2]University Hospital Cologne, Neurosurgery, Cologne, Germany, [3]Aretaieio University Hospital, Pain Unit, Athens, Greece, [4]Kunibertsklinik, Cologne, Germany

Introduction: Chronic pain affects more than 30% of people worldwide and requires a constant use of resources, that exceed any other disease. Among invasive treatments for chronic pain is using implantable pumps and neurostimulators. In order to track the progress of these patients in most cases several scales are used that record different aspects of the chronic pain patient, like pain itself, function, behaviour. We introduce a novel scale of long term evaluation of these patients.

Materials / Methods: This scale is called MODIFIED COLOGNE PAIN SCORE and is a modificaton of the COLOGNE SCORE SCALE, which was introduced in 1994 by A. Koulousakis with the acceptance of the German Pain Society for the evaluation of all interventional pain procedures at the Clinic for Stereotactic and Functional Neurosurgery at the University Hospital of Cologne, Germany. The new scale is divided in 4 parts. The first is referring to the scoring of Numerical Pain Rating Scale from 0 (no pain) to 10 (worst pain). The second refers to the percentage of reduction of previous medical treatment, marked as Medication, scoring from 0 (no medication) to 10 (no change in medication). The third part refers to the improvement of quality of life, marked as QoL, scoring from 0 (best quality, no complaints) to 10 (worst quality, no satisfaction). The fourth part refers to improvement of physical activity, scoring from 0 (completing all daily activities) to 10 (no change in activity). The total score ranges from 0 (best result) to 40 (worst result). We have used the modified scale for the last 2 years to evaluate efficacy and adjust treatments with implantable devices.

Results: Comparing the data from 55 patients (25 pumps, 30 stimulators) we determined that using the modified scale helps the physician to better understand and adjust more efficiently the treatment with implantable devices than using only specific or separate scales, which can be confusing. 80% of the patients showed better response and compliance in long term, than when used separate scales the previous years. 75% were more cooperative and willing to continue treatment after several years.

Discussion: Evaluation and treatment adjustments of the chronic pain patient with implanted devices can be difficult. Having a scale that can be efficient to both patient and health provider is crucial.

Conclusions: The "MODIFIED COLOGNE PAIN SCORE " can be a quick, easy, usefull and efficient scale that can assist health professionals provide better treatment for chronic pain patients with implanted devices.

Supplemental Data:

Part	Score
NPRS (Numerical pain rating scale)	0-10
MEDICATION REDUCTION	0-10
QoL (quality of life)	0-10
Activity	0-10
Total score	0-40

References: 1. Chronic pain: an update on burden, best practices, and new advances. Cohen et al. The Lancet, Vol. 397, No. 10289, May 29, 2021 2. Nociplastic pain: towards an understanding of prevalent pain conditions. Fitzcharles et al. The Lancet, Vol. 397, No. 10289, May 29, 2021 3. Neuromodulation for chronic pain. Knotkova et al. The Lancet, Vol. 397, No. 10289, May 29, 2021 4.https://www.britishpainsociety.org/static/uploads/resources/files/Outcome_Measures_January_2019.pdf 5.Cologne Score Scale-CSS (A. Koulousakis, 1992, DGNL, Wurzburg)

Acknowledgements:

Learning Objectives: 1. Introduce a novel pain scale 2. Share the experience of its use and note remarks 3. Propose the use and test from others

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

184

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

DISTINCT INFLUENCE OF BETA- AND GAMMA-TACS ON GRIP FORCE REGULATION IN HEALTHY OLDER ADULTS

Syed Qadri, MD[1], Seraphina Culp, BS[2], Megan Grainger, BS[1], Peter S. Lum, PhD[1,2], Shashwati Geed, PhD[1,3,4]
[1]Medstar Health, Physical Medicine & Rehabilitation, Washington DC, United States of America, [2]The Catholic University of America, Department Of Biomedical Engineering, Washington D.C., United States of America, [3]Georgetown University Medical Center, Department Of Rehabilitation Medicine, Washington D.C., United States of America, [4]The University of Texas at El Paso, Department Of Physical Therapy And Movement Sciences, El Paso, United States of America

Introduction: Synchronized firing of excitatory/inhibitory interneurons gives rise to cortical oscillations in the beta (13-30Hz), gamma (30-100Hz) bands. We tested if transcranial alternating current stimulation (tACS) in beta/gamma bands leads to systematic changes in different aspects of grip force regulation. We hypothesized that beta-tACS decreases the rate of rise and release of grip force whereas gamma-tACS increases the rates of grip force rise and release.

Materials / Methods: Seven adults (2 male; mean age±SD=65.5±20.9-yrs) received twenty minutes of beta (20Hz), gamma (70Hz), or sham-tACS using M1-contralateral-supraorbital montage (intensity just under threshold for phosphenes) during three visits one week apart. Participants performed 80 go/no-go grip-force-matching trials to a target force before and after tACS. Grip forces were processed into (1) grip onset reaction time; (2) rise time: duration to reach steady-state target grip force; (3) peak grip force velocity during rise; (4) reaction time to grip offset; (5) release time: duration to release grip to baseline. Paired-sample statistics were computed using the Wilcoxon signed-rank tests.

Results: Grip forces showed no difference pre/post gamma-tACS. Beta-tACS led to significant lowering of the grip offset reaction time (24.03±5.91msec, p=0.028) but significant increase in the duration of grip force release (50.51±5.9msec, p=0.043). Sham was associated with significant increase in grip force release time (21±4.7msec; p=0.028). When only the first block of go/no-go trials was tested, beta-tACS (80.13±5.9, p=0.043) and sham (102.42±4.77, p=0.028) showed significant increases in grip force release times, but gamma-tACS showed no change.

Discussion: Our task allows us to dissociate different aspects of grip force regulation, in particular, reaction time from the time for dynamic adjustments to desired grip force. Beta-tACS led to significantly faster release of an ongoing grip but slower relaxation of the grip forces to baseline. Upon testing the first 10 trials to eliminate effects of fatigue, beta-tACS still showed slower release of the ongoing grasp, but no change in reaction time to grip offset. Sham mirrored beta-tACS suggesting that fatigue may have led to these findings. However, gamma-tACS showed no change in grip force variables pre/post presenting two possibilities: (1) insufficient gamma-tACS intensity for this older adult population; (2) gamma-tACS accelerated grip force release to offset the delays observed in sham and beta-tACS. Data collection is ongoing, results from a larger sample will be presented.

Conclusions: beta-tACS contributes to faster release of an ongoing grasp but with prolonged duration of the actual grip-force relaxation to baseline. Gamma-tACS may accelerate the duration of grip force relaxation.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. Understand grip force regulation in older adults.
2. Understand the role of cortical beta and gamma oscillations in grip force control.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

185

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

MICROMAGNETIC STIMULATION OF THE RAT SPINAL CORD WITH SELECTIVE IPSILATERAL RECRUITMENT OF EMGS

Thomas Reilly, MD[1], Alpaslan Ersöz, PhD[2,3], Douglas Weber, Professor[2,3,4]
[1]Quantum NanoStim LLC, Research And Development, Palm Harbor, United States of America, [2]Carnegie Mellon University, Neuromechatronics Lab, Pittsburgh, United States of America, [3]Carnegie Mellon University, Department Of Mechanical Engineering, Pittsburgh, United States of America, [4]Carnegie Mellon University, Neuroscience Institute, Pittsburgh, United States of America

Introduction: Utilizing micromagnetic stimulation with a micro-coil (µcoil) presents an innovative alternative to traditional electrical stimulation for studying neurons within specific focal regions. This approach capitalizes on the induced electric field surrounding the tissues along the µcoil. This feature enables precise directionality and selectivity in the stimulation process. In the context of our research, we demonstrate the application of this technique in stimulating the L1 region of the rat spinal cord using a µcoil and subsequently recording evoked electromyography (EMG) in the biceps femoris.

Materials / Methods: We delivered pulses to the µcoil using an arbitrary function generator (AFG31000, Tektronix) and a power amplifier (Pyramid PB715X 1000 Watts 2 Channel Bridgeable Car Amplifier, Brooklyn, NY, 11204, USA). With *in vivo* validation experiments, the coil was stereotactically placed at the L1 region of the rodent spinal cord after laminectomy, and a recording electrode was inserted into the right and left biceps femoris muscle of rats. The evoked EMG responses were monitored in real-time with an Intan recording system (Intan RHD Recording System, Intan Technologies, Los Angeles, CA, USA).

Results: Micromagnetic spinal cord stimulation of the right and left lateral fibers at the L1 region of the rat spinal cord, evoked EMGs in the right and left biceps femoris, respectively. These results were reproducible and occurred at ~3ms after µMS.

Discussion: Forthcoming

Conclusions: Micromagnetic stimulation has emerged as a contactless, electrochemically safe stimulation technique. The insulated coil does not trigger any pH changes or have excessive charge accumulation, which is seen in traditional electrical spinal cord stimulation. The µcoil can induce precise ipsilateral stimulation in the spinal cord and trigger physiological responses.

Supplemental Data: Forthcoming

References: Forthcoming

Acknowledgements: This work has been funded by Quantum Nanostim through an award from the National Institute of Neurological Disorders and Stroke (NINDS) 1R43NS120335-01

Learning Objectives: (1) Mechanism of micromagnetic stimulation (2) Stimulation of the lateral dorsal spinal cord can induce ipsilateral evoked EMGs (3) Micromagnetic stimulation is a contactless, electrochemically safe stimulation technique.

Financial Disclosures: Thomas Reilly, Quantum Nanostim LLC, CEO, Owner of the above company Douglas J. Weber, PhD: Carnegie Mellon University, None Alpaslan Ersöz, PhD: Carnegie Mellon University, None

Disclosure: No significant relationships.

186

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

REVEALING CORTICAL DYNAMICS DURING ELECTROCONVULSIVE THERAPY IN A MOUSE MODEL

Zachary Rosenthal, MD, PhD[1], Joseph Majeski, PhD[2], Ala Somarowthu, PhD[3], Chris Favilla, MD[4], Golkoo Hosseini, MD[1], Jenny Rodriguez, MD[1], Mario Cristancho, MD[1], Arjun Yodh, MD[2], Ethan Goldberg, PhD[4,5]
[1]University of Pennsylvania Perelman School of Medicine, Department Of Psychiatry, Philadelphia, United States of America, [2]University of Pennsylvania, Department Of Physics, Philadelphia, United States of America, [3]Children's Hospital of Philadelphia (CHOP) Research Institute, Department Of Neurology, Philadelphia, United States of America, [4]University of Pennsylvania Perelman School of Medicine, Department Of Neurology, Philadelphia, United States of America, [5]Children's Hospital of Philadelphia, Department Of Neurology, Department Of Neuroscience, Philadelphia, United States of America

Introduction: Electroconvulsive therapy (ECT) is a life-saving treatment for medication-resistant depression. It has long been assumed that seizure is required for clinical benefit in ECT, but the underlying physiology is understudied.

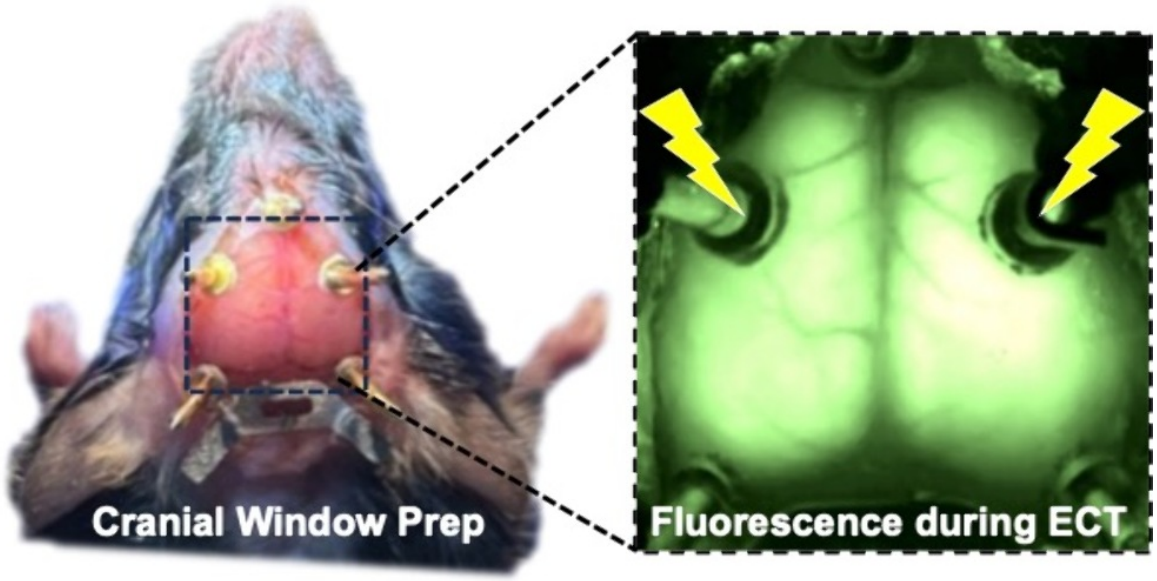
Materials / Methods: We performed the first ever recording of brain activity in a mouse model of ECT. We used transgenic Thy1-jRGeCO1a mice (n=10; 10-16 week old; mixed sex), which express a fluorescent reporter of intracellular calcium dynamics in excitatory neurons throughout the brain. Mice were implanted with 5 electrodes on the skull surface, as well as a clear polymer window overlying the intact skull to enable optical access to the cortex. We then visualized large-scale brain dynamics during ECT using a widefield fluorescence mesoscope.

Results: We reveal a second electrical event that reliably follows ECT seizure in mice: cortical spreading depolarization (CSD). We further show that high frequency stimulation generates briefer, higher amplitude seizures, that require less current to elicit a CSD. We also find that electrode configuration recruits seizure activity regionally during ECT and shapes which hemisphere CSD subsequently occurs in.

Discussion: It has long been assumed that seizure is necessary for the clinical benefit of ECT. However not all seizures are therapeutic, seizure properties have limited predictive value for clinical benefit, and non-convulsive stimulation may also be efficacious. The present investigation suggests that seizure is a means to another end: CSD. CSDs are primarily studied in brain injury and stroke, where they exacerbate injury. However, in the context of seizure, preclinical evidence suggests that CSDs can act as a protective, inhibitory ‘brake’ that terminates seizure and protects against future seizure. This is the first study to measure real-time brain activity during ECT pulse delivery in any species. Several opportunities were identified for refining stimulation – in particular high frequency pulse delivery elicits seizure and CSD more efficiently and with less current than low frequency pulse delivery. We also demonstrate the utility of current titration strategies to minimize the charge required for seizure, though modern ECT relies on fixed current.

Conclusions: This model system may enable future studies on parameter titration, circuit-level mechanisms of ECT, and novel neuromodulatory therapies.

Supplemental Data:



References: None

Acknowledgements: This work was supported by the University of Pennsylvania Educating Physician Scientists in Psychiatry (EPSP) Residency Research Track and award NIH R25MH119043. This work was also supported by the Institute for Translational Medicine and Therapeutics of the University of Pennsylvania and UL1TR001878 from the National Center for Advancing Translational Sciences.

Learning Objectives: 1. To establish a mouse widefield neuroimaging model for recording brain activity during electroconvulsive therapy (ECT) 2. To identify signatures of cortical activity during ECT that are associated with successful treatment 3. To identify biomarkers of plasticity in cortical dynamics over the course of serial treatment with ECT

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

187

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

EFFICACY AND SAFETY OF NEUROSTIMULATION IN A REAL-LIFE EVALUATION OF A THREE YEAR FOLLOW-UP COHORT STUDY IN A 295-PATIENT SUFFERING FROM NEUROPATHIC CHRONIC PAIN

Manuel Roulaud, MSc[1], Philippe Rigoard, MD[1], Amine Ounajim, PhD[1], Lisa Goudman, PhD[2], Bertille Lorgeoux, MSc[1], Sandrine Baron, RN[1], Sarah Borel, MSc[3], Nivole Kevin, MSc[1], Mathilde Many, MSc[1], Romain David, MD[1], Maarten Moens, MD[2], Maxime Billot, PhD[1]
[1]University Hospital Centre Poitiers, PRISMATICS Lab, Prismatics (predictive Research In Spine/neurostimulation Management And Thoracic Innovation In Cardiac Surgery), Poitiers, France, [2]Vrije Universiteit Brussel, Stimulus Research Group, Jette, Belgium, [3]Poitiers University Hospital, Prismatics Lab, Poitiers, France

Introduction: Implanted stimulation are applied since more than five decades to successfully relief neuropathic intractable chronic pain. Implanted neurostimulation techniques and pulse generator devices have evolved over time, now able to target spinal cord, dorsal root ganglion, peripheral nerve, sub-cutaneous, with different temporal settings such as tonic, high frequency, burst, high dose of stimulation. Data from long-term follow-up in real-life study are limited and focused on pain intensity. While new generation of objective and multidimensional pain assessment are now available, our study aimed to determine the efficacy and safety of implanted neurostimulation based on composite outcomes and long-term evaluation.

Materials / Methods: Data from the real-life retrospective observational PRISMAP study, including 295 patients with up to 3 years follow-up, were used. Our primary outcome was the efficacy of neurostimulation based on the Multidimensional Clinical Response Index (MCRI) ranging from 0 (worst possible global health status) to 10 (best potential global health status) with an Minimal Clinical Important Difference (MCID) of 1.05 [1]. In addition, pain intensity (NPRS), functional disability (ODI), quality of life (EQ-5D-5L) and pain surface were also assessed. The explantation rates over time was collected and analyzed using Kaplan-Meier curves.

Results: Among the 295 implanted patients, 174 had a 1-year follow-up, 98 had a 3-year follow-up and 50 had more than 3-year follow-up. The MCRI increased significantly from 3.34 ± 1.9 at baseline to 6.05 ± 2.5 at last follow-up ($p < 0.0001$). The MCRI responders' rate was 66.4%. Significant improvement was observed for pain intensity NPRS ($p < 0.0001$), ODI ($p < 0.0001$), EQ-5D-5L ($p < 0.0001$) and pain surface ($p < 0.0001$). The vast majority (67%) of patients reported a considerable improvement with a PGIC of 6 or 7. Using survival analysis, the rate of explant was 5.4% at 1 year, 9.3% at 2 years and 18.4% at 3 years follow-up considering unanticipated explants (i.e. excluding depleted batteries and non-rechargeable devices change).

Discussion: Our long-term real-life cohort study showed that neurostimulation was able to significantly improve global health (MCRI), quality of life and to significantly decrease pain intensity, functional disability and pain surface, with explanted rate up to 18.4% at 3-year follow-up. Our results reinforce the benefit of using implanted neurostimulation to relief neuropathic chronic pain.

Conclusions: Long-term real-life cohort study combine with multidimensional assessment are key point for demonstrating the potential benefits of implanted neurostimulation to treat neuropathic chronic pain in a near future.

Supplemental Data:

References: 1. Rigoard P, et al. A Novel Multi-Dimensional Clinical Response Index Dedicated to Improving Global Assessment of Pain in Patients with Persistent Spinal Pain Syndrome after Spinal

Surgery, Based on a Real-Life Prospective Multicentric Study (PREDIBACK) and Machine Learning Techniques. J Clin Med. 2021 Oct 24;10(21):4910.

Acknowledgements:

Learning Objectives: 1/ To get insights on the long-term efficacy of implanted neurostimulation using holistic evaluation tools. 2/ To estimate the explanation rates at 1, 2 and 3-year follow-ups after implantation 3/ Reinforce the use of real-life large cohorts of implanted patients to extract efficacy and safety estimates and improve the robustness of the literature.

Financial Disclosures: Moens M. reports speaker fees from Medtronic and Nevro, and Rigoard P. reports grants and personal fees from Medtronic, Abbott and Boston Scientific. Remaining authors have nothing to disclose.

Disclosure: No significant relationships.

188

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

USING AN AUTOMATED TOOL TO CHARACTERIZE AND DETECT EVOKED COMPOUND ACTION POTENTIALS IN RATS

Eline Versantvoort, MSc[1], Daniel Parker, BSc (Hons)[2], Zubin Nanavati, BBNSc (Hons)[2], Darayus Nanavati, BSc (Hons)[2], Birte Dietz, PhD[3], Peter Single, BSc (Hons)[2], Dave Mugan, BSc (Hons)[3], Quoc Vuong, PhD[4], Ilona Obara, PhD MSc[1]
[1]Newcastle University, School Of Pharmacy And Translational And Clinical Research Institute, Newcastle upon Tyne, United Kingdom, [2]Saluda Medical, Sydney, Australia, [3]Saluda Medical, Harrogate, United Kingdom, [4]Newcastle University, Biosciences Institute And School Of Psychology, Newcastle upon Tyne, United Kingdom

Introduction: The evoked compound action potential (ECAP) represents the neural recruitment of dorsal column fibers following spinal cord stimulation (SCS) and indicates the onset of SCS-induced sensations reported by humans[1]. Hence, the ECAP threshold (ECAPT) can be utilized as an objective surrogate to determine the optimal SCS dose[2] to improve translatability of preclinical SCS models. This study presents an automated methodology to improve accuracy, reliability and translatability of ECAP analyses in rats subjected to a model of neuropathic pain.

Materials / Methods: Adult male Sprague-Dawley rats (240-300 g; n = 15) were subjected to the spared nerve injury (SNI) model. A six-contact lead was implanted epidurally covering T11-L3. Stimulation and recordings were performed in anesthetized and freely behaving rats using a specially designed multi-channel system[3,4]. The stimulation current was increased in a stepwise manner from 0.0 mA (50 Hz 200 µs; 50 recordings/1 µA step size) until a motor response was detected. Manual processing of the recordings included the collection of input-output (IO) functions by interpolating the raw data points with an assumption-free spline curve (smoothing parameter=0.95). Manual ECAPTs were determined by **(Method 1)** offline visual inspection of the first observable ECAP; **(Method 2)** zero-crossing estimation of the fitted spline curve; **(Method 3)** linear extrapolation of IO functions to the y-intercept[4]. Finally, manual ECAPT estimates were compared to ECAPTs estimated by an automated tool.

Results: There was an overall difference in ECAPT estimates (current and amplitude) between anesthetized and freely behaving animals, in both sham and SNI groups (Fig. 1,2). Differences in mean current (mA) required to generate ECAPTs were observed in the anesthetized animals, but not in the freely behaving animals, when comparing Methods 2 and 3 to the automated method (Fig. 1). The reliability of the manually estimated ECAPT is dependent on several factors, such as the signal-to-noise ratio of the recording as well as the linearity of the IO function data.

Discussion: The automated tool may improve replicability and translatability of our findings, and overcome the challenges observed with the manual analysis of ECAP recordings. Moreover, the difference observed in the ECAPT current and amplitude between anaesthetised and freely behaving rats demonstrates the importance of accounting for multiple factors that could lead to variations in dorsal column activation.

Conclusions: Implementing an automated tool to estimate ECAPT may improve the application of SCS in preclinical models, as well as the replicability and translatability of findings.

Supplemental Data:

References: 1. Gmel GE, Santos Escapa R, Parker JL, Mugan D, Al-Kaisy A, Palmisani S. The Effect of Spinal Cord Stimulation Frequency on the Neural Response and Perceived Sensation in Patients With Chronic Pain. Front Neurosci. 2021;15:625835.
2. Parker J, Karantonis D, Single P. Hypothesis for the mechanism of action of ECAP-controlled

closed-loop systems for spinal cord stimulation. Healthc Technol Lett. 2020 Jun;7(3):76-80.
3. Dietz BE, Mugan D, Vuong QC, Obara I. Electrically Evoked Compound Action Potentials in Spinal Cord Stimulation: Implications for Preclinical Research Models. Neuromodulation. 2022 Jan;25(1):64-74.
4. Versantvoort EM, Dietz BE, Mugan D, Vuong QC, Luli S, Obara I. Evoked compound action potential (ECAP)-controlled closed-loop spinal cord stimulation in an experimental model of neuropathic pain in rats. Bioelectron Med. 2024 Jan 10;10(1):2.

Acknowledgements: Funding and equipment were provided by Saluda Medical.

Learning Objectives: 1. Be able to describe characteristics of ECAP recordings in anesthetized and freely behaving SNI rats. 2. Be able to recognize an automated tool allowing for reliable determination of ECAP amplitude and threshold. 3. Be able to identify translational values of preclinical SCS models.

Financial Disclosures: Darayus Nanavati ($20,001 - $100,000 USD; stock options), Zubin Nanavati ($20,001 - $100,000 USD; stock options), Daniel Parker ($20,001 - $100,000 USD; stock options), Birte Elisabeth Dietz ($20,001 - $100,000 USD; stock options), Peter Single (> $100,000 USD; stock options) and Dave Mugan (> $100,000 USD; stock options) are employed by Saluda Medical. Ilona Obara has received travel and research grants from Saluda Medical (> $100,000 USD). None of the authors have a commercial interest in the material presented here. There are no other relationships that might lead to a conflict of interest in the current study.

Disclosure: No significant relationships.

189

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

THE EFFECT OF DEEP BRAIN STIMULATION ON NEUROVASCULAR COUPLING IN HUMAN INTRACRANIAL RECORDINGS OF BASAL GANGLIA

Artur Vetkas, MD[1], Srdjan Sumarac, MSc[1], Mojgan Hodaie, MD[1], Suneil Kalia, MD[1], Andres Lozano, MD[1], William Hutchison, PhD[1], Luka Milosevic, PhD[2]
[1]Toronto Western Hospital - University of Toronto, Neurosurgery, Toronto, Canada, [2]University Health Network, Clinical And Computational Neuroscience, Toronto, Canada

Introduction: Deep brain stimulation (DBS) targeting the basal ganglia is an effective and well-established therapy for a range of neurological and psychiatric disorders. However, the precise mechanism of action and the range of physiological effects of DBS are not yet fully described. While neurovascular coupling has been suggested as a potential mechanism of action for DBS, very little research has been done to asses the impact of DBS on neurovascular responses, particular on the level of microcirculation.

Materials / Methods: Objective: This study aimed to investigate the impact of high-frequency neuronal microstimulation on cerebral vascular reactivty and through analysis of cardioballistic biomarker obtained from intracranial microelectrode recordings (MER).
Methods: We collected MER data from two electrodes (~600 µm away) and examined the effects of 100 Hz microstimulation on cardioballistic waveforms in 178 MER segments from 98 patients undergoing DBS surgery, including 59 recordings segments from the globus pallidus internus (GPi; n=29), 22 from the substantia nigra pars reticulata; SNr; n = 15;), 44 from the subthalamic nucleus (STN; n = 28;), and 53 from the ventral intermediate nucleus (Vim; n = 26). We used linear mixed models (LMM) to compare the changes in cardioballistic waveform amplitudes before and after HFS in both the proximal and distal electrode. The decay of the post-HFS cardioballistic amplitudes was quantified by the half-life derived from a decaying exponential model over a five-second period. Neurovascular coupling was assessed using LMM through pre- and post-HFS changes in high-frequency oscillations (HFO) and cardioballistic-HFO phase-amplitude coupling (PAC). A linear computation model was used to relate cardioballistic waveform changes to arteriole diameter variations.

Results: High-frequency stimulation led to a significant increase in vascular response within the STN (LMM; $p < .001$; average increase of 424%), in Vim (LMM; $p < .001$; 385%), in GPi (LMM; $p < .001$; 165%), and to a lesser extent in SNr (LMM; $p = .034$; 102%). No significant changes to cardioballistic waveform amplitudes were noted in recordings at the distal recording electrode (~600 µm away). Temporal dynamics analysis showed post-stimulation cardioballistic waveform amplitude exhibiting either persistent or decaying dynamics over 5 seconds, with no significant difference in the decay rates across the targets (LMM; Vim-GPi $p = .467$, Vim-SNr $p = .582$, Vim-STN $p = .482$). Neurovascular analysis at the proximal electrode showed a positive significant correlation between cardioballistic waveform changes and HFO power change ($p = .034$), but no significant effects were found in cardioballistic-HFO PAC ($p = .570$). Modeling of the dynamics of vessel walls in response to stimulation substantiated the hypothesis that vessel dilation can lead to an increased transmission of pulsatile forces to the microelectrode.

Discussion: Comprehensive evaluation of DBS, vascular reactivity, and NVC may offer ways to enhance cerebral perfusion, potentially serving as treatment for cerebrovascular and neurological diseases.

Conclusions: Our findings reveal a significant impact of electrical stimulation on local neurovascular reactivity in the STN, Vim, GPi, and SNr highlighting the potential therapeutic implications of DBS for neurodegenerative, as well as neurovascular diseases. Further research is warranted to investigate

the underlying mechanisms, optimize stimulation parameters, and explore novel applications in treating brain disorders involving impaired neurovascular function.

Learning Objectives: 1. Understand the effect of deep brain stimulation (DBS) on neurovascular coupling as measured by changes in cardiac signal prominence in intracranial microelectrode recordings. The study found that 100Hz microstimulation led to a significant increase in cardiac signal prominence across various brain structures including the VIM, STN, and GPi, as observed from the proximal microelectrode. This indicates that DBS has a profound impact on vascular reactivity in these regions as measured indirectly through changes in the cardiac signal artifact. 2. Comprehend the temporal dynamics of the vascular response following DBS as measured by the cardiac signal artifact. Analysis of the cardiac signal dynamics post-stimulation revealed segments were either persistent or decaying over 5 seconds. The average half-life of decaying segments was around 2 seconds with no significant differences between brain structures. This provides insight into how vascular reactivity returns to baseline levels after DBS. 3. Understand the potential mechanisms underlying the effect of DBS on neurovascular coupling. The study discusses potential mechanisms such as induced neural activity elevating metabolic demand, direct stimulation of vessel walls, or biochemical signaling pathways involving astrocytes. Further research is still needed to clarify the relationship, but the findings help advance understanding of DBS physiological effects beyond neurons.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

190

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

AMPLITUDE PROFILE OF EVOKED RESONANT NEURAL ACTIVITY IN GLOBUS PALLIDUS INTERNA OF PARKINSONS DISEASE PATIENTS

Luciano Branco, MSc[1], Hossein Heydari, BSc (Hons)[2], Chandra Swamy, MSc[2], Arjun Tarakad, MD[3], Nora Vanegas-Arroyave, MD[3], Lisa Yutong Taneff, MSN[3], Nuri Ince, PhD[2], Ashwin Viswanathan, MD[4]
[1]University of Houston, Biomedical Engineering, Houston, United States of America, [2]Mayo Clinic, Neurologic Surgery, Rochester, United States of America, [3]Baylor College of Medicine, Neurology, Houston, United States of America, [4]Baylor College of Medicine, Neurosurgery, Houston, United States of America

Introduction: Evoked resonant neural activity (ERNA) is a promising biomarker for identifying the globus pallidus interna (GPi) during deep brain stimulation (DBS) surgery. Key advantages of ERNA include the ability to record ERNA in the anesthetized patient, a large signal amplitude and local specificity.

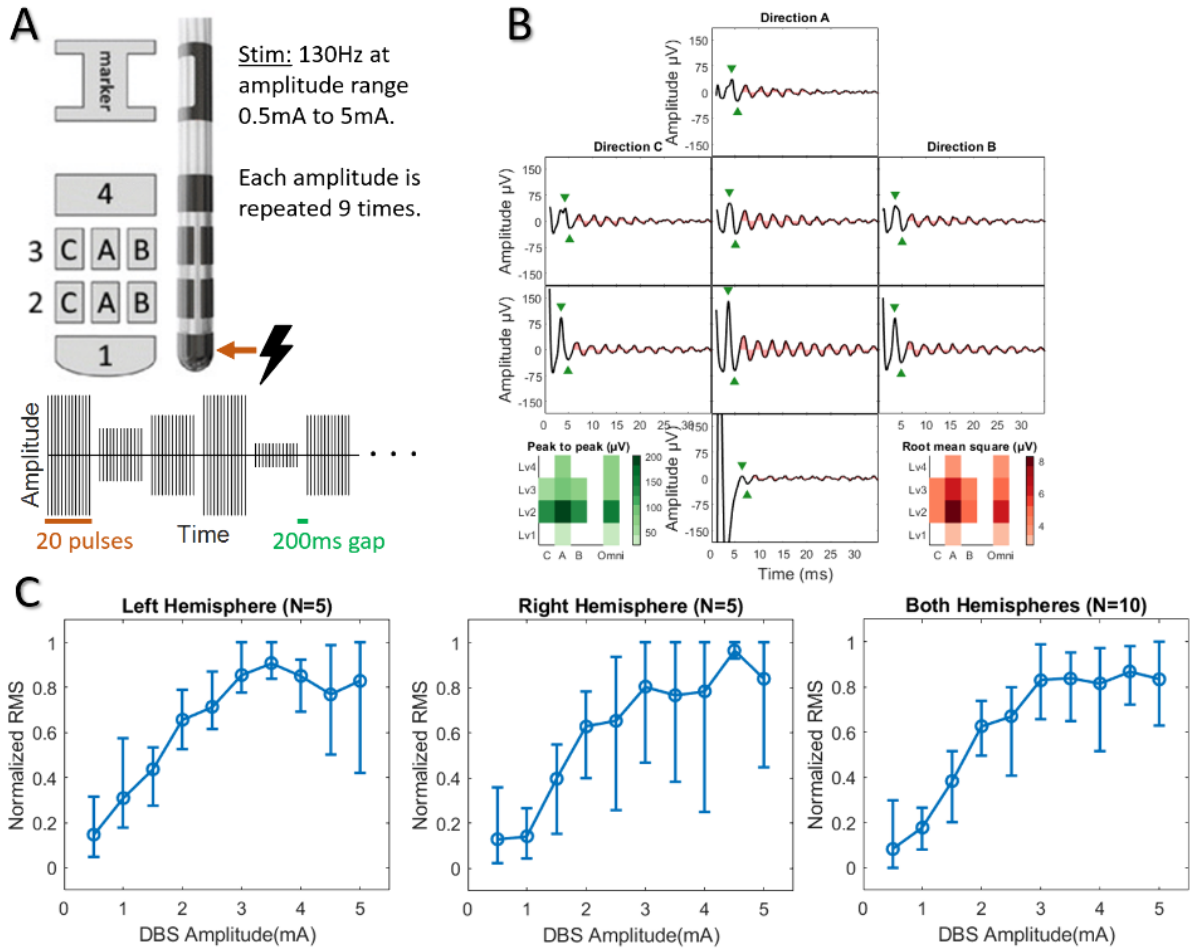
Materials / Methods: We recorded local field potentials (LFPs) from 6 patients intraoperatively during bilateral GPi-DBS surgery after securing the 8-channel, directional leads. Monopolar, biphasic, and charge-balanced stimulation (130Hz, 100µsec) was delivered (Ripple, Summit) at amplitudes varying between 0.5 to 5mA, in 0.5mA steps and randomized order, to the bottom contact of each lead. Stimulation was delivered in bursts of 20 pulses followed by a 200ms gap in which ERNA could be observed. Each amplitude was repeated for a total of 9 trials (Fig. A). Trials were averaged after detrending with Savitzky–Golay filter (3rd order, 5ms window), followed by peak to peak (P2P, taken from the largest positive deflection to the following trough) and root mean square (RMS) calculations. RMS values of each trial are calculated for a 100ms window, starting from the next zero-crossing point after the P2P (Fig. B).

Results: Out of the 12 GPi hemispheres, two were excluded due to an inability to detect resonance during DBS stimulation gaps. In the remaining 10 GPi hemispheres, RMS and P2P values showed a rapid increase within the initial amplitude range of 0-2.5mA, generally reaching a plateau in the 2.5-4mA range. In multiple cases, values decreased in the highest range of 4-5mA (see Fig. C).

Discussion: The results of this study suggest an optimal amplitude window for maximizing the induced ERNA biomarker. It is currently unclear if this optimal amplitude range correlates with the clinical therapeutic window. However, these findings open the door to the possibility of automatically determining stimulation parameters by actively probing the motor circuits with electrical stimulation while recording ERNA.

Conclusions: GPi ERNA profile reveals a non-linear relationship with DBS stimulation amplitude, indicating a saturation in the resonance carried by the motor networks

Supplemental Data:



References: [1] Sinclair, Nicholas C et al. “Subthalamic nucleus deep brain stimulation evokes resonant neural activity.” *Annals of neurology* vol. 83,5 (2018): 1027-1031. doi:10.1002/ana.25234 [2] Ozturk, Musa et al. “Electroceutically induced subthalamic high-frequency oscillations and evoked compound activity may explain the mechanism of therapeutic stimulation in Parkinson's disease.” *Communications biology* vol. 4,1 393. 23 Mar. 2021, doi:10.1038/s42003-021-01915-7

Acknowledgements: This work was sponsored by the National Institutes of Health—National Institute of Neurological Disorders and Stroke (Grant R01NS124650).

Learning Objectives: [1] Is it possible to induce ERNA at GPi of PD patients? Yes, ERNA is present in GPi. [2] Is ERNA in GPi a localized phenomenon? Yes, ERNA in GPi appears to be stronger in specific contacts in a directional DBS electrode. [3] How does ERNA gets modulated by DBS amplitude? ERNA in GPi increases rapidly at initial DBS amplitudes and saturates at higher intensities.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

191

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

PROLONGED HIPPOCAMPAL DEEP BRAIN STIMULATION LEADS TO HETEROGENEOUS CELLULAR RESPONSES IN CA1 NEURONS

Yangyang Wang, MSBmE, Cara Ravasio, MSc, Jiahe Niu, BEng, Sukhneet Bhogal, BS, Emily Pira, BEng, Rose Coviello, BEng, Abdullah Malik, BS, Xue Han, PhD
Boston University, Biomedical Engineering, Boston, United States of America

Introduction: Deep brain stimulation (DBS) is effective for managing various neurological and psychiatric disorders. However, the therapeutic mechanisms of DBS are unknown. Studies suggested that electrical stimulation can directly influence the activity of local neurons through axons.[1,2] We recently demonstrated that DBS-evoked membrane voltage changes led to informational lesion.[3] Intriguingly, the clinical outcome of DBS in epilepsy and movement disorders is consistent with tissue resection and pharmacological lesion, suggesting the inhibition theory. However, few studies examined the cellular and network effect of prolonged DBS directly related to clinical observations. We performed cellular calcium imaging from >16,000 CA1 neurons, free of electrical stimulation artifact, upon prolonged 39 minutes-long DBS.

Materials / Methods: We placed a custom imaging window coupled with an electrical stimulation electrode above the CA1 region in five C57BL/6 mice. AAV9-Syn-jGCaMP7f viruses were infused. DBS pulses were bipolar and 200 μs per pulse (115.2 ± 45.1μA, n=26 sessions, corresponding to ~3.8–17.0μC/cm^2 charge density per stimulation phase). Each recording session was 63 minutes long (Fig. 1).

Results: We recorded a total of 7299 neurons across 5 mice with DBS at 40Hz, and 9466 neurons with DBS at 140Hz. Our analysis suggested that many neurons exhibited a prominent and transient change within a few seconds of DBS onset delivered at either 40Hz or 140Hz, with the majority showing a reduction in activity, though some exhibiting an increase (Fig.2). Interestingly, this initial change dissipated soon after, with most neurons settled into similar patterns as during baseline period (Fig.2 B and D). However, a sizable fraction of neurons remained suppressed throughout the entire DBS period, and quickly recovered at DBS offset
(Fig.3).

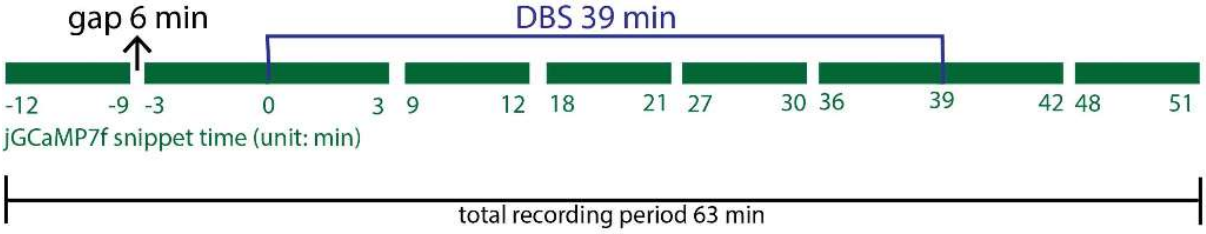


Figure 1, Schematic of recording protocol. During each 63 minutes long recording sessions, we sampled GCaMP7f fluorescence from many neurons periodically, starting at 12 minutes before DBS onset until 12 minutes after DBS offset, with DBS lasting for 39 minutes. DBS was at either 40Hz or 140Hz.The recording time is displayed relative to DBS onset (time 0). GCaMP7f fluorescence were imaged through a custom fluorescence microscope at 20Hz. Each recording period lasted for either 3 or 6 minutes, with 6-minutes between periods, and the total imaging duration was 27 minutes. This imaging strategy was designed to minimize GCaMP7f signal bleaching, while allowing us to sample CA1 neuron's responses throughout the entire 63 minutes long recording periods.

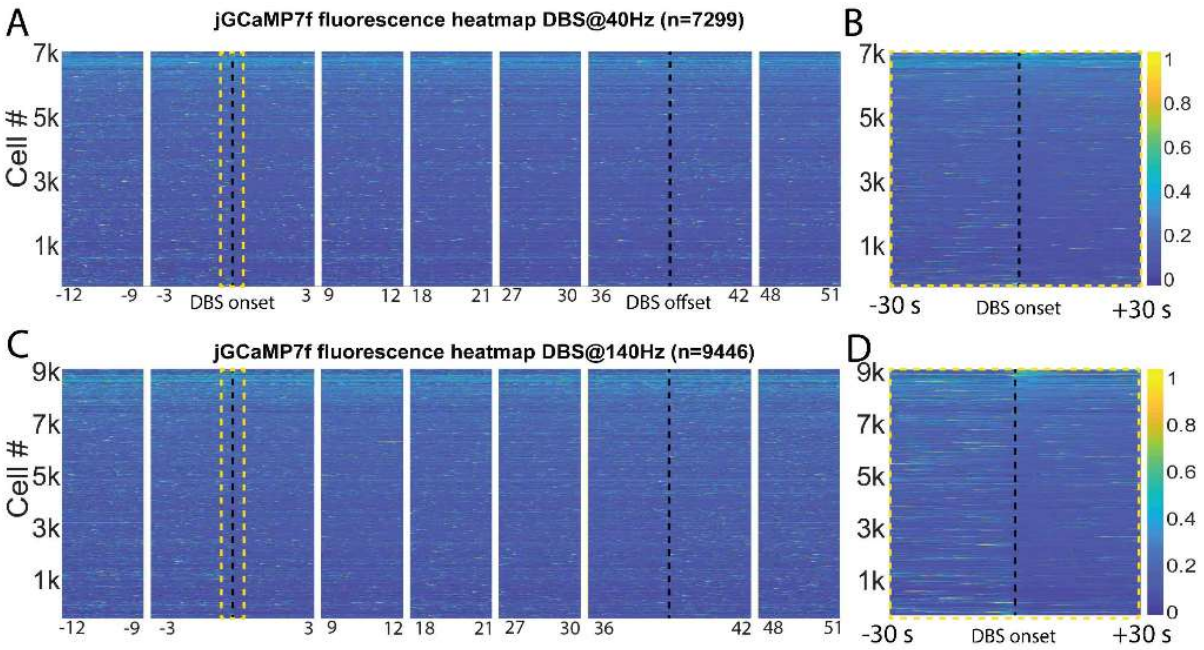


Figure 2. Transient changes in neural activity, measured as GCaMP7f fluorescence, at DBS onset. (A) Neural activity before, during and after 40Hz DBS. 7299 neurons were collected from 13 recording sessions in 5 mice. Neurons were sorted based on their fluorescence change during DBS compared to before DBS, with the highest on the top. The yellow box indicate the 1 min time window around the DBS onset. (B) Zoom-in heatmap at DBS onset, as highlighted by the yellow box in A. (C) Neural activity before, during and after 140Hz DBS across 9446 neurons collected from 13 recording sessions in 5 mice. (D) Zoom-in heatmap at DBS onset, as highlighted by the yellow box in C.

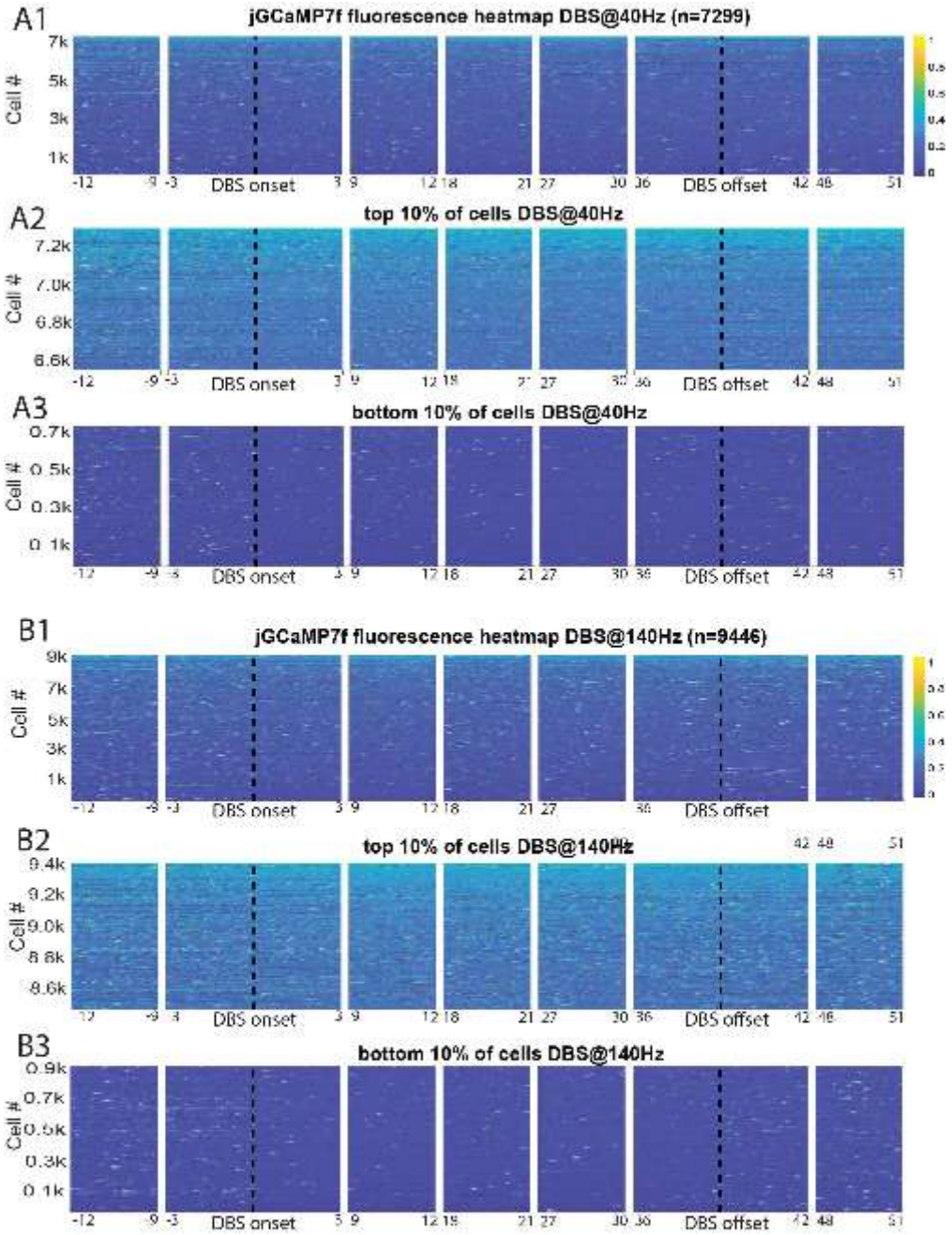


Figure 3. Prominent inhibitory effect during prolonged DBS. (A1, B1) The same raw dataset as Figure 2, but sorted based on the overall fluorescence during the entire DBS period, with the highest fluorescence on the top. (A2, B2) top 10% of neurons with the highest GCaMP7f fluorescence during DBS. (A3, B3) bottom 10% of the neurons with the lowest fluorescence during DBS.

Discussion: DBS at both 40Hz and 140Hz led to robust and transient suppression across a large fraction of neurons. There was a significant fraction of neurons that exhibit long lasting suppression throughout the entire DBS period. The results here extend our previous analysis[3] to >16,000 neurons, allowing us to probe the heterogeneity of DBS across neuronal populations. Our results revealed that DBS mediated transient effect is restricted to a few seconds of DBS onset, and the neural activity during prolonged DBS remain diverse across the population.

Conclusions: Our results demonstrate that DBS evokes transient and overall inhibitory cellular responses at onset followed by the return of dynamic responses across neurons within the network during prolonged DBS, suggesting that DBS does not synchronize neurons in the network. The observed suppressed neurons throughout the prolonged DBS supports a general inhibitory effect of DBS.

Supplemental Data:

References: [1] Benazzouz, A. & Hallett, M. Mechanism of action of deep brain stimulation. *Neurology* **55**, S13–S16 (2000). [2] Liu, L. D. et al. Frequency-dependent effects of electrical stimulation in the globus pallidus of dystonia patients. *J. Neurophysiol.* **108**, 5–17 (2012). [3] Lowet, E., Kondabolu, K., Zhou, S. *et al.* Deep brain stimulation creates informational lesion through membrane depolarization in mouse hippocampus. *Nat Commun* **13**, 7709 (2022).

Acknowledgements: NIH 5R01MH122971. 1RF1NS129520, 1R01NS119483

Learning Objectives: (1) what is the transient effect of prolonged DBS onset: many neurons exhibited a prominent and transient change within a few seconds of DBS onset delivered at either 40Hz or 140Hz, with the majority showing inhibitory effect, though some exhibiting an increase. The transient effects dissipated within a couple seconds, with most neurons settled into similar patterns as during baseline period. (2) what is the prominent effect during prolonged DBS: a sizable fraction of neurons remained suppressed throughout the entire prolonged DBS period, and quickly recovered at DBS offset. (3) how to relate the in vivo experiments to clinical observations: By performing cellular calcium imaging from >16,000 CA1 neurons, free of electrical stimulation artifact, upon prolonged 39 minutes-long DBS, we concluded that DBS does not produce uniform changes across neurons in the network. Many neurons showed transient and prolonged inhibitory effects, while some still showed excitatory effects.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

192

Poster on Board
POSTER ON BOARD: AS01. BASIC SCIENCE OF NEUROMODULATION
13-05-2024 08:00 - 19:00

EXPLORING THE IMPACT OF DIFFERENT TRANSCRANIAL ALTERNATING CURRENT STIMULATION (TACS) SETTINGS ON MOVEMENT-RELATED BETA DESYNCHRONIZATION ACROSS MOTOR HEMISPHERES

Xuanteng Yan, BSc (Hons)[1], Kenya Morales Fajardo, MSc[2], Georgios Mitsis, PhD[2], Marie-Hélène Boudrias, PhD[1]
[1]McGill University, Montréal, Canada, [2]McGill University, Bioengineering, Montréal, Canada

Introduction: The phenomenon of movement-related beta desynchronization (MRBD) in Electroencephalography (EEG) recordings, specifically the decrease in beta band power during movement, is well-established [1]. MRBD is closely linked to motor performance, making it pivotal in understanding neural processes [2]. Additionally, transcranial alternating current stimulation (tACS) has emerged as a tool influencing brain activity, particularly in the context of motor function [3]. Despite its potential, the precise quantitative impact of tACS on MRBD in healthy adults remains unclear, motivating our study to explore this relationship.

Materials / Methods: Fifteen healthy, right-handed adults participated in data collection, and data from a female participant were analyzed. Participants performed a hand-grip motor task in 50 trials, timed with tACS application: baseline, during, and 15/45/75 minutes post-tACS. Three tACS settings were applied: 70Hz, 20Hz, and a Sham control. A 1mA sinusoidal waveform was administered at electrode C3, with EEG recorded using a 64-channel ActiCap cap, sampled at 2.5KHz and referenced to FCz. Electrode impedances were maintained below 10kΩ. EEG data were filtered (0.1-100 Hz bandpass and 60Hz notch), and down-sample to 250Hz. We removed noisy epochs and channels by visual inspection. Independent component analysis was applied to identify and remove motion artifacts. EEG data during tACS were cleaned using the algorithm proposed by Yan et al., 2022 [4]. MRBD was calculated at contralateral and ipsilateral motor cortex electrodes (CP3 and CP4) by subtracting beta band power during trials from pre-movement resting state power, and subsequently normalized by the pre-movement resting power.

Results:

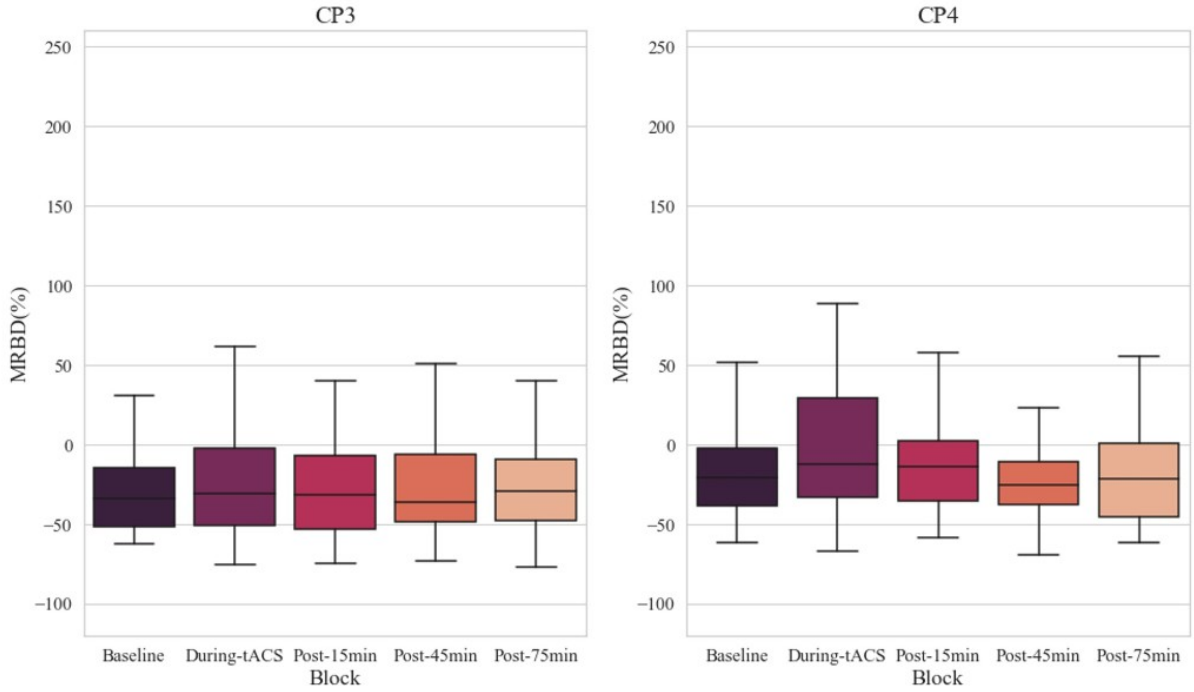


Fig. 1. Effects of Sham tACS on MRBD

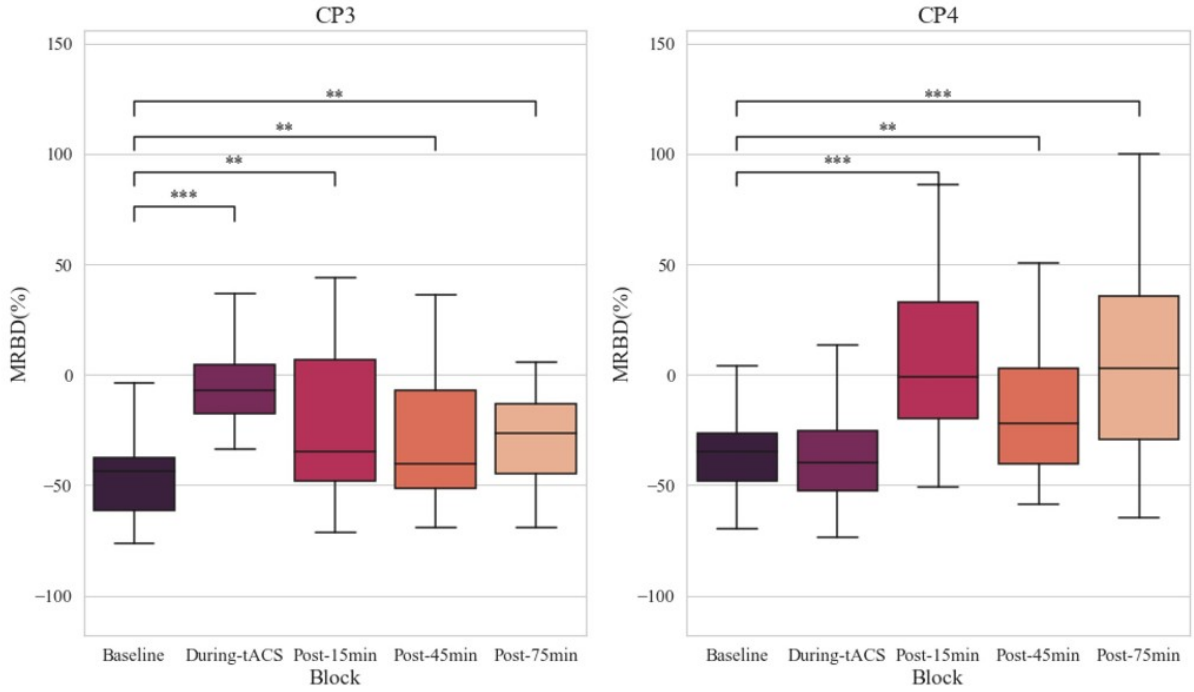


Fig. 2. Effects of 70Hz tACS on MRBD.

$*: p < 0.05, **: p < 0.005, ***: p < 0.001$

Sham tACS showed no significant modulation in MRBD magnitude (Fig. 1). In contrast, 70Hz tACS significantly decreased MRBD across all electrodes, with effects lasting up to 75 minutes post-tACS (Fig. 2).

Discussion: We reported less desynchronization in the beta band power after 70Hz tACS. As previous studies have reported that 70Hz tACS facilitates movement execution as less pronounced MRBD is associated with better motor function [5]. Our study suggests the link between tACS, MRBD and motor function, providing reference to future tACS applications in clinical trials. To our knowledge, it is also the first study trying to reveal the ongoing impacts of tACS in both motor hemispheres.

Conclusions: In the present study, we quantify the effects of tACS at different settings on MRBD, revealing a suppressive effects of 70Hz tACS on beta power desynchronization. Our study contributes valuable insights, laying a foundation for the application of tACS in therapeutic contexts and enhancing our understanding of its impact on motor function.

Supplemental Data: NA

References: [1] C. Neuper and G. Pfurtscheller, “Event-related dynamics of cortical rhythms: frequency-specific features and functional correlates,” *Int. J. Psychophysiol.*, vol. 43, no. 1, pp. 41–58, 2001. [2] V. Litvak et al., “Movement-related changes in local and long-range synchronization in parkinson’s disease revealed by simultaneous magnetoencephalography and intracranial recordings,” J. Neurosci., vol. 32, no. 31, pp. 10541–10553, 2012. [3] T. Yamaguchi et al., “Transcranial Alternating Current Stimulation of the Primary Motor Cortex after Skill Acquisition Improves Motor Memory Retention in Humans: A Double-Blinded Sham-Controlled Study,” Cereb. Cortex Commun., vol. 1, no. 1, pp. 1–11, 2020. [4] X. Yan, MH. Boudrias & G. D. Mitsis, ”Removal of Transcranial Alternating Current Stimulation EEG Artifacts Using Blind Source Separation and Wavelets”, IEEE Transactions on Biomedical Engineering, vol. 69, no. 10, pp. 3183-3192, 2022. [5] S. Miyaguchi et al., “Transcranial alternating current stimulation with gamma oscillations over the primary motor cortex and cerebellar hemisphere improved visuomotor performance,” Front. Behav. Neurosci., vol. 12, no. July, pp. 1–9, 2018.

Acknowledgements: This work was supported in part by the Fonds de Fonds de Recherche du Québec Nature et Technologies (FRQNT) awarded to XY.

Learning Objectives: 1. The beta band power in brain signals is related to the motor function: MRBD in the context of movement execution 2. tACS is capable of modulating brain activity and the beta power: 70Hz tACS decreases MRBD magnitude in both motor hemispheres 3. Lasting effects of tACS were found: Up to 75 minutes post tACS

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

193

Poster on Board
POSTER ON BOARD: AS02. NEUROPROSTHETICS / NEURAL ENGINEERING / BRAIN COMPUTER INTERFACE / ARTIFICIAL INTELLIGENCE
13-05-2024 08:00 - 19:00

EFFECTIVENESS OF SPINAL CORD AND L2 SYMPATHETIC GANGLION STIMULATION IN ALLEVIATING COMPLEX REGIONAL PAIN SYNDROME

Tae-Kyu Lee, MD, PhD, Min-Ho Lee, PhD
Uijeongbu St. Mary's Hospital, The Catholic University of Korea, Neurosurgery, Gyeongi-Do, Korea, Republic of

Introduction: Complex Regional Pain Syndrome (CRPS) demands a multi-pronged treatment approach encompassing education, self-management, physical rehabilitation, pain relief, and psychological support. When traditional medications fail to provide pain relief, alternatives such as Spinal Cord Stimulation (SCS) and Intrathecal Morphine Pump (ITP) may be explored. This study assesses the effect of SCS combined with L2 sympathetic ganglion stimulation (LSGS) in mitigating CRPS-related pain.

Materials / Methods: 62 CRPS patients, unresponsive to opioid medications and exhibiting neuropathic pain symptoms as per DN4 and LANSS Pain Scale, underwent SCS with LSGS in November 2015. To determine the suitability of SCS and LSGS, an epidural diagnostic block and an L2 sympathetic ganglion block were performed. Only those who experienced over 50% pain relief seven days post-diagnostic were considered. Pain levels were measured using the visual analog score (VAS), and daily morphine usage was tracked pre-and post-treatment.

Results: 55 of the 62 patients achieved significant pain relief lasting 12 months post-SCS and LSGS. On average, VAS scores gradually decreased over time, and daily morphine consumption reduced from the baseline. Pain relief (VAS 4.67±1.43 (mean ± SD)) had been achieved after SCS and LSGS and lasted for 12 months (4.43±0.72 after one month: 4.34±0.64 after 2months: 4.18±0.73 after six months: 5.12±1.36 after 12 months). Daily morphine consumption was reduced to a maximum of 62.13% after SCS and LSGS compared to the baseline. Complications during SCS and L2 LSGS did not occur in this study. No complications arose during the procedures. The remaining seven patients, reporting heightened pain, subsequently received morphine ITP, leading to substantially decreased VAS scores and minimal side effects due to low morphine doses.

Discussion: Neuropathic pain, resulting from damage to the somatosensory system, can manifest in several regions, including the peripheral nerves, spinal cord, or brain. Our study spotlighted the sympathetic maintained pain (SMP) subset of neuropathic pain, primarily seen in CRPS-I. Believed to be exacerbated by the sympathetic nervous system's activity, SMP often necessitates diverse treatment strategies. These include medications, physical therapy, sympathetic nerve blocks, and possibly spinal cord stimulation. If a patient with CRPS responded positively to the L2 sympathetic block, a combined approach of SCS and LSGS was adopted to manage their pain.

Conclusions: SCS, when combined with LSGS, has shown promise in effectively managing CRPS, emphasizing its value in treatment regimens.

Supplemental Data:

References: 1. Turner, Judith A., et al. "Spinal cord stimulation for patients with failed back surgery syndrome or complex regional pain syndrome: a systematic review of effectiveness and complications." *Pain* 108.1-2 (2004): 137-147. 2. Kemler, Marius A., et al. "Effect of spinal cord stimulation for chronic complex regional pain syndrome Type I: five-year final follow-up of patients in a randomized controlled trial." *Journal of neurosurgery* 108.2 (2008): 292-298. 3. Visnjevac, Ognjen, et al. "A comprehensive outcome-specific review of the use of spinal cord stimulation for complex regional pain syndrome." *Pain Practice* 17.4 (2017): 533-545. 4. Geurts, José W., et al. "Spinal cord

stimulation for complex regional pain syndrome type I: a prospective cohort study with long-term follow-up." *Neuromodulation: Technology at the Neural Interface* 16.6 (2013): 523-529. 5. Schattschneider, Jörn, et al. "Complex regional pain syndromes: the influence of cutaneous and deep somatic sympathetic innervation on pain." *The Clinical journal of pain* 22.3 (2006): 240-244. 6. Jensen, Troels S., and Ralf Baron. "Translation of symptoms and signs into mechanisms in neuropathic pain." *Pain* 102.1-2 (2003): 1-8. 7. Krumova, Elena K., et al. "Are sympathetic blocks useful for diagnostic purposes?." *Regional Anesthesia & Pain Medicine* 36.6 (2011): 560-567. 8. Bandyk, Dennis F., et al. "Surgical sympathectomy for reflex sympathetic dystrophy syndromes." *Journal of vascular surgery* 35.2 (2002): 269-277. 9. Fine, Perry G. "Pain Research and Basic Science: Pain and the Sympathetic Nervous System." *Anesthesiology and Pain Management*. Dordrecht: Springer Netherlands, 1994. 65-75.

Acknowledgements: I am grateful to my colleagues, especially Sei-yeon Yang and Professor Min-ho Lee, who sought the basic science and clinical evidence for the new attempt and established guidelines and treatment strategies.

Learning Objectives: 1. Understanding CRPS and Treatment Modalities: Learners will be able to describe the characteristics and challenges of Complex Regional Pain Syndrome (CRPS) and articulate the various treatment approaches, including Spinal Cord Stimulation (SCS) and Intrathecal Morphine Pump (ITP). **2. Appreciating the Role of SCS and LSGS in Pain Management:** Learners will understand the methodology and criteria for patient inclusion in SCS and L2 sympathetic ganglion stimulation (LSGS) treatments. They will be able to discuss the efficacy and safety of these procedures in reducing neuropathic pain in CRPS patients. **3. Differentiating between Types of Neuropathic Pain:** Learners can differentiate between sympathetic maintained pain (SMP) and other types of neuropathic pain, recognize their origins in the somatosensory system, and explain the rationale behind combined SCS and LSGS treatment for CRPS patients.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

194

Poster on Board
POSTER ON BOARD: AS02. NEUROPROSTHETICS / NEURAL ENGINEERING / BRAIN COMPUTER INTERFACE / ARTIFICIAL INTELLIGENCE
13-05-2024 08:00 - 19:00

BEST PRACTICE GUIDANCE FOR IMPLEMENTATION OF PHYSIOLOGICAL CLOSED-LOOP CONTROLLERS WITH IMPLANTABLE NEUROMODULATION SYSTEMS

Victoria Marks, PhD[1], John Fleming, PhD[1,2], Mayela Zamora, PhD[1], Lawrence Poree, MD, PhD[3,4], Tim Denison, PhD[1,5,6]
[1]Oxford University, Institute Of Biomedical Engineering, Oxford, United Kingdom, [2]Oxford University, Medical Research Council Brain Network Dynamics Unit, Oxford, United Kingdom, [3]University of California, Anesthesiology, San Francisco, United States of America, [4]Univeristy of California San Francisco, Department Of Anesthesiology And Pain Medicine., San Francisco, United States of America, [5]University of Oxford, Mrc Brain Networks Unit, Oxford, United Kingdom, [6]University of Oxford, Nuffield Deparment Of Clinical Neurosciences, Oxford, United Kingdom

Introduction: Homeostasis is maintained by living organisms at a variety of scales for healthy biological functioning. During healthy physiology, biological processes, such as heart rate or blood glucose concentration, are regulated to remain within a healthy range, or “setpoint,” to maintain a stable internal environment and ensure normal functioning of the organism. Dysregulation of processes outside of the healthy range can lead to abnormal behaviour and subsequently result in the emergence of pathological disease. To combat chronic deviations from homeostasis, physiological closed-loop controllers (PCLC) have emerged as a burgeoning sector of the medical device field. Common systems dependent on physiological feedback include anaesthesia machines, which respond to changes in the bispectral index to adjust propofol delivery[1], and continuous glucose monitors, which respond to changes in blood glucose by alarming to administer insulin or to eat. Advances in the sensing and stimulation capabilities of implantable neurostimulators allow for the breakthrough of PCLCs in the neuromodulation space.

Materials / Methods: We will examine obstacles to PCLC implementation in closing the loop in neurological disorders such as pain and epilepsy.

Results: This work will help research teams do the following: 1. select an appropriate input signal for a PCLC, 2. characterize the anticipated behaviour of the PCLC, 3. select appropriate fallback modes to mitigate risk in the event the PCLC fails, 4. implement checks on the device to prevent skill degradation, and 5. design in silico models to verify and test PCLC performance.

Discussion: The utility of such an application is exemplified by interim results of the ADAPT-PD trial which suggest better control of Parkinsonian symptoms through a biological, homeostatic, feedback mechanism[2], and the pivotal trials of spinal cord stimulation which uses a similar mechanism to combat chronic leg pain with therapeutic stimulation[3].

Conclusions: The goal of this work is to highlight the core principles and best practices of PCLC as applied to neurostimulation. Ultimately, we will provide a practical checklist for researchers to use when developing PCLC systems which follow the recently released guidance from the FDA for use in medical devices[4].

Supplemental Data:

References: 1. Mendez, Juan Albino, et al. "Improving the anesthetic process by a fuzzy rule based medical decision system." Artificial intelligence in medicine 84 (2018): 159-170. 2. Herrington, Todd, et al. “Enrollment phase sensing data from the Adaptive DBS Algorithm for Personalized Therapy in Parkinson’s Disease (ADAPT-PD) clinical trial.” International Congress of Movement Disorders (2023) 3. Mekhail N, Levy RM, Deer TR, et al. Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial.

Lancet Neurol. 2020;19(2):123-134. 4. “Technical Considerations for Medical Devices with Physiologic Closed-Loop Control Technology.” FDA Guidance Document Docket Number FDA-2021-D-0996 (2023)

Acknowledgements:

Learning Objectives: 1. Learners will be able to identify approproate target biomarkers for inputs into physiological closed-loop controllers. 2. Learners will be able to design systems that test for and mitigate risk in implementation of PCLCs. 3. Learners will be able to design and follow a checklist to remain compliant (with the regulatory body for medical devices in the country in which they conduct research) while working with PCLCs.

Financial Disclosures: Dr. Lawrence Poree is a Consultant for Medtronic, and he receives stock options and consulting fees from both Nalu and Saluda. Professor Tim Denison is a consultant for Cortec and director of Amber Tx Ltd, which manufacturers closed loop devices.

Disclosure: No significant relationships.

195

Poster on Board
POSTER ON BOARD: AS02. NEUROPROSTHETICS / NEURAL ENGINEERING / BRAIN COMPUTER INTERFACE / ARTIFICIAL INTELLIGENCE
13-05-2024 08:00 - 19:00

SIMPLIFYING CLOSED-LOOP BRAIN STIMULATION - AN OPEN-SOURCE APPROACH

Niels Peekhaus, MSc, Annalisa Colucci, MSc, Mareike Vermehren, MSc, David Haslacher, MSc, Surjo Soekadar, MD
Charité - Universitätsmedizin Berlin, Berlin, Germany

Introduction: Transcranial electrical or magnetic brain stimulation is widely used in neuroscience and clinical applications, but stimulation effects are variable and not fully understood. Typically, stimulation is applied in an open-loop fashion, i.e., irrespective of the ongoing brain activity or brain states. Such brain activity-informed (closed-loop) paradigm would be very desirable, however, to reduce variability and to improve effect sizes or treatment efficacy. First closed-loop stimulation setups were introduced but rely on expensive real-time computers and other hardware with limited accessibility. Here, we developed and implemented a closed-loop brain stimulation system that is based entirely on open-source software and runs on ordinary computers substantially increasing accessibility.

Materials / Methods: The developed setup consists of an electroencephalography (EEG) amplifier for data acquisition, a from-the-shelf computer performing the online data-analysis, a digital-to-analog (DA)-converter generating the stimulation waveform, and a brain stimulator applying an electric current. As these are all well accessible components, they are not optimized towards real-time applications and thus each component introduces considerable delays and jitter into the signal chain, which is not compatible with a millisecond-precise closed-loop brain stimulation design. We addressed this issue by estimating the delay of the system in real-time and by employing a short-term prediction of brain signals targeted by the stimulation. The prediction adjusts the stimulation waveform to the expected brain signal, compensating for the inaccuracies of the hardware and preserving millisecond-precise timing of the stimulation. The proposed setup was validated in technical tests as well as during application of median nerve stimulation linked to alpha oscillations recorded via EEG. We evaluated the total amount of delay present in the system, as well as the phase difference between the targeted brain oscillation and applied stimulation waveform that reflects the accuracy of the stimulation setup.

Results: The signal acquisition and processing introduced a delay of 14.6±3.8 ms. By applying delay-and-jitter compensation we linked the stimulation waveform to the alpha oscillations with an average phase error of 21.7±9.5°.

Discussion: The proposed system performed stable, and accuracy was comparable to a state-of-the-art real-time computer-based setups achieving 19.3±7.8° of phase error in average.

Conclusions: Establishing closed-looped neuromodulation experiments using low-cost, accessible hardware and open-source software is feasible. Increasing accessibility of such paradigm will foster adoption and development of novel applications for closed-loop brain stimulation.

Supplemental Data:

References:

Acknowledgements: This study was supported by the European Research Council (ERC) under the project NGBMI (759370), the Federal Ministry of Research and Education (BMBF) under the projects SSMART (01DR21025A), QHMI (03ZU1110DD) and NeuroQ (13N16486), as well as the Einstein Foundation Berlin (A-2019-558).

Learning Objectives: I would like to... 1. present my work publicly and receive feedback, hear about experiences, and receive criticism about the way I address challenges and intend to continue my research. 2. get in contact with more people who are facing similar challenges as I do and who are interested in continued exchange and collaboration. 3. learn about other peoples work and their strategies to deal with the many pitfalls that exist when working wihth neuromodulation. Ideally, I would get a lot of input and feel more confident about the work I do and the results I find.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

196

Poster on Board
POSTER ON BOARD: AS02. NEUROPROSTHETICS / NEURAL ENGINEERING / BRAIN COMPUTER INTERFACE / ARTIFICIAL INTELLIGENCE
13-05-2024 08:00 - 19:00

PHASE-LOCKED NONINVASIVE BRAIN STIMULATION: A USER FEASIBILITY STUDY

Nicolo Rossetti, MSc[1], Roberto Garcia Van Der Westen, MSc[1], John Morales Tellez, PhD[1], Vojkan Mihajlovic, PhD[2]
[1]IMEC, Eindhoven, Netherlands, [2]IMEC, Autonomous Therapeutics, Eindhoven, Netherlands

Introduction: Close loop brain stimulation holds the potential to enhance the effects of transcranial brain stimulation (tCS) by synchronizing the timing of the stimulation with respect to the underlying brain activity. This can be achieved by precise phase-locking of alternate current stimulation (tACS) and its variants such as interferential stimulation (tIS) to adapt brain waves with higher temporal and spatial precision. Phase-locked tACS requires precise control of the timing of stimulation and accurate computation of the phase lag between the stimulation and brain signals, with current state-of the-art approaches being affected by large accuracy and precision errors, calling for new closed loop solutions.

Materials / Methods: In our previous work, we have demonstrated an in-silico setup to characterize the accuracy of our new phase-locked tACS framework. It consists of signal generators and NeuroConn DC Stimulator Plus™ (Neurocare group, Munich, Germany) for tACS, IMEC's Mood 8™ EEG headset (IMEC, Leuven, Belgium) for signal recording, and a phantom head for positioning of the recording/stimulation electrodes. However, when translating this framework to in vivo settings, several challenges had to be overcome. The most obvious example is the positioning of the control and simulation signal electrodes with respect to the recording sites, which required dedicated optimization runs.

We have evolved and deployed the proposed phase-locked tCS framework on a poll of three healthy volunteers to test the performance in a real-case scenario. Furthermore, we have expanded the framework to also support phase-locked tIS, which allows operation without the external control signal but still achieving precise stimulus timing. Towards adhering to ethical requirements, Mood 8 EEG headset is replaced by Micromed Brain Quick™ EEG system (Micromed Group, Mogliano Veneto, Treviso, Italy) in the setup for recording brain activity.

Results: The complete close loop setup has been demonstrated and successfully applied on a total number of three subjects. The setup was continuously improved based on the preliminary results from the first subjects, and in its final version indicated reliable performance in terms of phase estimation errors of only $0.33 \pm 0.38^{\circ}$ for tACS and $2.84^{\circ} \pm 3.25^{\circ}$ for tIS, which is superior to state-of-the-art closed-loop solutions.

Discussion: The results demonstrate the feasibility of precise phase-locked non-invasive stimulation in humans and paves the way for future deployment of the technology to target specific applications in the field of neurostimulation.

Conclusions: We have demonstrated a novel method and setup for phase-locked brain stimulation achieving superior phase estimation errors in user trials.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1. Demonstrate superior phase-locking method in user trials: method developed and improved in user trials. 2. Develop a framework / setup for closed-loop brain stimulation: setup developed and deployed in user trials. 3. Introduce novel algorithm for real-time EEG phase estimation: medhod based on wavelets introduced.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

197

Poster on Board
POSTER ON BOARD: AS03. SOCIOECONOMICS OF NEUROMODULATION
13-05-2024 08:00 - 19:00

REAL- WORLD DATA COLLECTION USING REMOTE PROGRAMMING FOR DRG AND SCS PATIENTS

Andrea Dreyer, RN, Phyllis McPhillips, RN, Guilherme Santos Piedade, MD, Zarela Krause Molle, MD, Phillipp Slotty, MD, Jan Vesper, MD
University Medical Center, Heinrich Heine University, Functional Neurosurgery And Stereotaxy, Duesseldorf, Germany

Introduction: Spinal cord and dorsal root ganglion stimulation (SCS and DRG-S) are standard of care for patients with chronic neuropathic pain. Travel times, lack of financial resources and transportation options strongly influence the individual's decision on seeking healthcare. Telehealth in general refers to the exchange of medical information through electronic communication. However, it is usually restricted to video conferences, without interfering with implanted medical devices. A digital platform was recently introduced to enable remote programming in Neuromodulation. It is accessible via tablets/smartphones and allows direct contact between a patient and their doctor/pain nurse.

Materials / Methods: We designed a prospective cohort to evaluate safety and performance of remote care in patients with SCS or DRG-S. Between January and October 2023, 28 patients were included. We assess up pain scores (VAS), EQ5D, pain Detect, Patient Global Impression of Care (PGIC) and telehealth usability questionnaire (TUQ) to evaluate the preoperative status, the status at implantation of the system, and the postoperative course. The postoperative data are assessed in the context of video conferences for remote programming.

Results: This is an ongoing study. No travel or waiting time was assessed, since all patients received their appointment right in time at their home. The overall satisfaction with the telehealth system is high. TUQ 7/7 in all pats., mean PGIC 5 (4-6), mean VAS baseline/6mo (9/3). No lack of efficacy of stimulation or pain relief was found. In two out of the SCS patients, a mechanical problem was suspected, which led to an additional on-site visit, which was solved. Two patients reported technical difficulties dialing in due to limited abilities with smart devices.

Discussion: The general convenience with the system is high, which is conform to previously published data regarding telehealth in general. Witek et al. reported no statistical difference between virtual and in-person assessments and Powers et al showed that wearables can be used for an objective quantification of symptoms without the need for clinic facility time.

Conclusions: The general convenience with the system is high, which is conform to previously published data regarding telehealth in general. Witek et al. reported no statistical difference between virtual and in-person assessments and Powers et al showed that wearables can be used for an objective quantification of symptoms without the need for clinic facility time.

Supplemental Data:

References: Witek, Natalie, et al. "Remote telemedicine evaluation of deep brain stimulation candidacy: retrospective cohort analysis." Neurology: Clinical Practice 10.3 (2020): 199-205. Powers, Rob, et al. "Smartwatch inertial sensors continuously monitor real-world motor fluctuations in Parkinson's disease." Science translational medicine 13.579 (2021): eabd7865.

Acknowledgements: The previous study was supported by an ABBOTT grant. The current real world survey has not been supported by third parties.

Learning Objectives: value of telehealth during pandemics remote programming is safe and feasable

Financial Disclosures: JV, PS received research grants, JV serves as a consultant of ABBOTT, JV, AD, PMP, ZKM received travel grants from ABBOTT

Disclosure: No significant relationships.

198

Poster on Board
POSTER ON BOARD: AS03. SOCIOECONOMICS OF NEUROMODULATION
13-05-2024 08:00 - 19:00

THE EXPECTED AND UNEXPECTED VALUE OF INTEGRATING REMOTE PROGRAMMING INTO A NEUROMODULATION TREATMENT PATHWAY – A MODELLING OF PATIENT, HOSPITAL AND ENVIRONMENTAL COSTS

Naoufel Ouerchefani, MD[1], Johan Leguilloux, MD[2], Abdelssalem Chaar, MD[3], Riadh Ouerchefani, PhD[4]
[1]Foch Hospital, PARIS, France, [2]hôpital privé nord parisien, paris, France, [3]hopital privé evry, paris, France, [4]univ Angers, universite de Nantes, LPPL,SFR confluences, Angers, France

Introduction: In clinical practice, traditional neuromodulation therapy pathways have been proven to be effective. They cover the following phases: preoperative selection, perioperative trial and implant, followed by follow-up after surgery. Since the COVID pandemic, the acceptance of digital health technologies in healthcare has grown rapidly and they are considered to be a safer technique[1]. This study compared, using a survey, the traditional post-operative follow-up path with a new pathway integrating remote consultation, to determine all the benefits of this approach in patients and healthcare institutions for environment and cost.

Materials / Methods: Thirty patients who underwent either Spinal Cord Stimulation or Dorsal Root Ganglion Stimulation and were subject to face-to-face in-person follow-up, as well as thirty other patients who with remote programming follow-up, filled out the proposed survey. They were compared across 5 different domains (travel mode and distance; time; costs, experience of In-clinic appointments, experience with remote consultation) . A Cost Modelling Tool will be used to verify the expected efficiency gains based on the defined follow-up pathways with and without remote consultations and data taken from the patient survey. Modelling assumptions will be made by comparing the base case (in-clinic follow-up) with three scenarios: percentage of patients currently accessing remote programming and consultations, a target percentage, and a hypothetical scenario with 100% of patients using remote programming follow-up.

Results: Our results showed efficiency gains for our clinic including savings in time, cost and carbon footprint for patients followed-up remotely compared to patients exclusively followed-up in-clinic.

Discussion: Besides the gains justified by this remote technique, some other unexpected benefits of integrating remote programming into our neuromodulation treatment pathway could be highlighted a posteriori. However, we believe our results will not be dissimilar to those of other healthcare institutions that integrate this technology into their follow-up pathway for managing neuromodulated patients. Verified efficiency gains are likely to look different depending on geography, socioeconomic status, and societal differences.

Conclusions: Remote programming has the potential to add value compared with traditional neuromodulation therapy pathways by generating gains for both the healthcare institution and the patient.

Supplemental Data:

References: Pathak, YJ, et al. (2021). Digital Health Integration with Neuromodulation Therapies: The Future of Patient-Centric Innovation in Neuromodulation. Frontiers in Digital Health. 3, 1-14. doi: 10.3389/fdgth.2021

Acknowledgements: personal financial support

Learning Objectives: - improve patient care and the follow up of stimulated patient - facilitate the access to the spinal cord stimulation especially for patients who live far from hospitals - reduce medical costs

Financial Disclosures: I am a consultatnt for boston scientific, abott and medtronic

Disclosure: No significant relationships.

199

Poster on Board
POSTER ON BOARD: AS03. SOCIOECONOMICS OF NEUROMODULATION
13-05-2024 08:00 - 19:00

DORSAL SPINAL CORD STIMULATION VS MEDICAL MANAGEMENT FOR THE TREATMENT OF LOW BACK PAIN (DISTINCT)- A HEALTHCARE COST ANALYSIS.

Robert Heros, MD[1], James Yue, MD[2], Edward Tavel, MD[2], Sayed Wahezi, MD[3], Robert Funk, MD[2], Patrick Buchanan, MD[2], Jacqueline Weisbein, MD[2], Anne Christopher, MD[4], Christopher Gilligan, MD[5], Denis Patterson, DO[6], Ajay Antony, MD[2], Mohab Ibrahim, MD[2], Nathan Miller, MD[2], Keith Scarfo, MD[2], Michael Fishell, MD[2], Steven Falowski, MD[7], Derron Wilson, MD[2], Scott Kreiner, MD[2], Chi Lim, MD[2], Edward Braun, PhD[2], Jessica Jameson, MD[2], Robert Levy, PhD[8], David Dickerson, MD[9], Susan Moeschler, MD[10], Udoka Okaro, PhD[11], Mehul Desai, MD[2], Julie Pilitsis, MD, PhD[12], Thadcha Panchalingam, PhD[2], Scott Goates, PhD[2], Alex Benison, PhD[2], Timothy Deer, MD[13]
[1]Spinal Diagnostics, Oregon, United States of America, [2]TBA, Tba, TBA, United States of America, [3]Montefiore Multidisciplinary Pain Program, Pain Management, Bronx, United States of America, [4]St. Louis Pain Consultants, Pain, Chesterfield, United States of America, [5]Brigham and Women's Hospital Harvard Medical School, Division Of Pain Medicine, Boston, United States of America, [6]Nevada Advanced Pain Specialists, Pain, Denver, United States of America, [7]Neurosurgical Associates of Lancaster, Neurosurgical Associates Of Lancaster, Lancaster, United States of America, [8]Anesthesia Pain Care Consultants, Anesthesia Pain Care Consultants, Tamarac, United States of America, [9]NorthShore University Health System, Department Of Anesthesiology, Critical Care And Pain Medicine, Evanston, United States of America, [10]Mayo Clinic, Department Of Anesthesiology, Rochester, United States of America, [11]St Jude Medical, Neuromodulation, Austin, United States of America, [12]Florida Atlantic University, NY, United States of America, [13]The Spine and Nerve Center of the Americas, Pain, Charleston, United States of America

Introduction: Chronic low back pain is highly prevalent. While those with an identified anatomic pain source may benefit from back surgery, many patients without a surgically correctable pathology suffer due to limited effective treatment options. Non-surgical alternatives, such as physiotherapy, oral analgesics, and imaging-guided injections provide temporary relief. The DISTINCT (NCT04479787) study demonstrated superior outcomes in pain relief, function, and other symptoms with passive recharge burst Spinal Code Stimulation (SCS) compared to conventional medical management (CMM) in the treatment of persistent back pain in this patient group. The objective is to compare the healthcare utilization (HCU) and associated costs for SCS and CMM cohorts to a matched real-world cohort of similar chronic low back pain patients without surgical options.

Materials / Methods: DISTINCT is a prospective, multi-center, randomized, clinical study. An independent board-certified spine surgeon reviewed and confirmed a lack of appropriate corrective surgical options. Low back pain intensity (NRS), back pain-related disability (ODI), pain catastrophizing (PCS), PROMIS-29 and patient global impression of change (PGIC) are assessed. Responders are defined; 50% reduction on NRS, 13-point decrease on ODI, 40% decrease on PCS or a definite or considerable improvement in a subject's painful condition on PGIC. The real-world cohort selection from a payer claims database closely follows the DISTINCT study criteria and matches the control-arm of the primary analysis cohort based on baseline patient characteristics, pain diagnosis, and the number of years of pain. For the matched patients, HCU data is collected for opioid medication, anti-convulsants and other analgesics, injections, RF ablations, physical therapy, office visits, imaging, and other therapies. HCU is quantified by the proportion of patients who use each therapy or pain medication and the associated average cost per patient in the 6M follow-up. Both the HCU and average/patient costs from the

Results: To follow later

Discussion: To follow later

Conclusions: To follow later

Supplemental Data:

References:

Acknowledgements: This study is funded by Abbott

Learning Objectives: To follow later

Financial Disclosures: Okaro, Padgaliam, Goates, and Benison are employees of Abbott All other authors participated in the study

Disclosure: No significant relationships.

200

Poster on Board
POSTER ON BOARD: AS03. SOCIOECONOMICS OF NEUROMODULATION
13-05-2024 08:00 - 19:00

UTILIZATION STATUS AND EQUITY OF DEEP BRAIN STIMULATION FOR PARKINSON'S DISEASE: A LARGE-SCALE MULTICENTER CROSS-SECTIONAL SURVEY

Shu Wang, MD, Fangang Meng, MD, PhD, Jianguo Zhang, MD
Beijing Tiantan Hospital, Capital Medical University, Department Of Neurosurgery, Beijing, China

Introduction: To examine regional utilization, equity, and influential factors of deep brain stimulation (DBS), an emerging effective therapy, for Parkinson's disease (PD).

Materials / Methods: We conducted a large-scale multicenter cross-sectional study using a national census of 74 Chinese centers. We investigated the national DBS population and centers for PD from 1997 to 2021, and explored the regional sociodemographic characteristics, surgical population, related resources, and insurance policies in 2020.

Results: Totally, 38,122 PD patients from 349 centers received DBS by 2021, accounting for 1.118% (1.108-1.129) of patients and 0.954% (0.933-0.976) of centers. The annual surgical population and coverage showed significant upward trends with rapid growth rates, while the annual surgical center and coverage had two peaks in 2002-2006 and 2010-2018, associated with clinical approvals and new technologies. We projected that 103,070 (51,165-154,975) PD patients [2.088% (1.351-2.825) coverage] and 603 (72-1,134) centers [1.356% (1.126-1.586) coverage] would undergo DBS by 2030. Eastern and central provinces had better economic status, more surgical patients, higher insurance affordability, and more related resources than western and northeastern provinces. Higher GDP per capita (β=5.041, 3.324-6.758 and β=0.008, 0.004-0.012; all $P<0.001$) and more functional neurosurgery doctors (β=3.596, 0.353-6.839; $P=0.031$ and β=0.010, 0.002-0.017; $P=0.013$) positively influenced surgical population and coverage, while higher insurance level (β=128.888, 64.702-193.075; $P<0.001$) positively influenced surgical coverage.

Discussion: Although surgical populations, centers, and DBS coverage for PD have rapidly improved and are predicted to have a future increase, DBS coverage is still insufficient to cover potential eligible patients. Chinese regions faced major challenges such as regional imbalances, which should be given greater attention to promote universal health coverage equity and realize coordinated regional development. To increase the number of beneficiaries and coverage of DBS, adjustments should be made to the equity of economic development, DBS-related resources, and insurance policies.

Conclusions: Despite the rapid improvement and expected increase of surgical population, centers, and coverage of DBS for PD, they are still insufficient to meet the potential demand of eligible patients. Regional health disparities should be addressed to promote coordinated development.

Supplemental Data:

Learning Objectives: 1) This is the first multicenter study around the world to evaluate the utilization, surgical coverages and regional balance of DBS for PD involving 74 Chinese centers from 1997-2021. 2) From the first DBS surgery in 1997, surgical populations and DBS centers for PD improved rapidly, with approximately 1% coverage for all PD patients and centers by 2021, and were predicted to have a future increase to nearly 2% coverage by 2030. However, this is still insufficient to cover potential eligible patients. 3) To increase beneficiaries and coverage of DBS, adjustments should be made to the coordinated development in economic, surgical resources, and insurance policy.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

201

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

ACCURACY OF TECHNIQUES ESTIMATING PSEUDO-MONOPOLAR BETA POWER FROM BIPOLAR SUBTHALAMIC LFPS IN PARKINSON'S DISEASE PATIENTS WITH DBS

Jennifer Behnke, MD[1], Robert Peach, PhD[2], Moritz Gerster, MSc[3], Johannes Busch, MD[1], Jonathan Kaplan, MD[1], Gerd-Helge Schneider, MD[4], Katharina Faust, MD[4], Andrea Kuehn, MD[1]
[1]Charité University Medicine, Movement Disorders And Neuromodulation Unit, Berlin, Germany, [2]University Hospital Würzburg, Department Of Neurology, Würzburg, Germany, [3]Bernstein Center for Computational Neuroscience, Berlin, Germany, [4]Charité University Medicine, Department Of Neurosurgery, Berlin, Germany

Introduction: Subthalamic (STN) beta activity (13-35 Hz) has been instrumental in contact selection for deep brain stimulation (DBS) in Parkinson's disease (PD) (1-3). Sensing-enabled DBS devices now allow for short (20 s) derivations of bipolar local field potentials (LFPs) from multiple directional contact pairs. Despite advances in using these LFPs to guide contact-selection (4, 5), precisely selecting multiple directional contacts remains challenging. Our study introduces a new technique to estimate pseudo-monopolar beta power distributed across six directional contacts and tests its accuracy against existing contact-selection strategies and externalized lead LFPs.

Materials / Methods: We recorded LFPs from 23 PD patients at-rest with STN directional leads and sensing-enabled IPGs in a therapy-off state. First, we collected two minutes of LFPs from eight channels per externalized lead with the lowermost contact as a common reference. Second, from 16 of these patients, we recorded 20 seconds of LFPs shortly after IPG implantation from 12 available bipolar channels per hemisphere. These LFPs provide beta power from in-between contacts. To estimate the periodic beta power for each directional contact, we developed a method that weights beta activity based on the Euclidean distance to the central position of each bipolar recording. The sum of all weighted LFPs resulted in a beta power estimation for a directional contact. We compared this novel method with two prior strategies (5, 6) and validated them using re-referenced externalized LFPs.

Results: Beta power distributions calculated with all three methods showed positive correlation coefficients in most hemispheres compared to their distributions from re-referenced externalized LFPs. Between all three methods highest correlation resulted between Euclidean and Strelow et al. (5) calculated beta power. Using the Euclidean method we found good agreement with at least one contact matching between two contacts with maximal calculated beta power and maximal beta power of externalized re-referenced LFPs of the same hemispheres.

Discussion: Overall, the Euclidean method showed consensus with beta power distributions from externalized LFPs. Despite all methods correlating to the externalized re-referenced LFPs to a similar degree, the selection of two maximal beta contacts can vary between the different methods.

Conclusions: We have developed a method for estimating monopolar spectral beta power at all directional contacts, enabling objective and precise contact selection using bipolar LFPs. Despite variability to calculations of other methods, this study demonstrates its accuracy in externalized LFPs. Its clinical efficacy merits future investigation.

Supplemental Data:

References: 1. Ince NF, Gupte A, Wichmann T, Ashe J, Henry T, Bebler M, et al. Selection of optimal programming contacts based on local field potential recordings from subthalamic nucleus in patients with Parkinson's disease. Neurosurgery. 2010;67(2):390-7.
2. Tinkhauser G, Pogosyan A, Debove I, Nowacki A, Shah SA, Seidel K, et al. Directional local field potentials: A tool to optimize deep brain stimulation. Mov Disord. 2018;33(1):159-64.

3. Fernandez-Garcia C, Monje MHG, Gomez-Mayordomo V, Foffani G, Herranz R, Catalan MJ, et al. Long-term directional deep brain stimulation: Monopolar review vs. local field potential guided programming. Brain Stimul. 2022;15(3):727-36.
4. Binder T, Lange F, Pozzi N, Mussacchio T, Daniels C, Odorfer T, et al. Feasibility of local field potential-guided programming for deep brain stimulation in Parkinson's disease: A comparison with clinical and neuro-imaging guided approaches in a randomized, controlled pilot trial. Brain Stimul. 2023.
5. Strelow JN, Dembek TA, Baldermann JC, Andrade P, Jergas H, Visser-Vandewalle V, Barbe MT. Local Field Potential-Guided Contact Selection Using Chronically Implanted Sensing Devices for Deep Brain Stimulation in Parkinson's Disease. Brain Sci. 2022;12(12).
6. Busch JL, Kaplan J, Bahners BH, Roediger J, Faust K, Schneider GH, et al. Local Field Potentials Predict Motor Performance in Deep Brain Stimulation for Parkinson's Disease. Mov Disord. 2023.

Acknowledgements: This study was funded by the Deutsche Forschungsgemeinschaft (German Research Foundation) Project-ID 424778381 TRR 295.

Learning Objectives: 1. To understand the significance and challenge of utilizing chronically derived LFPs for precise directional contact selection in DBS Sensing-enabled DBS devices and directional leads provide us with chronically available LFPs useful for guiding contact selection after IPG implantation. However, challenges of utilizing these LFPs for contact selection include pre-defined bipolar recording montages, which provide oscillatory information from locations between contacts and not directly from individual contacts. 2. To introduce a method for calculating beta power at individual directional contacts post-IPG implantation Listeners will discover that our method utilizes all 9 segmental bipolar LFPs per lead to calculate an estimate for beta power at a single directional contact, which might result in a more precise estimation of monopolar beta power compared to existing techniques. 3. To verify the presented method as a beta-guided contact selection tool through comparisons with other approaches using post-IPG LFPs and externalized LFPs The comparison of the new method to prior methods using post-IPG LFPs should elaborate similarities and differences between the methods and assess the usability of the new method for future automatized contact selection algorithms. The comparison to the externalized LFPs should verify all methods using post-IPG LFPs. We will assess differences between the externalized and post-IPG recordings, that need to be considered.

Financial Disclosures: Andrea A. Kühn: a) Medtronic, b) Advisory Board, honoraria, c) 5,000 - 20,000 USD a) Boston Scientific, b) honoraria, c) 5,000 USD All other authors declare no significant relationships.

Disclosure: No significant relationships.

202

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

ASSESSING OUTCOME MEASURES OF DEEP BRAIN STIMULATION IN TREMOR WITH A WEARABLE SENSOR

Philipp Capetian, MD, Franziska Gross, MD, Nicolo Pozzi, MD, Jens Volkmann, MD
University Hospital of Wuerzburg, Dept. Of Neurology, Würzburg, Germany

Introduction: Assessing the outcomes of Deep Brain Stimulation procedures in tremor syndromes poses a notable challenge, primarily due to the fluctuating nature of tremor severity throughout the day, which is influenced by daily activities. To enhance the accuracy and comprehensiveness of this assessment, the integration of wearable sensors capable of measuring tremor severity over extended periods might be advantageous.

Materials / Methods: Eight patients afflicted with tremor syndromes, including essential tremor and Parkinson's disease, underwent Deep Brain Stimulation (DBS) procedures. The assessment was conducted both before and after the operation, employing the "Quality of Life in Essential Tremor Questionnaire" (QUEST). Tremor severity was evaluated using two distinct methods: firstly, through a brief 30-second measurement using a gyroscopic sensor, and secondly, through an extended 8-hour measurement facilitated by a wearable patient sensor, both of which were provided by EvokAI Inc. The analysis encompassed the reduction in tremor severity, gauged by a proprietary movement disorder index (MDI), the augmentation in quality of life, and an exploration of the correlation between the alterations in quality of life and tremor severity.

Results: A noticeable trend towards reduced tremor severity was observed post-operation, while there were no significant changes in the quality of life scale. We were unable to identify any correlation between the two assessment tools or establish a clear link with changes in quality of life.

Discussion: The limited number of patients, each presenting with two distinct tremor syndromes and targeted brain regions (VIM and subthalamic nucleus), introduced a notable level of heterogeneity. This diversity may have hindered our ability to detect subtle changes effectively. Furthermore, the intermittent nature of measurements conducted with the wearable sensor might have caused us to miss specific time intervals in patients who did not exhibit continuous tremor activity.

Conclusions: Wearable sensors have the potential to capture tremor severity throughout the daily lives of patients. To establish the true significance of the data collected in relation to patient satisfaction, larger and more uniform patient groups will be required.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: Explore the application of wearable tremor measurement devices in DBS patients. Investigate the specific challenges associated with capturing tremor severity and establishing its correlation with patient satisfaction. Offer an opinion on whether wearables, at this juncture, can serve as a viable means of evaluating tremor severity.

Financial Disclosures: PC received travel funds and consultant fees of EvokAI.

Disclosure: The author of this abstract receives consulting fees from the company producing the sensors employed in this study. The study was financially sponsored by the company. No direct influence on the results were taken by the company.

203

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

CONNECTIVITY CORRELATES OF TREATMENT RESPONSE IN PEDUNCULOPONTINE NUCLEUS DEEP BRAIN STIMULATION FOR MULTIPLE SYSTEM ATROPHY

Amir Divanbeighi Zand, BA BM BCh[1], Sean Martin, FRCS(SN)[1], John Eraifej, MB ChB[2], Alceste Deli, MD, MSc, DPhil[1,3], Nagaraja Sarangmat, MD[4], Marko Bogdanovic, PhD[5], Michele Hu, PhD[5], Tipu Aziz, FMedSci[1], Tim Denison, PhD[5,6], James Fitzgerald, MB ChB, PhD[1], Alexander Green, PhD FRCS(SN)[1]
[1]University of Oxford, Nuffield Department Of Surgical Sciences, Oxford, United Kingdom, [2]University of Oxford, Nuffield Department Of Clinical Neurosciences, Oxford, United Kingdom, [3]University of Oxford, Sir Jules Thorn Sleep And Circadian Neuroscience Institute, QU, United Kingdom, [4]Oxford University Hospitals, Neurology, Oxford, United Kingdom, [5]University of Oxford, Nuffield Deparment Of Clinical Neurosciences, Oxford, United Kingdom, [6]Oxford University, Institute Of Biomedical Engineering, Oxford, United Kingdom

Introduction: The pedunculopontine nucleus (PPN) is a deep brain stimulation (DBS) target for axial motor deficits in Parkinson's disease and under investigation for other disorders (1). Anatomically, the PPN region is reciprocally connected to basal ganglia and motor cortical areas, and receives projections from deep cerebellar nuclei (2). The PPN could therefore be a point of interaction between these components of the motor network, which may be modulated by DBS. Additionally, connections with limbic and hypothalamic areas are strongly involved in the descending modulation of autonomic activity (3), raising the possibility of autonomic neuromodulation with DBS of this region. We have presented results of a first-in-man, five-patient trial (abstract #591) showing PPN DBS can improve gait and autonomic symtpoms in multiple system atrophy (MSA), a progressive neurodegenerative condition characterised by parkinsonism, ataxia, and prominent autonomic dysfunction. A follow-on study is currently recruiting (Motion Adaptive Deep Brain Stimulation for MSA, NCT05197816). Here, we investigate the optimal functional connectivity profiles of treatment efficacy across multiple autonomic and motor symptom domains in the seven patients implanted to date.

Materials / Methods: Participants (n = 7) underwent PPN DBS for MSA as part of two clinical trials. LEAD-DBS v3.0 (4) was used to reconstruct DBS Electrodes and resulting volumes of activated tissue (VATs). Resting state fMRI data from 1000 healthy participants (5) was utilised in the DBS network mapping method. The resulting functional DBS networks were correlated with changes in in motor and autonomic questionnaires, as well as physiologic autonomic and motor testing, at follow-up (6 months) compared to baseline. Patient-level correlations of connectivity profile with response were combined in a group-level analysis to identify networks associated with symptomatic improvement. Permutation tests and cross-validation were then used to estimate the validity of these networks.

Results: Full results to follow (late-breaking). Figure 1 (below) shows electrode localisation for all participants in MNI 2009b
space:

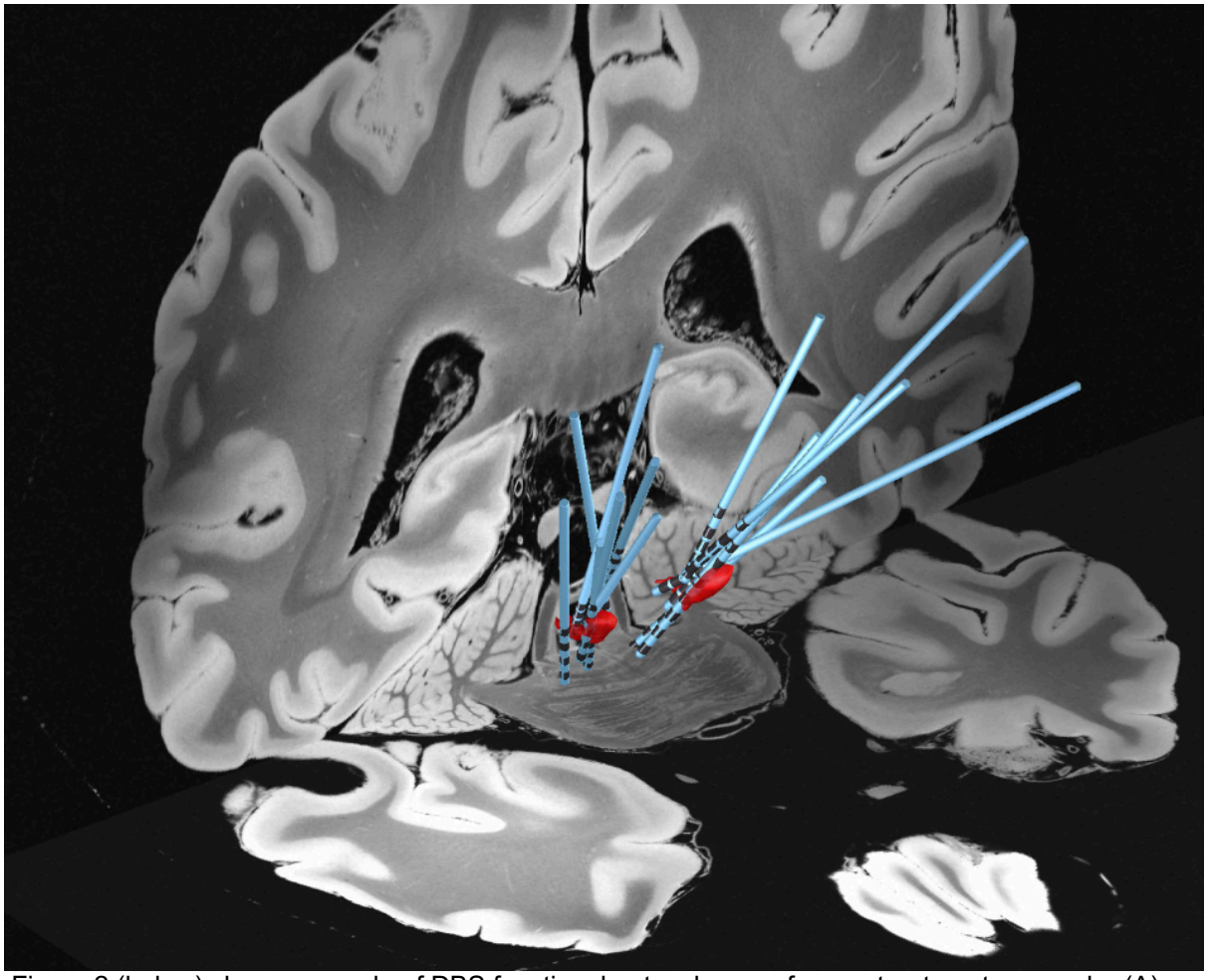
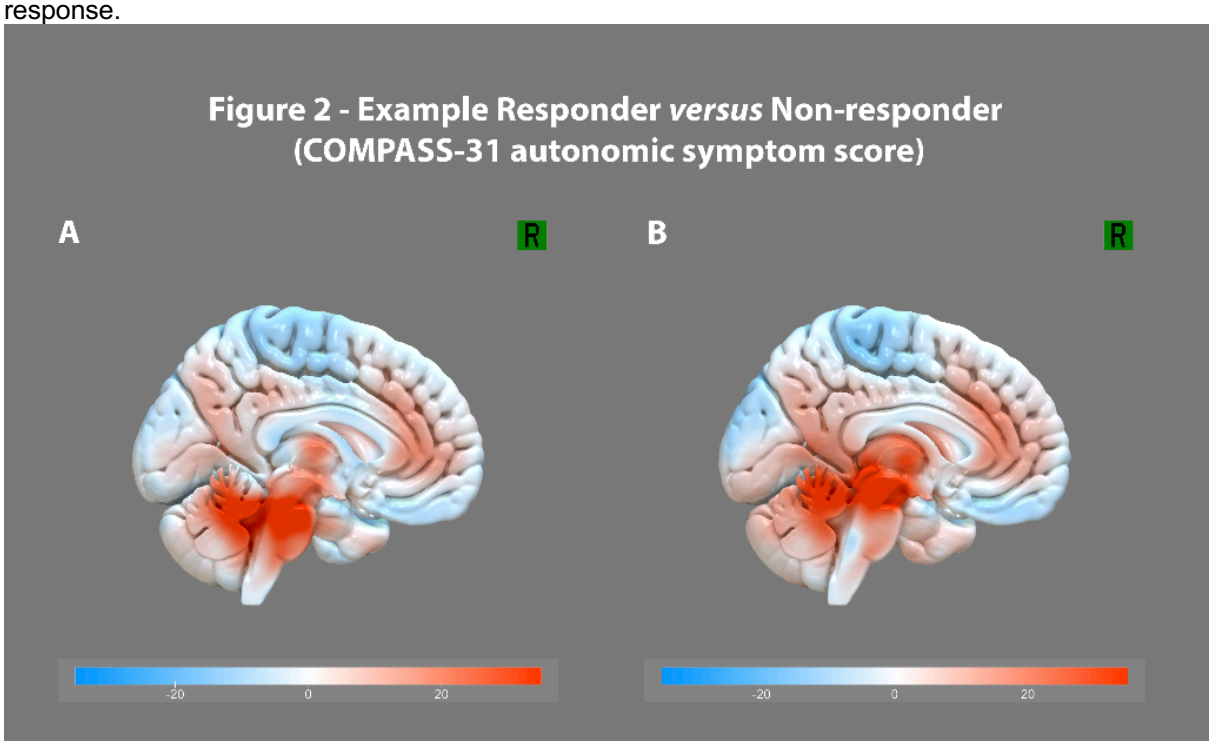


Figure 2 (below) shows example of DBS functional network maps for one treatment responder (A) and one non-responder (B) in the COMPASS-31 autonomic symptom score, showing distinct connectivity profiles. Red-coloured brain regions indicate a positive correlation with the patient's volume of activated tissue (VAT), and vice-versa for blue, with intensity representing the strength of correlation (t-stat maps are presented, with corresponding numeric values in the scale bar below). The study will use the entire dataset to investigate networks associated with treatment

response.



Discussion: To follow (late-breaking)

Conclusions: To follow (late-breaking)

Supplemental Data: To follow (late-breaking)

References: 1. Thevathasan W, Debu B, Aziz T, Bloem BR, Blahak C, Butson C, Czernecki V, Foltynie T, Fraix V, Grabli D, Joint C, Lozano AM, Okun MS, Ostrem J, Pavese N, Schrader C, Tai CH, Krauss JK, Moro E; Movement Disorders Society PPN DBS Working Groupin collaboration with the World Society for Stereotactic and Functional Neurosurgery. Pedunculopontine nucleus deep brain stimulation in Parkinson's disease: A clinical review. Mov Disord. 2018 Jan;33(1):10-20. doi: 10.1002/mds.27098. Epub 2017 Sep 28. PMID: 28960543. 2. Thevathasan W, Moro E. What is the therapeutic mechanism of pedunculopontine nucleus stimulation in Parkinson's disease? Neurobiol Dis. 2019 Aug;128:67-74. doi: 10.1016/j.nbd.2018.06.014. Epub 2018 Jun 19. PMID: 29933055. 3. Jenkinson N, Nandi D, Muthusamy K, Ray NJ, Gregory R, Stein JF, Aziz TZ. Anatomy, physiology, and pathophysiology of the pedunculopontine nucleus. Mov Disord. 2009 Feb 15;24(3):319-28. doi: 10.1002/mds.22189. PMID: 19097193. 4. Neudorfer C, Butenko K, Oxenford S, Rajamani N, Achtzehn J, Goede L, Hollunder B, Ríos AS, Hart L, Tasserie J, Fernando KB, Nguyen TAK, Al-Fatly B, Vissani M, Fox M, Richardson RM, van Rienen U, Kühn AA, Husch AD, Opri E, Dembek T, Li N, Horn A. Lead-DBS v3.0: Mapping deep brain stimulation effects to local anatomy and global networks. Neuroimage. 2023 Mar;268:119862. doi: 10.1016/j.neuroimage.2023.119862. Epub 2023 Jan 5. PMID: 36610682; PMCID: PMC10144063. 5. Yeo BT, Krienen FM, Sepulcre J, Sabuncu MR, Lashkari D, Hollinshead M, Roffman JL, Smoller JW, Zöllei L, Polimeni JR, Fischl B, Liu H, Buckner RL. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiol. 2011 Sep;106(3):1125-65. doi: 10.1152/jn.00338.2011. Epub 2011 Jun 8. PMID: 21653723; PMCID: PMC3174820.

Acknowledgements:

Learning Objectives: (Late-breaking - results, discussion and conclusions to follow. This may alter the below objectives, however it is likey they will remain similar) 1. Motor and autonomic effects of PPN DBS in MSA depend on distinct distributed networks of brain regions 2. Connectivity to these networks may be used to predict outcomes of PPN DBS 3. These findings provide further insight into the mechanisms of PPN DBS, which is the subject of active study

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

204

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

TREMOR REDUCTION USING DBS: OUTCOMES OF A REAL-WORLD, PROSPECTIVE, MULTICENTER ESSENTIAL TREMOR REGISTRY

Günther Deuschl, MD[1], Griet Loret, MD[2], Norbert Kovacs, MD[3], Marta Blazquez-Estrada, MD[4], Frederik Clement, MD[5], Jung-Il Lee, MD[6], Pr Schuurman, MD[7], Lilly Chen, MD[8], Rajat Shivacharan, PhD[8], Edward Goldberg, MD[8]
[1]University Hospital Schleswig-Holstein, Neurology, Kiel, Germany, [2]AZ Sint Lucas, Neurology, Brugge, Belgium, [3]University of Pécs, Neurology, Pécs, Hungary, [4]Hospital Universitario Central de Asturias, Neurology, Oviedo, Spain, [5]AZ Delta, Neurology, Ghent, Belgium, [6]Samsung Medical Center, Sungkyunkwan University, Neurology, Seoul, Korea, Republic of, [7]Academic Medical Center (Amsterdam UMC), Neurosurgery, Amsterdam, Netherlands, [8]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: Large, multicenter patient outcome registries are an important source from which to collect real-world evidence (RWE). Ventral intermediate nucleus (Vim) Deep Brain Stimulation (DBS) is an increasingly recommended therapeutic approach in properly selected candidates to manage Essential Tremor (ET). This clinical evaluation will help provide RWE in patients implanted with a DBS system for ET. Here, we evaluate on-going registry outcomes derived from patients implanted with directional Deep Brain Stimulation systems with Multiple Independent Current Control (MICC) technology for treatment of Essential Tremor.

Materials / Methods: In this prospective, on-label, multi-center, international DBS registry, enrolled patients are implanted with a directional MICC-based DBS system (Vercise™, Boston Scientific, Marlborough, MA USA). Patients are followed up to 3-years where ET symptoms and overall improvement in quality of life are evaluated. Clinical endpoints evaluated at baseline and during study follow-up timepoints include Fahn-Tolosa-Marin Rating Scale (FTMTRS), the Essential Tremor Rating Assessment Scale (TETRAS), Quality of Life in Essential Tremor Questionnaire (QUEST), and Global Impression of change. Adverse events are also being collected.

Results: from this ongoing, prospective, multicenter, international outcomes study demonstrate significant improvement in ET related symptoms and quality of life up to 12-month follow-up. A total of 50 subjects (27 males, mean age= 65.3 years, mean disease duration = 19.5 years) received DBS. At the 12-month follow-up, a mean 8.9-hours reduction in tremor was noted (self-reported, QUEST) in a typical day. Additionally, regarding tremor severity, no subject reported marked disability while 82.6% reported mild disability (FTMTRS), and subjects saw a 63.7% mean-improvement in activities of daily living (TETRAS) at 12-months compared to baseline. No lead breakages/fractures were reported.

Discussion: Results from this ongoing, prospective, multicenter, international real-world outcomes study using multiple-source constant-current Directional DBS Systems for the treatment of Essential Tremor continue to demonstrate positive outcomes out to 12-months follow-up.

Conclusions: Results from this ongoing, prospective, multicenter, international real-world outcomes study using multiple-source constant-current Directional DBS Systems for the treatment of Essential Tremor continue to demonstrate positive outcomes out to 12-months follow-up.

References:

Learning Objectives: To assess registry participants with Essential Tremor according to the following: 1) Fahn-Tolosa-Marin Rating Scale (FTMTRS); the Essential Tremor Rating Assessment Scale (TETRAS), 2) Quality of Life in Essential Tremor Questionnaire (QUEST) 3) Global Impression of change

Financial Disclosures: Prof. Deuschl has a consulting agreement with Boston Scientific. a) Boston Scientiifc b) consultant c) 5-20k

Disclosure: This study is sposnored by Boston Scientific. Lilly Chen and Edward Goldberg are employees of Boston Scientific.

205

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

LOCALIZATION OF POSTERIOR SUBTHALAMIC AREA USING DENTATORUBROTHALAMIC TRACT

Hyun Ho Jung, MD, PhD
Yonsei University, Neurosurgery, Seoul, Korea, Republic of

Introduction: To analyze the precise location of the posterior subthalamic area (PSA) by using dentatorubrothalamic tract (DRTT) tractography to account for individual patient differences.

Materials / Methods: We used 31 patients' MRI who underwent Magnetic Resonance guided Focus Ultrasound (MRgFUS) thalamotomy for the treatment of essential tremor. Using BrainLab Elements (BrainLab, Munich, Germany), we depicted bilateral tractography, delineating the DRTT at the level of Red nucleus. By adjusting the region of interest (ROI) of the DRTT, we selected fibers passing through the PSA, dentate nucleus of cerebellum and thalamus, and marked their coordinates at the level of the equator of the red nucleus. To compute the coordinates for conventional targeting, we calculated the average of the X coordinate values from the anterior commissure-posterior commissure (AC-PC) line and the Y coordinate values based on the mid-commissural line. For direct targeting, we plotted the X and Y coordinates from the center of the red nucleus as a ratio of the red nucleus radius to account for interpatient variations.

Results: Using the conventional targeting method, the X coordinate was found to be 11.08±0.96 mm lateral to the anterior commissure-posterior commissure (AC-PC) line, and the Y coordinate was 7.64±1.24 mm posterior to the mid-commissural line. When considering the direct target location relative to the center of the Red nucleus, the X and Y coordinates were situated laterally at 183.70±30.70% and posteriorly at 48.99±29.68% of the Red nucleus radius, respectively.

Discussion: Though the evidence for a relation between stimulation of the DRTT and tremor improvement remained inconclusive, fewer amplitudes are needed in cases close to DRTT. The stimulation of the PSA might lead to at least equivalent or even better tremor suppression than VIM DBS. So finding the exact location of DRTT in the PSA is needed for the direct targeting paradigm.

Conclusions: The PSA is a crucial target for the treatment of patients with tremors. Through the application of DRTT tractography, it is possible to account for individual patient differences and establish a more personalized targeting strategy.

Supplemental Data:

References: 1. Barbe, M.T.; Reker, P.; Hamacher, S.; Franklin, J.; Kraus, D.; Dembek, T.A.; Becker, J.; Steffen, J.K.; Allert, N.; Wirths, J.; et al. DBS of the PSA and the VIM in essential tremor. Neurology 2018, 91, e543–e550 2. Blomstedt, P.; Sandvik, U.; Tisch, S. Deep brain stimulation in the posterior subthalamic area in the treatment of essential tremor. Mov. Disord. 2010, 25, 1350–1356.

Acknowledgements: None

Learning Objectives: 1. To localize PSA, DRTT could be used at the level of the largest Red nucleus radius 2. DRTT was located at laterally at 183.70±30.70% and posteriorly at 48.99±29.68% of the Red nucleus radius, respectively 3. DRTT at PSA could be the target for tremor control

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

206

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

RISK FACTORS FOR PERIOPERATIVE COMPLICATIONS IN MOVEMENT DISORDER DBS PATIENTS

Zarela Krause Molle, MD[1], Louisa Lobkowicz, Student[1], Phyllis McPhillips, RN[1], Andrea Dreyer, RN[1], Phillipp Slotty, MD[2,3], Guilherme Santos Piedade, MD[4], Jan Vesper, MD[1]
[1]University Medical Center, Heinrich Heine University, Functional Neurosurgery And Stereotaxy, Duesseldorf, Germany, [2]Helios Krefeld, Department Of Orthopaedics, Trauma Surgery And Hand Unit, Krefeld, Germany, [3]Heinrich-Heine University, Duesseldorf, Germany, [4]Nicklaus Children´s Hospital, Department Of Pediatric Neurosurgery, Miami, United States of America

Introduction: Deep brain stimulation (DBS) is an established and safe treatment option for selected movement disorders, such as idiopathic Parkinson's syndrome (IPS), essential tremor (ET) and dystonia. Although very rare, there are specific complications in DBS surgery. This study retrospectively investigates possible pre- and intraoperative conditions for their predictive value anticipating these complications. The investigated factors are disease duration, H/Y stage, UPDRS III score and non-disease-specific factors (age, diagnosis, secondary diseases, and duration of surgery).

Materials / Methods: Between January 2016 and October 2020, a total of 181 patients DBS were treated in our center with primary DBS implantation. Out of them, 160 were operated under general anesthesia and 21 patients underwent an awake procedure. We retrospectively reviewed patients' charts for surgical complications, such as intracranial hemorrhage, hematoma at the IPG site and infections. Neurological complications, such as postoperative delirium and mild cognitive impairment, were also included.

Results: In the postoperative cCT, a hemorrhage was seen in 5 patients (3.1%, four SAH, one ICH), all asymptomatic not requiring additional treatment. Hematoma at the IPG side occurred in 8 patients (5%), none of them requiring surgical revision. Infection and prolonged wound healing at the IPG site was found in 9 patients (5.6%) and electrode infections occurred in three patients (one intracerebral, two extracerebral (1.9%)). Neurological complications independent from stimulation were rare. Confusion was noted in 8 patients (5%), all of them following an awake procedure. Mild cognitive impairment was also seen following awake surgery only (two patients, 9.5%)

Discussion: DBS is a very effective long-term treatment in PD, dystonia and ET and complications are generally rare. However, intensified preoperative care should be considered in the presence of specific risk profiles. ICH was rare, all affected patients were asymptomatic and the hemorrhage was found in the routinely performed postoperative CT(3.1% vs. 0.2- 5.6% in the literature). IPG related impaired wound healing was rare compared to available references (5- 6.6%), as well as electrode infections (1.9 % vs. up to 12% in the literature). Confusion and de novo mild cognitive impairment were only seen in awake DBS patients, casting doubt on the usefulness of awake DBS procedures. Due to the low incidence of complications, no statistical significant association could be found with age, gender, or previous medical conditions.

Conclusions: In this retrospective review in a large cohort of patients, we failed to identify specific predictors for complications in DBS de novo surgery. Larger prospective real-world data registers are required as effect sizes are small. Standardized procedures and follow-up questionnaires might additionally be helpful.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1) Possible complications in DBS 2) Connection between surgical setting, underlying condition and complications

Financial Disclosures: Travel grants and reimbursement from Medtronic

Disclosure: No significant relationships.

207

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

ACUTE FEASIBILITY OF NOVEL STIMULATION PATTERN FOR THE TREATMENT OF PARKINSON'S DISEASE

Rene Molina, PhD[1], Dulce Maroni, PhD[2], Carolin Curtze, PhD[3], Abbey Holt-Becker, PhD[1], Erin Smith, MD[4], Katie Burcal, MSc[2], Robert Raike, PhD[1], Aviva Absoch, MD[2]
[1]Medtronic, Neuromodulation, Minneapolis, United States of America, [2]University of Nebraska Medical Center, Neurosurgery, Omaha, United States of America, [3]University of Nebraska at Omaha, Biomechanics, Omaha, United States of America, [4]University of Nebraska Medical Center, Neurological Sciences, Omaha, United States of America

Introduction: Deep brain stimulation (DBS) is a well-established treatment of Parkinson's disease (PD). Today, there is a commercially approved DBS implantable neural stimulator (INS enabled with technology that can sense brain signals during stimulation. Sensed brain signals in PD patients have identified pathological neural oscillations as potential biomarkers that can be used towards personalized and even adaptive 'closed-loop' stimulation. An alternative or even complementary approach may be to utilize biomarkers to design patient-customized non-continuous stimulation patterns. Several feasibility studies have shown promising results with various stimulation patterns[1-4], albeit without tuning to the patient's individual physiology. We hypothesize stimulation patterns designed to target patient-specific neural signals will result in more efficient and potentially superior therapy compared to standard DBS stimulation.

Materials / Methods: This was an acute feasibility study whereby stimulation patterns that switch electrodes and deliver bursts of stimulation at cycle frequencies tuned to the patient's specific beta peak were evaluated during an in-clinic setting. To deliver the patterned stimulation, a novel research system (Medtronic) was used to temporarily upload investigational firmware on previously implanted Percept™ PC systems in PD subjects with stable optimized DBS therapy settings, targeting the subthalamic nucleus (STN). Testing was conducted in the OFF PD medication state, and clinical outcomes were assessed with patterned stimulation, optimized clinical stimulation, and off stimulation in pseudorandomized order with subjects and raters blinded to the treatment condition. A final assessment was conducted in the ON medication state with clinical stimulation. Neuroimaging was used to retrospectively analyze volume of tissue activation (VTA) relative to lead placement and the sense signals. After study completion, the subjects were returned to their previous clinical stimulation settings.

Results: All patterns were successfully delivered and tolerated in all subjects without any adverse events. Stimulation patterns were assessed through motor testing using UPDRS scores, wearable inertial sensors, and sensed brain signals. Preliminary analysis reveals early differences in clinical efficacy between patterns compared to baseline ($p=0.0021$). Contact spacing (1.5 mm vs. 0.5 mm) was the primary driver of VTA results which may inform titration strategies. Further analysis into correlation with patient-specific oscillations and wearables will provide more insight.

Discussion: Practical tuning of a stimulation pattern may be accomplished with sensed brain signals. However, if further refinement is required, VTA may provide additional information.

Conclusions: Our findings fill critical evidence gaps in the feasibility and safety of delivering novel patterned stimulation. To date, results confirm that novel stimulation patterns can be tailored by patient-specific neural signals and delivered safely in PD patients.

Supplemental Data:

References: 1. De Jesus, S., Okun, M. S., Foote, K. D., Martinez-Ramirez, D., Roper, J. A., Hass, C. J., Shahgholi, L., Akbar, U., Wagle Shukla, A., Raike, R. S., & Almeida, L. (2019). Square Biphasic

Pulse Deep Brain Stimulation for Parkinson's Disease: The BiP-PD Study. *Frontiers in Human Neuroscience*, *13*. https://doi.org/10.3389/FNHUM.2019.00368 2. Adamchic, I., Hauptmann, C., Barnikol, U. B., Pawelczyk, N., Popovych, O., Barnikol, T. T., Silchenko, A., Volkmann, J., Deuschl, G., Meissner, W. G., Maarouf, M., Sturm, V., Freund, H. J., & Tass, P. A. (2014). Coordinated reset neuromodulation for Parkinson's disease: Proof-of-concept study: CR Neuromodulation of the Subthalamic Nucleus. *Movement Disorders*, *29*(13), 1679–1684. https://doi.org/10.1002/mds.25923 3. Brocker, D. T., Swan, B. D., So, R. Q., Turner, D. A., Gross, R. E., & Grill, W. M. (2017). Optimized temporal pattern of brain stimulation designed by computational evolution. *Science Translational Medicine*, *9*(371), eaah3532. https://doi.org/10.1126/scitranslmed.aah3532 4. Okun, M. S., Hickey, P. T., Machado, A. G., Kuncel, A. M., & Grill, W. M. (2022). Temporally optimized patterned stimulation (TOPS®) as a therapy to personalize deep brain stimulation treatment of Parkinson's disease. *Frontiers in Human Neuroscience*, *16*(August), 1–13. https://doi.org/10.3389/fnhum.2022.92950

Acknowledgements:

Learning Objectives: In the acute setting, patient-tailored novel stimulation patterns can - well-tolerated - provide motor symptom benefit comparable to standard clinical stimulation (baseline setting) - exhibit a side-effect profile comparable to standard clinical stimulation (baseline setting)

Financial Disclosures: Rene Molina, Medtronic, Company Employee, > $100,000 USD Dulce Maroni, No significant relationships Carolin Curtze, No significant relationships Abbey Holt-Becker, Medtronic, Company Employee, > $100,000 USD Erin Smith, No significant relationships Katie Burcal, No significant relationships Robert S. Raike, Medtronic, Company Employee, > $100,000 USD Aviva Abosch, Education/Research, > $100,000 USD

Disclosure: I am a Medtronic employee

208

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

SENSING EVOKED RESPONSE IN DEEP BRAIN STIMULATION SURGERY UNDER ANESTHESIA

Rene Molina, PhD[1], Alan Bush, PhD[2], Matteo Vissani, PhD[2], Kristin Hageman, PhD[1], Paul Stypulkowski, PhD[1], Abbey Holt-Becker, PhD[1], Scott Stanslaski, MSc[1], Robert Raike, PhD[1], Todd Herrington, MD, PhD[3], R. Mark Richardson, MD, PhD[2]
[1]Medtronic, Neuromodulation, Minneapolis, United States of America, [2]Massachusetts General Hospital, Neurosurgery, Boston, United States of America, [3]Massachusetts General Hospital, Harvard Medical School, Neurology, Boston, United States of America

Introduction: Deep brain stimulation (DBS) is a well-established treatment for movement disorders, in particular Parkinson's disease (PD). Local field potentials (LFP) and single unit recordings in relevant DBS targets have shown utility in lead localization, guided programming, biomarkers of symptom severity, and as control signals for adaptive DBS. A recently described evoked signal, evoked resonant neural activity (ERNA) [1], may provide added value in anesthetized DBS surgery and beyond.

Materials / Methods: Preclinical data were collected in three ovine subjects implanted with Medtronic 3389 leads in the left hemisphere and Medtronic SenSight leads in the right. An investigational research system delivered stimulation and recorded the ERNA response [2]. Stimulation was delivered in both continuous and bursted patterns. This same system was then used intra-operatively to collect evoked responses in five patients undergoing subthalamic nucleus (STN) DBS surgery for PD under anesthesia. Please note that Medtronic DBS systems are not approved for implant under general anesthesia in patients with PD; intraoperative test stimulation for symptom suppression is required. Evoked responses to different amplitudes and frequencies of stimulation were obtained and analyzed. LFP recordings were also collected with the implanted DBS device during initial programming sessions and compared to the intraoperative datasets.

Results: ERNA was successfully recorded under general anesthesia in the STN in both pre-clinical ovine subjects as well as five human participants. These recordings were obtained with implantable grade hardware and confirm that these signals are present under anesthesia. This work suggests that ERNA has potential as a method for functional confirmation of DBS lead placement under general anesthesia. LFP recordings from the implanted device recorded at initial programming were compared with the intra-operative recordings and showed correlation between strength of signal in the two recording modes.

Discussion: Our results confirm that ERNA can be recorded with investigational, implantable grade hardware. Additionally, intra-operative recordings are shown to correlate with LFP signals measured from the implanted DBS system.

Conclusions: Recording ERNA under anesthesia is feasible and may provide a viable signal to confirm DBS lead placement.

References: 1. Sinclair, N. C., McDermott, H. J., Bulluss, K. J., Fallon, J. B., Perera, T., Xu, S. S., Brown, P., & Thevathasan, W. (2018). Subthalamic nucleus deep brain stimulation evokes resonant neural activity. *Annals of Neurology*, *83*(5), 1027–1031. https://doi.org/10.1002/ana.25234 2. Hageman, K., Peterson, E., Stypulkowski, P., Corey, R., Jensen, R., Billstrom, T., Netoff, T., and Stanslaski, S. (April 17, 2023). "A Translatable System for Bi-Directional Stimulation and Evoked Response Measurement to Enable Neuronal Network Exploration." ASME. J. Med. Devices. June 2023; 17(2): 021007. https://doi.org/10.1115/1.4056945

Learning Objectives: - Determine if evoked neural responses can be captured with the Argus 1 ERNA System during DBS surgery under anesthesia. - Compare evoked signals with local field potentials and clinical stimulation settings. - Compare evoked signals with neuroimaging and localize evoked responses.

Financial Disclosures: Rene Molina, Medtronic, Company Employee, > $100,000 USD

Alan Bush, No significant relationships

Matteo Vissani, No significant relationships

Kristin Hageman, Medtronic, Company Employee, > $100,000 USD

Paul Stypulkowski, Medtronic, Company Employee, > $100,000 USD

Abbey Holt-Becker, Medtronic, Company Employee, > $100,000 USD

Scott Stanslaski, Medtronic, Company Employee, > $100,000 USD

Robert S. Raike, Medtronic, Company Employee, > $100,000 USD

Todd Herrington, Medtronic, Consultant/Advisory Board and Research, $500-$5000; MarvelBiome, Consultant/Advisory Board, Stock Options <5% (no public valuation); Boston Scientific, Sponsored Research, $5,001-$20,000

R. Mark Richardson, Education/Research, $20,001 - $100,000 USD

Disclosure: I am a Medtronic employee.

209

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

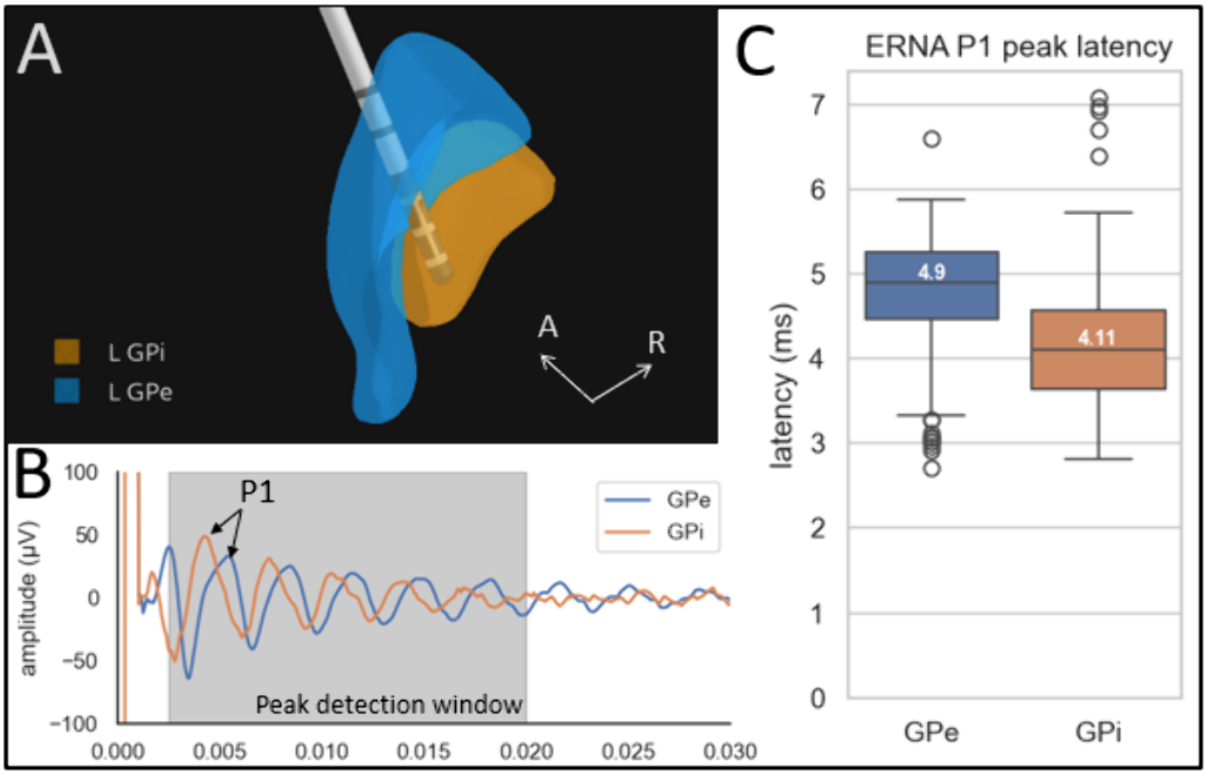
DEEP BRAIN STIMULATION EVOKED RESONANT NEURAL ACTIVITY IS DISTINGUISHABLE BETWEEN PALLIDAL SUB-STRUCTURES

Ashton Moorhead, MSBmE[1], Wee-Lih Lee, PhD[1,2], Thushara Perera, PhD[1,2,3], Kiaran Lawson, PhD[1], Thomas Tonroe, BEng(Hons)[1,4], Hugh McDermott, PhD[2,3], Kristian Bulluss, PhD[1,3,5,6,7], Wesley Thevathasan, PhD[1,3,8,9], Matthew Petoe, PhD[1,2]
[1]Bionics Institute, Melbourne, Australia, [2]University of Melbourne, Medical Bionics Department, Melbourne, Australia, [3]Deep Brain Stimulation Technologies, Melbourne, Australia, [4]RMIT University, School Of Engineering, Melbourne, Australia, [5]Austin Hospital, Department Of Neurosurgery, Melbourne, Australia, [6]Cabrini Hospital, Department Of Neurosurgery, Melbourne, Australia, [7]St Vincent's Hospital Melbourne, Department Of Neurosurgery, Melbourne, Australia, [8]Austin Hospital, Department Of Neurology, Melbourne, Australia, [9]The Royal Melbourne Hospital, Department Of Neurology, Melbourne, Australia

Introduction: Deep Brain Stimulation (DBS) is a common treatment for medication-refractory movement disorders, often targeting the globus pallidus internus (GPi) and subthalamic nucleus (STN). We have previously demonstrated the utility of evoked resonant neural activity (ERNA) as a biomarker to guide STN DBS implantation and stimulation settings [1]. ERNA is modulated by DBS parameters suggesting a direct relationship to the mechanisms of DBS [2]. Following recent reports describing the subcortical network possibly involved in generating ERNA [3, 4], we further investigated ERNA dynamics within the pallidum.

Materials / Methods: Five patients received bilateral GPi DBS electrode arrays (Vercise™ Cartesia™, Boston Scientific, Marlborough, Massachusetts, United States) for either Parkinson's disease (n=2) or dystonia (n=3). Intra-operative monopolar recordings were acquired, applying ten stimulation bursts (10 pulses per burst at 130Hz) to each electrode while simultaneously recording across the entire electrode array. Data was re-referenced to the contra-lateral hemisphere, filtered (130-1000Hz), and averaged across 10 measurements per electrode (Figure 1B). Pre-operative MRI and post-operative CT images were co-registered to the MNI152 NLIN 2009b template brain, and the DISTAL Atlas [5] was used to label electrodes as in the GPi or GPe, electrodes outside both structures were excluded from further analysis. ERNA peak amplitude and latency were determined using SciPy (find_peaks) and manually verified, then used to estimate ERNA peak frequency. ERNA characteristics were compared between GPi and GPe pallidal sub-

structures.



Results: ERNA was found in all hemispheres with a median peak frequency of 312 (IQR: 21) Hz and mean peak-to-peak amplitude of 61.2 (IQR: 37.7) μV. In electrode arrays spanning both GPi and GPe (n=8), median ERNA P1 peak latencies were 4.11 (IQR 0.87) ms and 4.90 (IQR 0.789) ms at GPi and GPe, respectively. Latency differences were significant ($p<0.001$, Mann-Whitney).

Discussion: With reference to recent publications hypothesizing that GPi-ERNA arises from recurrent inhibitory input from the GPe [3, 4] we found a 0.79 ms reduction in ERNA P1 peak latency recorded from the GPi compared to the GPe. This latency difference is similar to a single synaptic transmission.

Conclusions: These results are consistent with the hypothesis that GPi ERNA arises from recurrent GPe inhibition.

Supplemental Data:

References: [1] S. S. Xu *et al.*, “Can brain signals and anatomy refine contact choice for deep brain stimulation in Parkinson’s disease?,” *J. Neurol. Neurosurg. Psychiatry*, p. jnnp-2021-327708, May 2022, doi: 10.1136/jnnp-2021-327708. [2] C. Wiest *et al.*, “Evoked resonant neural activity in subthalamic local field potentials reflects basal ganglia network dynamics,” *Neurobiol. Dis.*, vol. 178, p. 106019, Mar. 2023, doi: 10.1016/j.nbd.2023.106019. [3] L. A. Steiner and L. Milosevic, “A convergent subcortical signature to explain the common efficacy of subthalamic and pallidal deep brain stimulation,” *Brain Commun.*, vol. 5, no. 2, p. fcad033, Apr. 2023, doi: 10.1093/braincomms/fcad033. [4] S. L. Schmidt, D. T. Brocker, B. D. Swan, D. A. Turner, and W. M. Grill, “Evoked potentials reveal neural circuits engaged by human deep brain stimulation,” *Brain Stimulat.*, vol. 13, no. 6, pp. 1706–1718, Nov. 2020, doi: 10.1016/j.brs.2020.09.028. [5] S. Ewert *et al.*, “Toward defining deep brain stimulation targets in MNI space: A subcortical atlas based on multimodal MRI, histology and structural connectivity,” *NeuroImage*, vol. 170, pp. 271–282, Apr. 2018, doi: 10.1016/j.neuroimage.2017.05.015.

Acknowledgements: The authors acknowledge Amanda Goy, Deanne Dawe, Jennifer Nagao, Joy Tan, Paul Minty and San San Xu for their contributions to the
ERNA studies. The support of Deep Brain Stimulation Technologies for this project is gratefully acknowledged.

Learning Objectives: Understand the defining features of ERNA in response to DBS of the pallidum. Recognize the potential use of ERNA as a tool to interrogate activation of basal ganglia circuitry through DBS. Understand how ERNA latencies within the pallidum relate to models explaining ERNA generation as activation of reciprocal connections between the STN and pallidum.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

210

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

A CLINICAL REPORT ON DEEP BRAIN STIMULATION OF THE GLOBUS PALLIDUS INTERNUS IN A PEDIATRIC PATIENT WITH KMT2B-ASSOCIATED DYSTONIA

Iroda Mammadinova, MD, Chingiz Nurimanov, MD, Seitzhan Aidarov, MD, Nurtay Nurakay, MD
National Centre for Neurosurgery, Vascular And Functional Neurosurgery, Astana, Kazakhstan

Introduction: Pediatric dystonia is characterized by the manifestation of dystonia before the age of 21 and is estimated to occur at a prevalence rate ranging from 2 to 50 cases per million individuals[1,2]. This case study highlights a unique instance of KMT2B-related dystonia in an 8-year-old girl, which was successfully treated with bilateral deep brain stimulation (DBS) of the globus pallidus internus (GPi).

Materials / Methods: The patient is an 8-year-old girl who first experienced dystonia symptoms at the age of 5, primarily affecting the distal parts of lower limbs. She also exhibited dysarthria and myoclonus in the shoulders and proximal parts of the upper limbs during purposeful movements. There was a dystonic posture characterized by inward rotation of the feet in the lower limbs, with no other neurological abnormalities detected. Prior treatment attempts using medications proved ineffective. The severity of the dystonia was evaluated using three scoring systems: the Unified Dystonia Rating Scale (UDRS), the Global Dystonia Severity Rating Scale (GDS), and the Burke-Fahn-Marsden (BFM) scale. Genomic sequencing identified a heterozygous mutation in the KMT2B gene (606834) located on chromosome 19p13. To address the dystonia symptoms, bilateral DBS of the GPi was performed under general anesthesia.

Results: This case report emphasizes the favorable results witnessed six months after the DBS procedure. Prior to surgery, the patient received scores of 8 on the UDRS, 36 on the GDS, and 13 on the BFM scale. Following the operation, notable clinical improvements were observed, particularly in motor symptoms affecting the arms and legs. However, the progress in speech and laryngeal function was less pronounced, resulting in an overall postoperative UDRS score of 4, GDS score of 26, and BFM score of 7.

Discussion: Numerous studies have consistently reported significant benefits following DBS targeting the GPi in individuals with dystonia associated with KMT2B mutations [3,4]. This highlights an important characteristic of KMT2B-related dystonia, namely its favorable response to DBS, which positions it as a preferred treatment option for severely affected patients.DBS has demonstrated effectiveness across various anatomical regions, leading to noticeable improvements in motor symptoms.

Conclusions: In conclusion, this case has provided valuable insights into the genetic understanding and treatment of dystonia, specifically highlighting the effectiveness of DBS. Therefore, genetic testing may be beneficial prior to considering surgery. However, further research and advancements are still needed to enhance our understanding of the underlying genetic mechanisms of dystonia and optimize the use of DBS as a treatment option.

Supplemental Data:

References: 1. Fernández-Alvarez, E.; Nardocci, N. Update on Pediatric Dystonias: Etiology, Epidemiology, and Management. *Degener Neurol Neuromuscul Dis* **2012**, *2*, 29–41, doi:10.2147/DNND.S16082. 2. Meyer, E.; Carss, K.J.; Rankin, J.; Nichols, J.M.E.; Grozeva, D.; Joseph, A.P.; Mencacci, N.E.; Papandreou, A.; Ng, J.; Barral, S.; et al. Mutations in the Histone Methyltransferase Gene KMT2B Cause Complex Early-Onset Dystonia. *Nat Genet* **2017**, *49*, 223–237, doi:10.1038/ng.3740. 3. Mun, J.K.; Kim, A.R.; Ahn, J.H.; Kim, M.; Cho, J.W.; Lee, J.-I.; Cho, K.R.; Youn, J. Successful Pallidal Stimulation in a Patient with KMT2B-Related Dystonia. *J Mov*

Disord **2020**, *13*, 154–158, doi:10.14802/jmd.19087. 9. Li, X.-Y.; Dai, L.-F.; Wan, X.-H.; Guo, Y.; Dai, Y.; Li, S.-L.; Fang, F.; Wang, X.-H.; Zhang, W.-H.; Liu, T.-H.; et al. Clinical Phenotypes, Genotypes and Treatment in Chinese Dystonia Patients with KMT2B Variants. *Parkinsonism Relat Disord* **2020**, *77*, 76–82, doi:10.1016/j.parkreldis.2020.06.002.

Acknowledgements: none

Learning Objectives: Objective 1: Enhance Knowledge of KMT2B-Related Dystonia and Treatment Options. **Desired Result**: This objective seeks to provide a comprehensive understanding of KMT2B-related dystonia, its clinical manifestations, and the potential treatments available, including the use of bilateral GPi DBS. **Objective 2**: Promote the Importance of Genetic Testing and Precise Treatment Planning. **Desired Result**: This objective emphasizes the significance of genetic testing in diagnosing dystonia and the critical role of precise electrode placement in DBS procedures. Learners will appreciate how these factors can lead to significant improvements in motor symptoms and overall quality of life in gene-associated dystonias. **Objective 3**: Deepen Knowledge of Genetic Factors in Dystonia and Treatment Strategies. **Desired Result**: This objective aims to expand the understanding of the genetic underpinnings of dystonia, with a particular focus on KMT2B-related dystonia. It also seeks to educate healthcare professionals and researchers on various treatment strategies, including the use of bilateral GPi DBS as an effective intervention.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

211

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

EVOLUTION OF DEEP BRAIN STIMULATION TECHNIQUES

Ryan Mayer, BS, Kishan Desai, BS, Rodrigo Salmeron De Toledo Aguiar, MD, Jesse McClure, MD, Nicholas Kato, BS, Cheyenne Kalman, BS, Julie Pilitsis, MD, PhD
Florida Atlantic University, Boca Raton, United States of America

Introduction: Complication mitigation in Deep Brain Stimulation (DBS) has been a topic matter of much discussion in the literature. Here we examine how neurosurgeons as individuals and as a field adapted the techniques they used to prevent the complications of infection, lead fracture/lead migration and suboptimal outcomes acutely and over time.

Materials / Methods: The authors performed a MEDLINE search inclusive of articles from 1987 to June 2023 including human, modeling, and animal studies written in English. Using the Rayyan platform, two reviewers (J.P. and R.M.) performed a title screen. Of the 943 articles, 252 were selected by title screen and 172 from abstract review for full text evolution. Ultimately 129 publications were evaluated. We describe initial complications and inefficiencies at the advent of DBS and speak to the changes instituted by surgeons and the field that reduced these complications.

Results: Specifically lead fractures occurred in ~10% of cases and infection in ~8% of cases. Changes in where extensions were positioned and infection control techniques resulted in incidence of <3% for both. Symptomatic hematomas occurred in nearly all multi-center studies at ~1-2% incidence and has decreased to a rare complication due to management of blood pressure, anti-coagulations, and improved trajectory selection. Post-operative confusion has been reduced with a decrease in operative time and in amount of time off medications.

Discussion: This scoping review adds to the literature as a guide to new neurosurgeons to understand what innovations have been trialed over time and to seasoned neurosurgeons as we embark on novel targets and neuromodulatory technologies.

Conclusions: DBS has evolved from 1987 as have surgical techniques and guidelines.

Supplemental Data:

References: 1. Conti A, Gambadauro NM, Mantovani P, Picciano CP, Rosetti V, Magnani M, Lucerna S, Tuleasca C, Cortelli P, Giannini G. A Brief History of Stereotactic Atlases: Their Evolution and Importance in Stereotactic Neurosurgery. Brain Sci. 2023 May 21;13(5):830. doi: 10.3390/brainsci13050830. PMID: 37239302; PMCID: PMC10216792. 2. Rahman M, Murad GJ, Mocco J. Early history of the stereotactic apparatus in neurosurgery. Neurosurg Focus. 2009 Sep;27(3):E12. doi: 10.3171/2009.7.FOCUS09118. PMID: 19722814. 3.Wycis HT, Spiegel EA. The effect of thalamotomy and pallidotomy upon involuntary movements in chorea and athetosis. Surg Forum. 1950:329-32. PMID: 14828513. 4.Couldwell WT, Apuzzo ML. Initial experience related to the use of the Cosman-Roberts-Wells stereotactic instrument. Technical note. J Neurosurg. 1990 Jan;72(1):145-8. doi: 10.3171/jns.1990.72.1.0145. PMID: 2403588. 5. Shealy CN, Mortimer JT, Reswick JB. Electrical inhibition of pain by stimulation of the dorsal columns: preliminary clinical report. Anesth Analg. Jul-Aug 1967;46(4):489-91.

Acknowledgements: N/A

Learning Objectives: 1. Understand the advancements in surgical technique of DBS 2. Understand the problems that arose with DBS and solutions to overcome them 3. Understand the novel targets and neuromodulatory technologies

Financial Disclosures: JGP receives grant support from Medtronic, Boston Scientific, Abbott, NIH 2R01CA166379, 3U54EB 015408-09 and NIH U44NS115111. She is a medical advisor for AIM Medical Robotics and has stock equity. RTA receives fellowship funding from Medtronic, Boston Scientific and Abbott.

Disclosure: No significant relationships.

212

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

DEEP BRAIN STIMULATION MODULATES OSCILLATORY BETA DYNAMICS AND QUANTIFIED MOVEMENT KINEMATICS IN PARKINSON'S DISEASE: A CASE STUDY

Erin Radcliffe, BSc (Hons)[1,2], Drew Kern, MD[1,3], Daniel Kramer, MD[1], John Thompson, PhD[1,3,4]
[1]University of Colorado Anschutz Medical Campus, Neurosurgery, Aurora, United States of America, [2]University of Colorado Anschutz Medical Campus, Bioengineering, Aurora, United States of America, [3]University of Colorado Anschutz Medical Campus, Neurology, Aurora, United States of America, [4]University of Colorado Anschutz Medical Campus, Psychiatry, Aurora, United States of America

Introduction: Parkinson's disease (PD) is characterized by dopaminergic neuron loss, basal ganglia dysregulation, and progressive impairments. Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is standard-of-care for medication-refractory PD. STN local field potential (LFP) features within the beta frequency range (13-30 Hz) correlate with impaired movement regulation in PD. Few studies have correlated objectively computed kinematics with oscillatory beta dynamics across clinical states.

Materials / Methods: We examined how DBS therapy modulated oscillatory beta dynamics and movement kinematics in a PD patient (N=2 hemispheres) across Off- and On-stimulation states while Off medication. STN-LFP and video-derived kinematic data were collected from each DBS-implanted hemisphere and contralateral limb, respectively, while the patient performed repeated trials of hand movements (Movement Disorder Society Unified Parkinson's Disease Rating Scale [MDS-UPDRS], item 3.5). Computer vision, markerless motion tracking, and trained neural networks quantified neuromotor behavior from 2D coordinate timeseries data composed of anatomically labeled points utilized to compute fingertip displacement amplitude, speed, and initiation latency.

Results: In both hemispheres, distinct DBS conditions significantly altered motor performance. For the left STN (right body), in the Off-stimulation condition, movement amplitudes averaged 60.79 mm with a standard deviation (SD) of 10.72, intra-movement cycle durations averaged 0.085 seconds (SD=0.023), and inter-movement cycle durations averaged 0.52 seconds (SD=0.16). Under the On-stimulation condition, amplitudes increased to an average 68.50 mm (SD=14.17), intra-movement durations decreased to average 0.069 seconds (SD=0.016), and inter-movement durations shortened to average 0.41 seconds (SD=0.08). For the right STN (left body), in the Off-stimulation condition, amplitudes averaged 84.78 mm (SD=10.78), intra-movement durations averaged 0.067 seconds (SD=0.011), and inter-movement durations averaged 0.47 seconds (SD=0.18). In the On-stimulation state, amplitudes increased to average 96.59 mm (SD=12.67), intra-movement durations decreased to average 0.057 seconds (SD=0.008), and inter-movement durations increased to average 0.63 seconds (SD=0.14). Statistical comparisons between DBS conditions for the left STN highlight the significance of increased movement amplitudes (p-value=0.05) suggesting augmented movement strength/fluidity, decreased intra-movement durations (p-value=0.02) indicating increased movement speed, and reduced inter-movement durations (p-value=0.01) implying quicker movement initiation when On-stimulation. For the right STN, DBS response differences were only significant for movement amplitudes (p-value=0.03).

Discussion: Our computational approach provides nuanced characterizations of PD motor behavior correlated with beta oscillatory dynamics to permit objective assessment of motor ability in distinct clinical states.

Conclusions: Preliminary results provide quantitative methods for determining clinical responses to neuromodulation parameters in PD. Subsequent analyses may inform DBS programming strategies and optimized control algorithms for adaptive DBS systems.

Supplemental Data:

References: 1. Yin, Z., Zhu, G., Zhao, B., Bai, Y., Jiang, Y., Neumann, W.-J., Kühn, A. A., & Zhang, J. (2021). Local field potentials in Parkinson's disease: A frequency-based review. *Neurobiology of Disease*, *155*, 105372. https://doi.org/10.1016/j.nbd.2021.105372 2. Radcliffe, E. M., Baumgartner, A. J., Kern, D. S., Borno, M. A., Ojemann, S., Kramer, D. R., & Thompson, J. A. (2023). Oscillatory beta dynamics inform biomarker-driven treatment optimization for Parkinson's disease. *Journal of Neurophysiology*, *129*(6), 1492-1504. https://doi.org/10.1152/jn.00055.2023 3. Cagnan, H., Denison, T., McIntyre, C., & Brown, P. (2019). Emerging technologies for improved deep brain stimulation. *Nature Biotechnology*, *37*(9), 1024-1033. https://doi.org/10.1038/s41587-019-0244-6 4. Torrecillos, F., Tinkhauser, G., Fischer, P., Green, A. L., Aziz, T. Z., Foltynie, T., Limousin, P., Zrinzo, L., Ashkan, K., Brown, P., & Tan, H. (2018). Modulation of Beta Bursts in the Subthalamic Nucleus Predicts Motor Performance. *Journal of Neuroscience, 38*(41), 8905-8917. https://doi.org/10.1523/jneurosci.1314-18.2018 5. Tien, R. N., Tekriwal, A., Calame, D. J., Platt, J. P., Baker, S., Seeberger, L. C., Kern, D. S., Person, A. L., Ojemann, S. G., Thompson, J. A., & Kramer, D. R. (2022). Deep learning based markerless motion tracking as a clinical tool for movement disorders: Utility, feasibility and early experience [Perspective]. *Frontiers in Signal Processing, 2*. https://doi.org/10.3389/frsip.2022.884384

Acknowledgements:

Learning Objectives: 1. Objective: Gain an overview of Parkinson's disease (PD), the role of deep brain stimulation (DBS) in its treatment, and the significance of local field potential (LFP) features within the beta frequency range (13-30 Hz) in relation to PD symptom severity. **Desired Result**: Attendees will gain an understanding of general PD characteristics, the therapeutic purpose of DBS, and how oscillatory beta features correlate with PD motor symptoms. **2. Objective**: Learn about computational tools and methods used to quantify neuromotor behavior and neuromodulation responses in PD. **Desired Result**: Attendees will become familiar with the use of computer vision, motion tracking, and signal processing for assessing PD motor performance correlated with electrophysiological dynamics. **3. Objective**: Recognize the potential value of utilizing quantitative methods for evaluating PD clinical outcomes and DBS responses. **Desired Result**: Attendees will comprehend how objective assessments can potentially guide enhancements in DBS therapy approaches for improved patient outcomes.

Financial Disclosures: D.S.K. has served as an advisor for the Colorado Clinical and Translational Sciences Institute (CCTSI) Data Safety Monitoring Board, Medical Boards for Boston Scientific, Medtronic, and AbbVie Pharmaceutics, has received honorarium from AbbVie Pharmaceutics, Abbott, and Boston Scientific, and receives research funding from Boston Scientific, Medtronic, University of Colorado Department of Neurology, and the Parkinson's Foundation. J.A.T. has received speaker honorarium from Medtronic and receives research funding from Boston Scientific, Medtronic, and the National Institute of Health (NIH). The presenting author and remaining co-author have no financial relationships to disclose.

Disclosure: No significant relationships.

213

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

DEEP BRAIN ELECTRODES AND DENTATO-RUBRO-THALAMIC TRACT: RELATIONSHIP BETWEEN ACTIVATED TISSUE VOLUME AND THERAPEUTIC EFFECT

Beatriz Mansilla, MD[1,2], María Román De Aragón, MD[1], Jose Paz Solis, MD[1], Laura González Martín, MD[3]
[1]University Hospital La Paz, Neurosurgery, Madrid, Spain, [2]University Hospital La Paz, Neurosurgery, MADRID, Spain, [3]University Hospital La Paz, Neurology, MADRID, Spain

Introduction: Stimulation of the dentato-rubro-thalamic tract (DRT) at the level of the ventral intermediate nucleus (VIM) is gaining a prominent role in the treatment of refractory essential tremor through deep brain stimulation (DBS). We aime to establish the importance of the DRT in the treatment of tremor with DBS. Correlate the activated tissue volume (ATV) with the therapeutic effect achieved.

Materials / Methods: We present two cases of refractory essential tremor treated with deep brain stimulation by stimulating the thalamic ventral intermediate nucleus (VIM) bilaterally. The VIM was localized using indirect calculation with the stereotactic planning program (brainlab elements). After micro-recording, two segmented electrodes were implanted. The electrode positions, dentato-rubro-thalamic tract, and activated tissue volume (ATV) were defined using the Guide XT program. We analyzed the relationship of the ATV of each electrode to the percentage of stimulated tract included.

Results: Case 1, 77-year-old female: - Left VIM electrode: Contacts 2, 3, 4 were activated at 33%, with settings of 2.6 mA, 60 pulses, and 130 Hz, resulting in a significant reduction of tremor with occasional, mild tremor and no adverse effects. The ATV encompassed 50% of stimulated DRT fibers. - Right VIM electrode: Using the same contacts and parameters, optimal results were achieved, with the ATV including 75% of fibers in the tract. Case 2, 73-year-old male: - Left VIM electrode: Contacts 4 (50%) and 7 (50%) were used, with settings of 2.2 mA, 100 pulses, and 130 Hz, resulting in poor therapeutic effect on tremor. The ATV included 15% of fibers. - Right VIM electrode: Contacts 2, 3, 4 (33%) were activated with intensity 1.9 mA, 60 pulses, and 130 Hz, resulting in a significant reduction of tremor. The ATV encompassed 75% of the tract.

Discussion: The objective of deep brain stimulation is to find the sweet spot or most specific target to achieve the best therapeutic effect without adverse effects. In the case of tremor, the sweet spot or true target could be related to a minimum percentage of stimulation of the dentato-rubro-thalamic tract, rather than focusing solely on the ventralis intermediate nucleus.

Conclusions: The dentato-rubro-thalamic tract is a crucial target in the treatment of refractory essential tremor with Deep Brain Stimulation. Suboptimal stimulation in our cases is related to electrode position further from the dentato-rubro-thalamic tract and a lower percentage of tract fibers included in the activated tissular volume.

Supplemental Data:

References: 1. Yang AI, Buch VP, Heman-Ackah SM, Ramayya AG, Hitti FL, Beatson N, Chaibainou H, Yates M, Wang S, Verma R, Wolf RL, Baltuch GH, Thalamic deep brain stimulation for essential tremor: relation of the dentato-rubro-thalamic tract with stimulation parameters, World Neurosurgery (2020), doi: https://doi.org/10.1016/j.wneu.2020.01.039. 2. Kruger M, Kurtev-Rittstieg R, Kagi G, Naseri Y, Hagele-Link S, Brugger F. Evaluation of automatic segmentation of thalamic nuclei through clinical effects using directional deep brain stimulation leads: a technical note. Brain Sci. (2020) 10, 642; doi: 10.3390/brainsci10090642. 3. Akram H, Dayal V, Mahlknecht P, Georgiev D, Hyam J, Foltynie T et al. Connectivity derived thalamic segmentation in deep brain stimulation for tremor. NeuroImage: Clinical 18 (2018): 130-142. 4. Koeglsperger T, Palleis C, Hell F, Mehrkens J, Botzel K.

Deep brain stimulation programming for movement disorders: current concepts and evidence-based strategies. Frontiers in neurology (2019): Vol 10. 5. Bryant J, De salles A, Cabatan C, Frysinger R, Behnke E, Bronstein J. The impact of thalamic stimulation on activities of daily living for essential tremor. Surg Neurol (2003); 59:479-85.

Acknowledgements:

Learning Objectives: 1. To establish the importance of the DRT in the treatment of tremor with DBS. Correlate the activated tissue volume (ATV) with the therapeutic effect achieved.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

214

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

HYBRID DBS SYSTEMS FOLLOWING IPG REPLACEMENT – FIRST EXPERIENCES IN 23 PATIENTS

Phillipp Slotty, MD[1,2], Zarela Krause Molle, MD[3], Phyllis McPhillips, RN[3], Andrea Dreyer, RN[3], Jan Vesper, MD[3]
[1]Helios Krefeld, Department Of Orthopaedics, Trauma Surgery And Hand Unit, Krefeld, Germany, [2]Heinrich-Heine University, Duesseldorf, Germany, [3]University Medical Center, Heinrich Heine University, Functional Neurosurgery And Stereotaxy, Duesseldorf, Germany

Introduction: Until recently, DBS cross-over devices, as switching the IPG from one company to another during replacement procedures, were not an option. Since 2022, adapters for switching from conventional Medtronic DBS systems are available. They allow the connection to Medtronic extensions and leads and connect to Boston Scientific DBS IPGs.

Materials / Methods: We report our first experiences using this adapter regarding the surgical procedures, safety and programming, especially related to the conversion from single-source IPGs to Multiple Independent Current Control (MICC) IPGs. Intra- and postoperative complications were assessed as well as adverse effects following conversion. The rationale for switching the manufacturer and the device were patient's preference, limited longevity of the prior IPG (< 3 year battery life), smaller IPG size options and limitations due to side effects with the prior system. The average IPG longevity prior to conversion was 2.7 y (0.9 – 4.8 yrs)

Results: 23 consecutive patients underwent IPG hybrid device implantation at our University hospital. All patients were discussed preoperatively by our interdisciplinary movement disorder board. We included 11 male and 12 female patients, PD (STN) n=14, Dystonia (GPI) n=5, ET (VIM) n=3, epilepsy /tremor (VIM/ANT) n=1. No surgical complications occurred, impedances were within range in all patients. All patients received postoperative programming by a movement neurologist. All patients were switched to the multiple independent current setting the day after surgery. Out of the total of 23 patients, 11 reported an unchanged status, 12 patients improved significantly compared to the preoperative status in at least one symptom or as a reduction of stimulation side effects at the first post op visit. All of the patients in the single visit subgroup received > 2 active electrodes, 18/23 of the patients in the multi visit subgroup received > 2 active electrodes.

Discussion: The high number of patients using more than 1 active contact shows the significance of the change to a MICC system. 54.4% (n=12) of the patients experienced a reduction in at least one symptom or side effect, a reduction in tremor, bradykinesia or rigidity. Final data on IPG longevity is not available yet, but calculation show a clear improvement to be expected. No surgical complications occurred.

Conclusions: DBS system cross-over IPG replacement is safe and technically easy. Clinical improvement was observed in a significant number of patients adding benefit beyond the smaller IPG size and improved battery life.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1) Options for inter-manufacturer IPG replacement exist and might be beneficial for the patient 2) These options can be considered for various reasons on an individual basis 3) Approved options exist, including MRI safety

Financial Disclosures: Philipp J. Slotty received speaker honoraria and travel reimbursement from Abbott, Boston Scientific, Uniqure, Photonamics and Saluda

Disclosure: No significant relationships.

215

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

DEEP BRAIN STIMULATION BATTERY LONGEVITY IN PARKINSON DISEASE AND ESSENTIAL TREMOR: A REAL-WORLD SINGLE CENTER COHORT

Manuel Tardáguila Serrano, MD[1], Lourdes Ispierto González, PhD[2], Dolores Vilas Rolan, PhD[2], Antonio González Crespo, MD[1], Jorge Luís Muñoz Aguiar, PhD[1], Ramiro Álvarez Ramo, PhD[2], Mónica Millan Torné, PhD[2], Carlos Javier Domínguez Alonso, MD[1]
[1]Hospital Universitari Germans Trias i Pujol, Neurosurgery, Badalona, Spain, [2]Hospital Universitari Germans Trias i Pujol, Neurology, Badalona, Spain

Introduction: Deep Brain Stimulation (DBS) is a well-established treatment for Parkinson disease (PD) and Essential Tremor (ET)[1 2]. This retrospective study from Hospital Universitario Germans Trias i Pujol (Barcelona, Spain) evaluated the longevity of the Infinity 7 (Abbott, TX, USA) in a single center real world setting.

Materials / Methods: Between 2017 and 2023 we retrospectively analyzed the longevity of 32 denovo DBS implants with Infinity 7 (n=22 for PD, n=10 for ET) and bilateral directional leads. Data was collected from denovo implants until battery replacement. The data collected included programming and device parameters, diagnosis, implanted target, and number of connections between the implanted device and the clinician programmer. This analysis did not consider devices that are still actively implanted (since 2017) .
2 devices were excluded (1= infection, 1= damage to device due to a surgery unrelated to DBS)

Results: Average Battery duration was 4.2 years (min: 2.1 years max: 5.1 years). The reviewed longevity was above 4 years in 21 patients (65.6%) and below 4 years in 11 patients (34.4%). Directional programming showed the highest longevity: Average longevity was 4.5 years, and 100% of patients with directional programming had >4 years battery longevity; whereas patients with omnidirectional programming had 4.0 years average longevity, and 53.3% of patients had a longevity >4 years.
PD had a higher longevity (4.3 years on average, 72.7% above 4 years) than ET (3.8 years average, 50% above 4 years).29 devices demonstrated a median longevity of 4.18 years [2.07– 5.06]. 14 devices were programmed in ring mode and demonstrated a longevity of 3.95 years [2.07 – 5.04], whereas 15 devices that used directionality demonstrated a longevity of 4.42 years [3.25 – 5.06]
In addition, the data demonstrated a 3.1% infection (32 devices, 1 infection) and no lead migration or fractures were reported

Discussion: Results are based on a single center experience. Programming techniques could differ between different centers[3] which could demonstrate different longevity outcomes.
Having observed a higher longevity with Single Segment Directional settings was an expected outcome (lower current strength required to achieve therapeutic benefit)[5,6]
Programming parameters from each device were not considered, even though Frequency, amplitude and pulse width also impact the longevity of the battery[4], these settings change over time making it very challenging to evaluate the exact impact on each device. In addition, impedance values impact battery longevity as well and these values are changing over time[7], making it challenging to evaluate the impedance impact on longevity throughout the whole device life.

Conclusions: Average longevity of the Infinity™ 7 reaches a real-world average outcome of 4.2 years. There is a tendency to a higher longevity when using directional programming. This single center study also demonstrated aan infection rate of 3.1% in DeNovo implants, which is in line with published material[8,9]

Supplemental Data:

References: 1 Limousin P, Krack P, Pollak P, Benazzouz A, Ardouin C, Hoffmann D, et al. Electrical stimulation of the subthalamic nucleus in advanced Parkinson's disease. N Engl J Med **2** Vesper J, Klostermann F, Stockhammer F, Funk T, Brock M. Results of chronic subthalamic nucleus stimulation for Parkinson's disease: a 1-year follow-up study. Surg Neurol 2002;57:306e11. discussion 311-313. **3** Aubignat M, et al. Deep brain stimulation programming in Parkinson's disease: Introduction of current issues and perspectives. Revue neurologique (2020), https://doi.org/10.1016/j.neurol.2020.02.009 **4** K Knudsen et al, Programming parameters of subthalamic deep brain stimulators in Parkinson's disease from a controlled trial. Parkinsonism and Related Disorders, 2019-08-01, Volume 65, Pages 217-223, **5** Schniztlez et al, Directional Deep Brain Stimulation for Parkinson's Disease: Results of an International Crossover Study With Randomized, Double-Blind Primary Endpoint; Neuromodulation 2022 Aug, 25(6):817-828 . https://doi.org/10.1111/ner.13407 **6** Soh et al, Therapeutic Window of Deep Brain Stimulation Using Cathodic Monopolar, Bipolar, Semi-Bipolar, and Anodic Stimulation. Neuromodulation 2019 Jun;22(4):451-455. doi: 10.1111/ner.12957. Epub 2019 Apr 5. https://doi.org/10.1111/ner.12957 **7** Cheung et al, Longitudinal Impedance Variability in Patients with Chronically Implanted DBS Devices. Deep Brain Stimulation, volume 6, issue 5, P746-751, Sep 2013. https://www.brainstimjrnl.com/article/S1935-861X(13)00092-2/fulltext **8** Atchley et al,68 2020, Surgical Site Infections Associated With Implanted Pulse Generators for Deep Brain Stimulation: Meta-Analysis and Systematic Review. Neuromodulation, Volume 26, issue 2, P280-281, Feb 2023. https://www.neuromodulationjournal.org/article/S1094-7159(22)00751-6/fulltext **9** Pepper et al, The Risk of Hardware Infection in Deep Brain Stimulation Surgery Is Greater at Impulse Generator Replacement than at the Primary Procedure. Stereotact Funct Neurosurg 2013;91:56–65 https://doi.org/10.1159/000343202

Acknowledgements:

Learning Objectives: 1. Learn about the importance of a precise implantation of deep brain stimulation leads, in order to achieve higher longevity battery life. 2. Learn about the difference between ring mode and directional mode. 3. Learn about the importance or programming parameters in order to achieve higher longevity battery life.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

216

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

ASSESSMENT OF IMAGE-GUIDED PROGRAMMING (IGP) ON BILATERAL STN AND GPI DEEP BRAIN STIMULATION PROGRAMMING TIME

Jason Aldred, MD[1], Theresa Zesiewicz, MD[2], Michael Okun, MD[3], Juan Ramirez-Castaneda, MD[4], Leo Verhagen Metman, MD, PhD[5], Corneliu Luca, MD[6], Ritesh Ramdhani, MD[7], Jennifer Durphy, MD[8], Yarema Bezchlibnyk, MD[9], Jonathan Carlson, MD[10], Kelly Foote, MD[11], Sepehr Sani, MD[12], Alexander Papanastassiou, MD[13], Jonathan Jagid, MD[14], David Weintraub, MD[15], Julie Pilitsis, MD, PhD[16], Benjamin Reese, MD[17], Rajat Shivacharan, PhD[17], Lilly Chen, MD[17], Edward Goldberg, MD[17]
[1]Selkirk Neurology, Neurology, Spokane, United States of America, [2]University of South Florida, Neurology, Tampa, United States of America, [3]Norman Fixel Institute for Neurological Disease, University Of Florida, Neurology, Gainesville, United States of America, [4]University of Texas, San Antonio, Neurosurgery, San Antonio, United States of America, [5]Northwestern University Medical Center, Neurology, Chicago, United States of America, [6]University of Miami School of Medicine, Neurology, Miami, United States of America, [7]Northwell Health, Neurosurgery, New York City, United States of America, [8]Albany Medical Center, Neurology, Albany, United States of America, [9]University of South Florida, Neurosurgery, Tampa, United States of America, [10]Inland Neurosurgery and Spine, Neurosurgery, Spokane, United States of America, [11]University of Florida, Neurosurgery, Gainesville, United States of America, [12]Rush University Medical Center, Neurosurgery, Chicago, United States of America, [13]University of Texas, San Antonio, Neurology, San Antonio, United States of America, [14]University of Miami School of Medicine, Neurosurgery, Miami, United States of America, [15]Northwell Health, Neurology, New York City, United States of America, [16]Florida Atlantic University School of Medicine, Neurosurgery, Boca Raton, United States of America, [17]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: Optimization of Deep Brain Stimulation (DBS) programming can be a lengthy, empirical trial-and-error process potentially leading to extended programming sessions and frequent visits. An image-guided programming (IGP)-based platform can help visualize lead location relative to anatomy with capability of reducing programming times and aiding active contact(s) selection through direct visualization and targeting of Stimulation Field Models (SFMs). Here, we describe assessment of Parkinson's disease (PD) patient outcomes using an IGP tool utilized during initial DBS programming, either with STN or GPi as brain target.

Materials / Methods: Novel IGP software (GUIDE XT™, Boston Scientific, Marlborough, MA USA) was evaluated from an ongoing prospective, multicenter, registry (NCT02071134) in which pre-operative MRI and post-operative CT scans were provided to localize the DBS lead relative to each subject's anatomy and to select programming parameters per alignment with SFMs. Time to reach effective DBS settings during the initial programming session was collected, along with device-aided suggested stimulation settings.

Results: To date, 57-subjects (mean age 62.9-years, 77% male) with 10.1-years of disease duration have been enrolled. Initial programming sessions (post-implant), where IGP provided settings for directional leads, lasted 39.4±4.4 minutes (mean±SE). Fifty-five percent (31/56) completed initial programming of bilateral directional leads with the IGP in <30-minutes. Motor function (mean MDS-UPDRS III scores [Meds OFF]) was significantly improved by 55% (n=45) and 45% (n=37) at 6-and 12-months, respectively. Of 21 patients for whom follow-up programming information out to 6- and 12-months was available, 52% and 43% of DBS programs remained unchanged from initial setting (i.e., no change in active contact(s) and cathodic/anodic distribution of current), respectively, as suggested by IGP.

Discussion: Though optimization was subjective in this evaluation, and there was no control group, this tool revealed promising time-based and motor outcomes.

Conclusions: These results indicate that use of this tool is associated with rapid initial programming sessions and clinically significant motor improvement.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: Patients using an IGP-based tool were assessed per the following:

1) Time to complete initial DBS programming

2) Motor function assessment in patients who used an IGP tool

3) To assess programming at follow-up visits to determine if programming has changed since initial use of IGP

Financial Disclosures: Drs. Aldred and Okun have consulting agreements with Boston Scientific. a) Boston Scientific b) consultant c) 5-20k

Disclosure: This study is sponsored by Boston Scientific. Lilly Chen, Rajat Shivacharan, and Edward Goldberg are employees of Boston Scientific.

217

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

REAL-WORLD OUTCOMES USING DBS SYSTEMS WITH DIRECTIONALITY AND MULTIPLE INDEPENDENT CURRENT CONTROL: USA EXPERIENCE

Michael Okun, MD[1], Kelly Foote, MD[1], Theresa Zesiewicz, MD[2], Yarema Bezchlibnyk, MD[3], Alexander Papanastassiou, MD[4], Juan Ramirez-Castaneda, MD[5], Jonathan Carlson, MD[6], Jason Aldred, MD[7], Vibhor Krishna, MD[8], Corneliu Luca, MD[9], Jonathan Jagid, MD[10], Jennifer Durphy, MD[11], Leo Verhagen Metman, MD, PhD[12], Sepehr Sani, MD[13], Steven Ojemann, MD[14], Drew Kern, MD[15], David Weintraub, MD[16], Ritesh Ramdhani, MD[17], Abdolreza Siadati, MD[18], Bharathy Sundaram, MD[19], Cong Zhao, MD[20], Derek Martinez, MD[21], Mustafa Siddiqui, MD[22], Stephen Tatter, MD[23], Lilly Chen, MD[24], Rajat Shivacharan, PhD[24], Edward Goldberg, MD[24]
[1]Norman Fixel Institute for Neurological Disease, University Of Florida, Neurology, Gainesville, United States of America, [2]University of South Florida, Neurology, Tampa, United States of America, [3]University of South Florida, Neurosurgery, Tampa, United States of America, [4]University of Texas, San Antonio, Neurology, San Antonio, United States of America, [5]University of Texas, San Antonio, Neurosurgery, San Antonio, United States of America, [6]Inland Neurosurgery and Spine, Neurosurgery, Spokane, United States of America, [7]Selkirk Neurology, Neurology, Spokane, United States of America, [8]University of North Carolina, Chapel Hill, Neurosurgery, Chapel Hill, United States of America, [9]University of Miami School of Medicine, Neurology, Miami, United States of America, [10]University of Miami School of Medicine, Neurosurgery, Miami, United States of America, [11]Albany Medical Center, Neurology, Albany, United States of America, [12]Northwestern University Medical Center, Neurology, Chicago, United States of America, [13]Rush University Medical Center, Neurosurgery, Chicago, United States of America, [14]University of Colorado Anschutz Campus, Neurosurgery, Denver, United States of America, [15]University of Colorado Anschutz Campus, Neurology, Denver, United States of America, [16]Northwell Health, Neurology, New York City, United States of America, [17]Northwell Health, Neurosurgery, New York City, United States of America, [18]Forth Worth Brain and Spine Institute, Neurosurgery, Fort Worth, United States of America, [19]Texas Institute for Neurological Disorders, Neurology, Sherman, United States of America, [20]St. Luke's Regional Medical Center, Neurology, Boise, United States of America, [21]St. Luke's Regional Medical Center, Neurosurgery, Boise, United States of America, [22]Wake Forest University School of Medicine, Neurology, Winston-Salem, United States of America, [23]Wake Forest University School of Medicine, Neurosurgery, Winston-Salem, United States of America, [24]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: Deep Brain Stimulation (DBS) is an effective strategy for reducing the motor complications in Parkinson's disease (PD). Clinical data collected from a wide variety of implanting centers (based on standard of care) treating PD patients may help provide addtional insights regarding the real-world, clinical use and outcomes of DBS. Here, we present preliminary outcomes from an ongoing prospective, multicenter outcomes study conducted in the United States consisting of patients implanted with directional DBS Systems capable of multiple independent current control (MICC) for use in the management of the motor signs and symptoms in levodopa-responsive PD.

Materials / Methods: Prospectively-enrolled participants were implanted with Vercise DBS systems (Boston Scientific), a multiple-source, constant- current system, and were assessed up to 3-years post-implantation. Clinical measures recorded at baseline and during the follow-up included MOS-Unified Parkinson's disease Rating Scale (MDS-UPDRS), Parkinson's Disease Questionnaire (PDQ-39), Global Impression of Change (GIC), and the Non-Motor Symptom Assessment Scale (NMSS). Adverse events and device-related complications were also collected.

Results: To date, a total of 141-subjects (mean age: 64.0 ± 9.0 years, 71.5% male, disease duration 9.4 ± 5.1 years, n = 137) have been enrolled to date, and 116 of these have undergone device activation. A 53.4% improvement (27-points, $p<0.0001$) in motor function was noted at 6-months as assessed by the MDS-UPDRS III in the "off" medication condition. At 6-months follow-up, over 95% of subjects and over 90% of clinicians noted improvement as compared with Baseline. To date, no lead

fractures or unanticipated adverse events were reported. Additional and updated data will be presented.

Discussion: Data from this study will continue to provide insight regarding the application of the MICC-based directional DBS Systems for PD as applied in real-world settings.

Conclusions: Real-world outcomes from this large, prospective, multicenter outcomes study demonstrated improvement in motor function, quality-of-life, and satisfaction following DBS.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: To assess registry participants according to the following: 1) motor function 2) impression of change 3) adverse events

Financial Disclosures: Dr. Okun has a consulting agreement with Bsoton Scientific. a) Boston Scientiific b) consultant c) 5-20k

Disclosure: This study is sponsored by Boston Scientific. Lilly Chen and Edward Goldberg are employees of Boston Scientific.

218

Poster on Board
POSTER ON BOARD: AS04AA. BRAIN - INVASIVE: MOVEMENT DISORDERS
13-05-2024 08:00 - 19:00

IMPACT OF NEUROPSYCHOLOGICAL TESTING ON SURGICAL DECISION MAKING AND TARGETING IN PARKINSON'S DISEASE

Lutz Weise, MD[1], Rachel Vaughn, MD[1], John Fisk, PhD[2], Thomas Van Essen, MD[1]
[1]Dalhousie University, Neurosurgery, Halifax, Canada, [2]Dalhousie University, Psychology, Halifax, Canada

Introduction: Deep brain stimulation (DBS) improves motor symptoms and quality of life in Parkinson's Disease (PD), but this is offset against the risk of cognitive deterioration. Preoperative neuropsychological screening is widely employed to minimize this risk, but integration of cognitive test resultsin the DBS evaluation varies. Here, we describe how preoperative neuropsychological status may impact the surgical decision-making process.

Materials / Methods: Methods We conducted a single-center, observational cohort study using data from patients enrolled in a local neuromodulation registry. Consecutive patients who were assessed for DBS implantation between 2016 and 2023 were included. A multidisciplinary team, including a trained neuropsychologist, convened bimonthly to review PD patient cases. Patients underwent multi-domain pre-operative neuropsychological assessments to evaluate cognitive functioning and were categorized into those with Mild Cognitive Impairment (MCI) or Parkinson's Disease Dementia (PDD) and those with preserved cognition.

Results: Of 95 PD patients evaluated, 75 (79%) underwent DBS placement. 45 (47%) had MCI and 4 (4%) had PDD. Notably, 14 (29%) patients with MCI were excluded, which comprised 70% of patient exclusions. 27 (56%) had altered DBS targets and 8 (16%) proceeded as planned. Among PDD patients, 3 (75%) were excluded, and 1 (25%) received modified targets. Neuropsychological testing led to a modification of surgical strategy from planned bilateral subthalamic nucleus stimulation in 41 out of 49 (84%) patients with cognitive impairment, which was significant when compared to the 14 of 46 (30%) patients with preserved cognition who required modification (for dystonia/unilateral symptoms) ($p < .001$).

Discussion: Neuropsychological test results significantly impact the surgical decision-making process for DBS patients, in terms of patient eligibility or treatment modification. Preoperative neuropsychological screening may be clinically relevant to mitigate the risk of cognitive decline in PD patients undergoing DBS. In future research we will analyse one-year neuropsychological follow and develop a prognostic model to predict cognitive decline post-DBS

Conclusions: Neuropsychological test results significantly impact the surgical decision-making process for DBS patients, in terms of patient eligibility or treatment modification. Preoperative neuropsychological screening may be clinically relevant to mitigate the risk of cognitive decline in PD patients undergoing DBS. In future research we will analyse one-year neuropsychological follow and develop a prognostic model to predict cognitive decline post-DBS

Supplemental Data:

	Patients with Cognitive Impairment (MCI/PDD)	**Patients without Cognitive Impairment**	**Total**	**P-value**
Evaluated Patients	49 (52%)	46 (48%)	95	
MCI	45 (47%)	-	45	
PDD	4 (4%)	-	4	
Excluded	14 (28%)	6 (13%)	20	0.13

Altered Targets	27 (56%)	8 (17%)	35	< 0.01
As planned	8 (16%)	39 (85%)	47	< 0.01
Bilateral Gpi	14 (29%)	6 (13%)	20	
Bilateral VIM	1 (2%)	-	1	
Unilateral VIM	12 (24%)	6 (13%)	18	
Unilateral STN	1 (2%)	-	1	

References:

Acknowledgements:

Learning Objectives: 1. Impact of Neuropsychological testing on patient selection 2. Impact of Neuropsychological testing on target selection 3. Importance of Neuropsychological assessment and follow up

Financial Disclosures: The main (L.W.) author has received research funding and speakers honoraria from Medtronic and Boston Scientific.

Disclosure: The presenting author received research grants and speakers' honoraria from Medtronic and Boston Scientific

220

Poster on Board
POSTER ON BOARD: AS04AB. BRAIN - INVASIVE: PSYCHIATRIC DISORDERS
13-05-2024 08:00 - 19:00

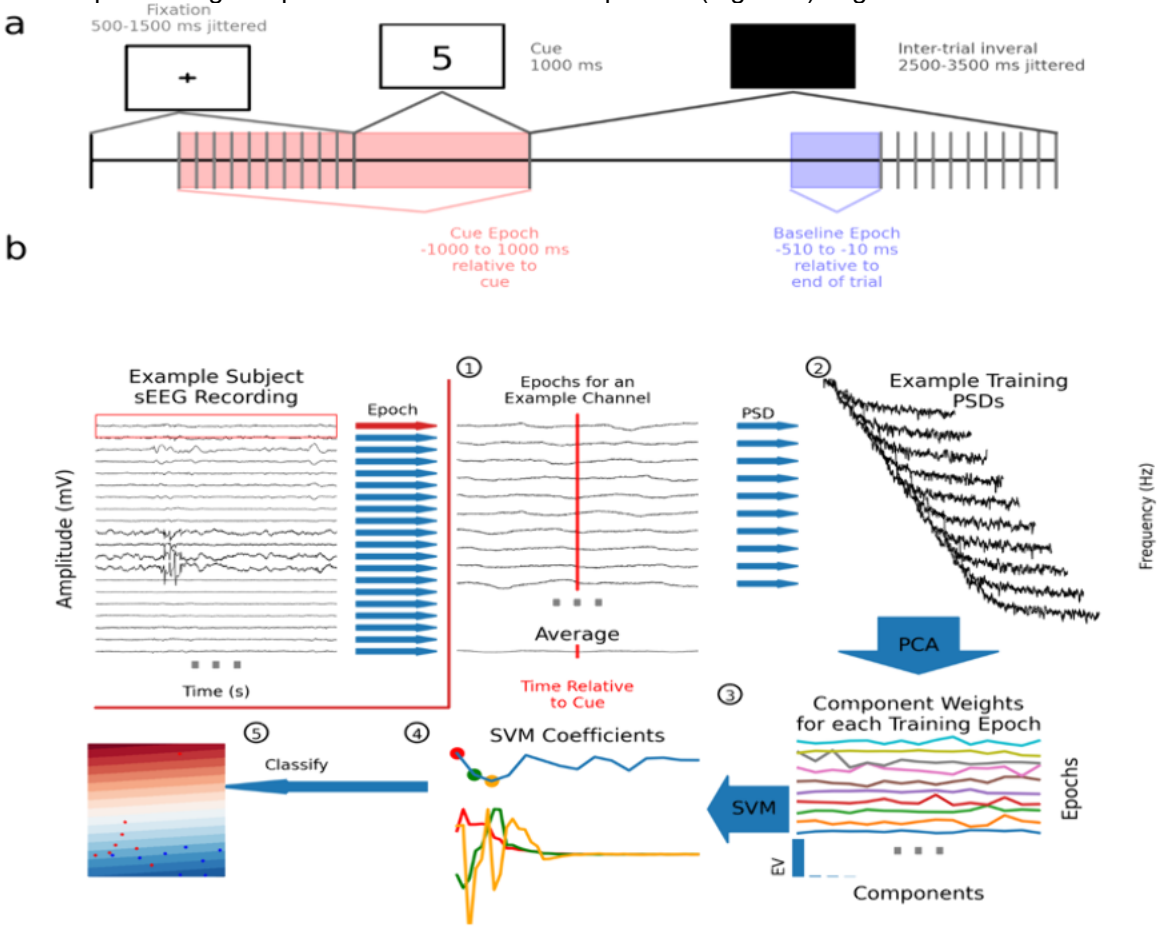
INVESTIGATING THE TRIPLE CODE MODEL IN NUMERICAL COGNITION USING INTRACRANIAL ELECTROENCEPHALOGRAPHY

Hao Tan, BSc (Hons), Alex Rockhill, PhD, Christian Lopez Ramos, MD, Maryam Shahin, MD, Erin Yamamoto, MD, Caleb Nerison, BSc (Hons), Ahmed Raslan, MD
Oregon Health & Science University, Portland, United States of America

Introduction: Comprehending numerical quantities is an essential human trait. Given the deleterious consequences associated with numeracy deficits, enhancing our knowledge of number processing is critical. The “Triple Code Model” (TCM) of numerical cognition theorizes that different neural substrates encode the processing of visual, auditory, and nonsymbolic numerical representation formats. While studies such as fMRI and TMS have supported this model, limited studies have examined the TCM using intracranial electroencephalography. In this study, we utilized human intracranial recordings to identify the neural correlates of symbolic and non-symbolic number processing.

Materials / Methods: We recorded from intracranial stereotactic EEG electrodes implanted in 13 patients with epilepsy. Subjects performed a passive numerical recognition task with numbers 1 to 9 presented in two representation formats: auditory (spoken numbers, sequential beeps) and visual (Arabic numeral, assortment of dots). Power spectral densities were computed for each task epoch and dimensionally reduced with principal component analysis (PCA). The PCA components were then passed into a linear support vector machine (SVM) classification algorithm to identify neural correlates

of number processing compared to inter-trial baseline periods (Figure 1). Figure 1:



Results: A total of 2,482 electrode contacts were analyzed. For visual numerical stimuli, the bilateral fusiform and left occipital regions demonstrated the highest classification accuracy (Figure 2). When stratified, Arabic numerical processing was greatest in the bilateral superior frontal, left parietal, and left superior temporal cortices. In contrast, accuracy was highest in the right supramarginal gyrus and left fusiform in response to numbers presented as dots. Auditory number stimuli were highly represented in the right fusiform, the left parietal, and left superior and inferior temporal regions. Stimuli presented as beeps were encoded in the left fusiform and left inferotemporal and superior parietal areas. In contrast, the left superior temporal and left superior frontal cortices showed the best classification values for spoken numbers. In response to numerical stimuli, irrespective of delivery modality, the temporal onset of high-frequency activity initially occurred in the superior temporal and inferior temporal regions, peaking later in the parietal region (Figure 3). Figure
2:

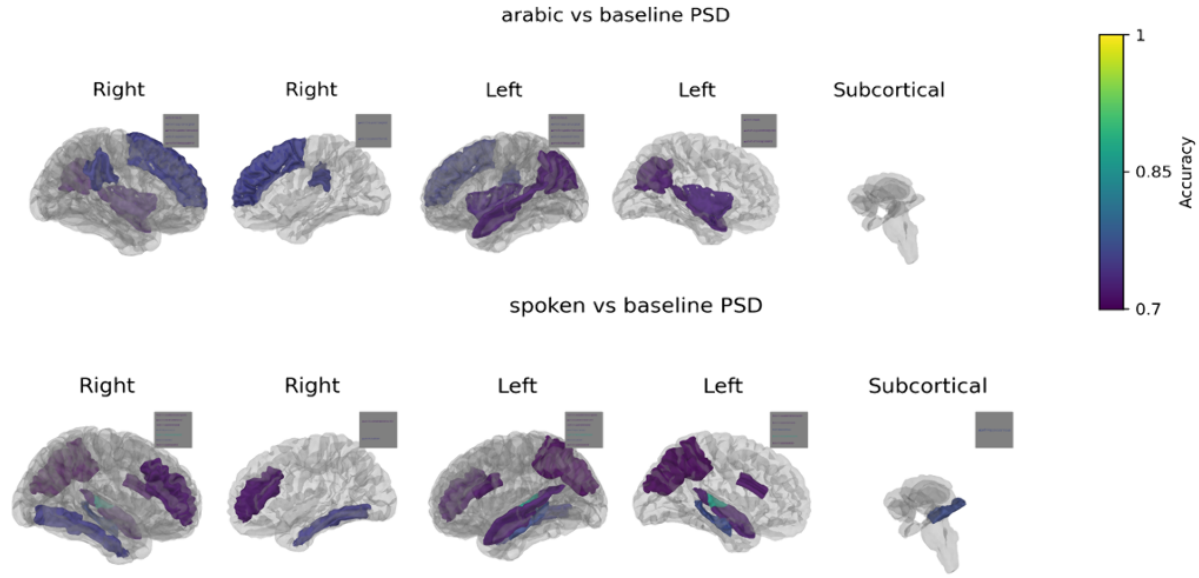
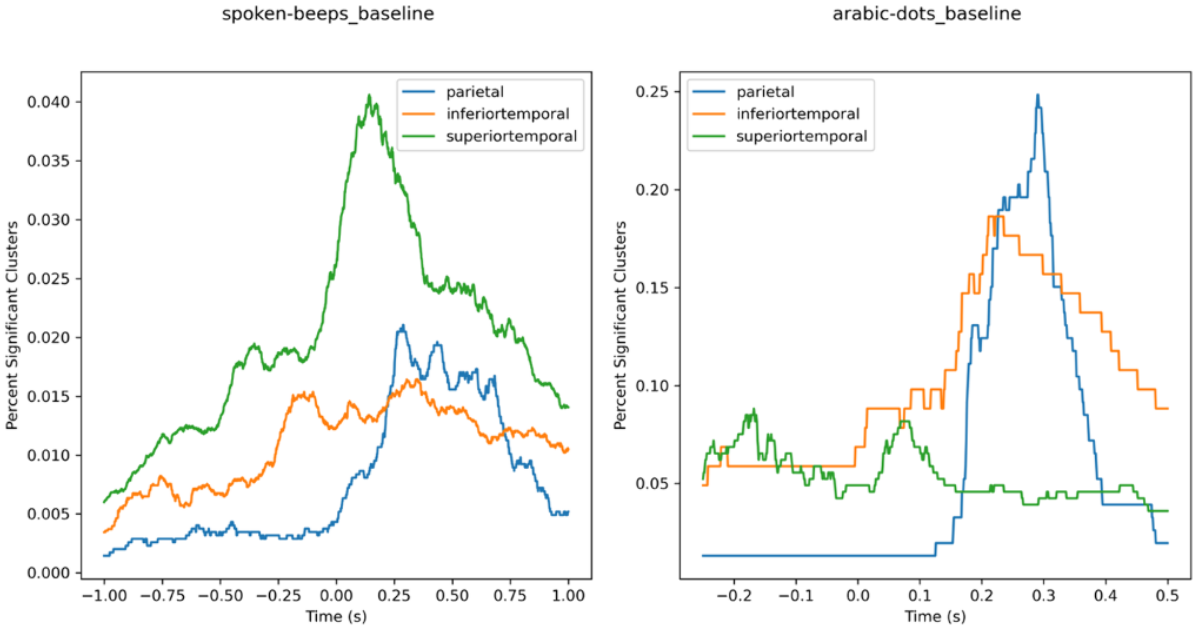


Figure 3:



Discussion: Using intracranial recordings, we found evidence that the superior temporal, inferior temporal, and parietal cortices are important in encoding visual, superior, and non-symbolic representation number formats, supporting the role of neural correlates postulated by the TCM.

Conclusions: Implementing a linear SVM classifier with PCA, we examined the Triple Code Model in numerical cognition and identified several neural structures with high classification values involved in number processing.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1. Identify neural correlates related to numerical processing from intracranial human recordings 2. Understand machine learning classification algorithm to decode neural

structures involved in number processing 3. Compare the Triple Code Model theory to neural correlates identified using intracranial EEG in the processing of auditory, visual, and non-symbolic representation formats

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

221

Poster on Board
POSTER ON BOARD: AS04AC. BRAIN - INVASIVE: EPILEPSY
13-05-2024 08:00 - 19:00

ASSESSING FUNCTIONAL THALAMO-CORTICAL CONNECTIVITY IN ADULTS WITH FRONTAL AND TEMPORAL LOBE EPILEPSY

Ana Marta Dias, MSc[1], João Paulo Cunha, PhD[1], Jan-Hinnerk Mehrkens, MD[2], Elisabeth Kaufmann, MD[2]
[1]INESC TEC, Porto, Portugal, [2]Ludwig-Maximilan's University, Munich, Neurology, Munich, Germany

Introduction: Epilepsy is a neurological disease characterized by recurrent and unpredictable seizures. It affects over 65 million people worldwide, from which over 1/3 are resistant to antiseizure medication [1,2]. For these cases, neuromodulation comes up as a promising alternative therapy, from which deep brain stimulation of the anterior thalamic nuclei (ANT-DBS) has been established as a safe and effective treatment [3,4]. The ANT has been proven to play a key role in epileptic seizure propagation, however, unravelling the exact mechanisms underlying ANT-DBS in epilepsy and predicting outcome remains a challenge [5]. Current evidence suggests that ANT-DBS in epilepsy induces cortical alterations that may support the corresponding antiseizure effect [6]. From these, the activation of regions associated with the default mode network (DMN) must be highlighted [7].

Materials / Methods: Simultaneous scalp and thalamic electroencephalography (EEG) signals were collected from two refractory epilepsy patients receiving ANT-DBS with a Percept™ PC neurostimulator, one with temporal lobe epilepsy (TLE) and the other with frontal lobe epilepsy (FLE). Resting-state awake EEGs were pre-processed in three steps: bandpass (1-70Hz) and notch (50Hz) filtering, noisy epoch removal, and independent component analysis. The latter step was not performed for thalamic channels. Further, frequency-dependent functional connectivity was estimated in a threefold manner: firstly, between the thalamus and cortex; secondly, limited to DMN regions post brain source reconstruction; and thirdly, exclusively for thalamic regions.

Results: Generally, interactions were stronger when in theta (4-8Hz) and alpha (8-13Hz) rhythms, irrespective of the epilepsy subtype. In alpha, information flows more prominently from the ANT to the cortex, particularly to regions associated with the DMN. Activation was observed, not only in the DMN, but also in regions beyond. Functional connectivity values were overall higher for the TLE patient. Finally, we were not able to define a consistent activation pattern within the thalamus.

Discussion: Results show that thalamo-cortical functional connectivity is largely dependent on the considered EEG rhythm. Higher connectivity values for the TLE patient may explain the associated better clinical outcomes in ANT-DBS. Other canonical brain networks may be associated with ANT-DBS in epilepsy, given the observed activation of several regions.

Conclusions: This work may shed light on the potential of studying thalamocortical connectivity and the brain rhythms modulating these in ANT-DBS, to better understand the fundamentals behind the clinical effectiveness of ANT-DBS. Nevertheless, a bigger cohort is needed to validate the findings across epilepsy subtypes.

Supplemental Data:

References: [1] Stafstrom C. E. and Carmant L. Seizures and Epilepsy: An Overview for Neuroscientists. Cold Spring Harb Perspect Med, 5(6):1–18, 2015. [2] Devinsky O., Vezzani A., Jette N., Curtis M., and Perucca P. Epilepsy. Nature Reviews Disease Primers 4, 3(18024), 2018. [3] Thijs D. R., Surges R., O'Brien T. J., and Sander J. W. Epilepsy in adults. Lancet, 393(10172):689–701, 2019 [4] Nasser Zangiabadi, Lady Diana Ladino, Farzad Sina, Juan Pablo Orozco-Hernández, Alexandra Carter, and José Francisco Téllez-Zenteno. Deep brain stimulation and drug-resistant epilepsy: A review of the literature. Frontiers in Neurology, 10, 2019. [5] Piper R. J., Richardson R. M., Worrell G., Carmichael D. W., Litt B. Baldeweg T., Denison T., and Tisdall M. M. Towards network-

guided neuromodulation for epilepsy. Brain, 145(10):3347–3362, 2022. [6] Giovanna Aiello, Debora Ledergeber, Tena Dubcek, Lennart Stieglitz, Christian Baumann, Rafael Polanìa, and Lukas Imbach. Functional network dynamics between the anterior thalamus and the cortex in deep brain stimulation for epilepsy. Brain, page awad211, 06 2023. [7] Artur Vetkas, Jürgen Germann, Gavin Elias, Aaron Loh, Alexandre Boutet, Kazuaki Yamamoto, Can Sarica, Nardin Samuel, Vanessa Milano, Anton Fomenko, Brendan Santyr, Jordy Tasserie, Dave Gwun, Hyun Ho Jung, Taufik Valiante, George M Ibrahim, Richard Wennberg, Suneil K Kalia, and Andres M Lozano. Identifying the neural network for neuromodulation in epilepsy through connectomics and graphs. Brain Communications, 4(3), 04 2022.

Acknowledgements: The authors would like to acknowledge the participants of this study, by contributing to the scientific advancement of the research area. This work is financed by National Funds through the Portuguese funding agency, FCT - Fundação para a Ciência e a Tecnologia, within project LA/P/0063/2020.

Learning Objectives: 1. Attendees will analyse a contribution to the definition of putative biomarkers for various applications in DBS. 2. Participants will break down specific thalamo-cortical connectivity patterns distinguishing frontal versus temporal lobe epilepsy. 3. Attendees will be able to recognise the potential of functional connectivity studies as a huge asset to understand the mechanisms underlying ANT-DBS.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

222

Poster on Board
POSTER ON BOARD: AS04AC. BRAIN - INVASIVE: EPILEPSY
13-05-2024 08:00 - 19:00

FEASIBILITY OF DETECTION OF AN EPILEPTIC SEIZURE BIOMARKER ON THE VAGUS NERVE IN PIGS

Ilya Tarotin, PhD[1], Benjamin Metcalfe, PhD[2], Christopher Beach, PhD[1], Justin Perkins, BVetMed MS CertES Dip ECVS MRCVS[3], Mafalda Ribeiro, MSc[2], Sud Sivaneswaran, MSc[1], Matthew Zhang, -[1], Hannah Claridge, PhD[1], Alex Stokoe, MSc[1]
[1]TTP plc, Ttp Campus, Melbourn, United Kingdom, [2]University of Bath, Electronic & Electrical Engineering, Bath, United Kingdom, [3]The Royal Veterinary College, Clinical Science And Services, Hatfield, United Kingdom

Introduction: Epilepsy is a major neurological condition affecting 1% of the global population, with about 1/3rd of the cases not responding to conventional drug treatment [1]. VNS (vagus nerve stimulation) is an approved treatment modality for drug-resistant epilepsy, but it lacks selectivity resulting in non-optimal treatment outcomes and multiple side effects [2]. This study aims at the detection and characterisation of a biomarker of epileptic seizures on the vagus nerve (VN) using the porcine model in vivo. The results will inform the feasibility of real-time closed-loop VNS for epilepsy based on the primary biomarker.

Materials / Methods: Three anaesthetised pigs were used for simultaneous electroneurogram (ENG) and electrocorticogram (ECoG) recordings (Fs=50kHz). For ENG, nerve cuffs with ten longitudinally placed ring electrodes were implanted on both branches of the VN. For ECoG, 2x1 subdural electrodes were placed on the temporal lobe to monitor seizures. Seizures were induced by an intracranial injection of 0.1-0.2 mL of procaine benzylpenicillin (300 mg/ml). All animals were given pancuronium for muscle relaxation. The presence of biomarker was initially investigated by measurement of the correlation of the ENG signal in the frequency domain with seizures represented as 0-1 steps, where 0 – the time before seizure, and “1” – after seizure.

Results: Multiple seizures were observed during each experimental day. The average RMS noise in the ENG over a 10-ms window was <15 μV in all experiments. One-second window moving variance analysis of ENG has uncovered patterns correlated with breathing (Figure 1a) in accordance with [3]. Correlation analysis of ENG frequency spectra with seizure starting time did not reveal obvious biomarkers of seizure versus pre-seizure activity (Figure 1b). The reason may be that penicillin induces a pre-seizure state straight after injection, as seen in the alteration of baseline ECoG (Figure 1c).

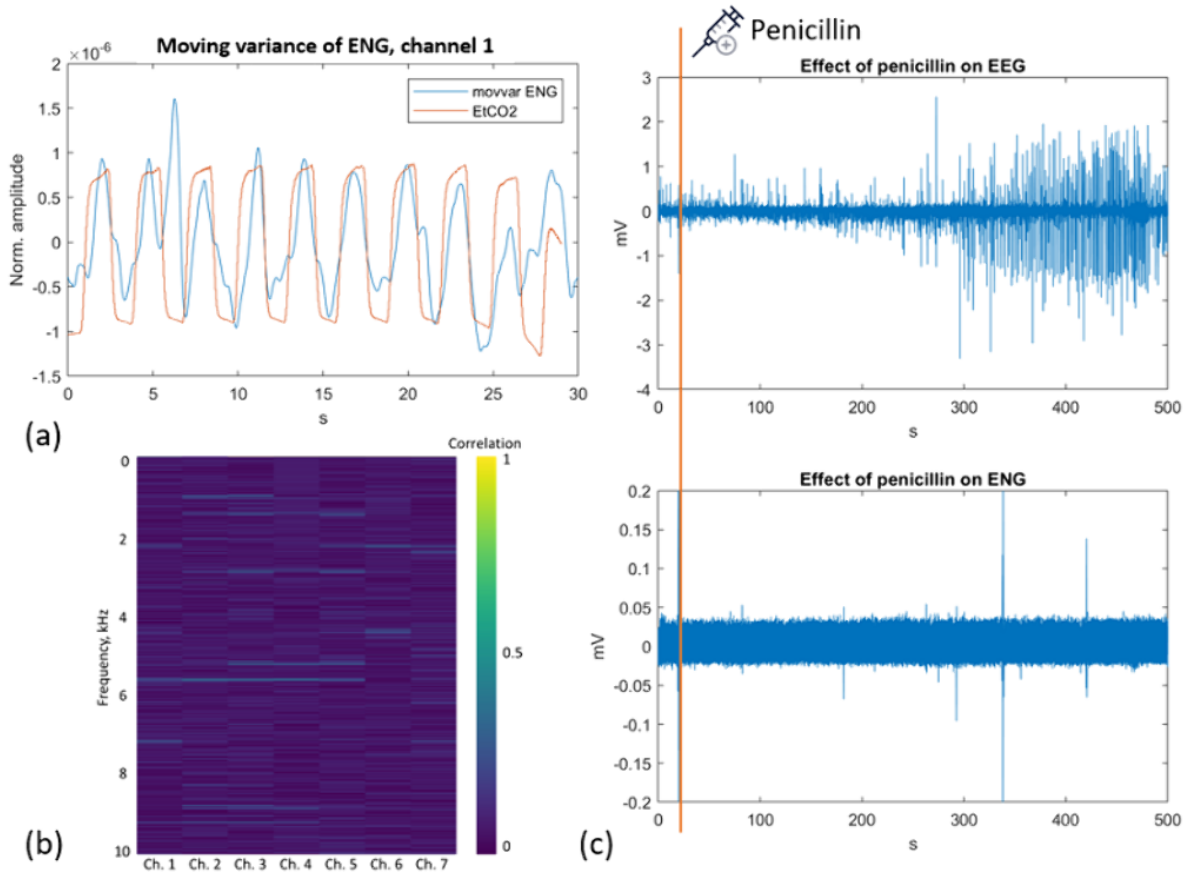


Figure 1. (a) Moving variance of 0.25-10 kHz filtered ENG signal (blue) and respiration signal (red); (b) Correlation of right VN ENG Fourier spectra with the seizure (0-1 step); (c) Change in ECoG and ENG activity after penicillin injection.

Discussion: This study develops an approach and experimental protocol to detect a biomarker of epileptic seizures in pigs to unlock closed-loop VNS for epilepsy. Future work includes further data analysis including Bayesian and Fourier methods.

Conclusions: The experimental protocol developed in this study can be utilised for studying the VN response during epilepsy in various settings. The closed-loop VNS based on seizure biomarker recorded on the VN will improve therapy efficacy and reduce side effects.

Supplemental Data:

References: 1. WHO. Epilepsy, https://www.who.int/news-room/fact-sheets/detail/epilepsy 2. Ryvlin, Philippe, et al. "Neuromodulation in epilepsy: state-of-the-art approved therapies." The Lancet Neurology 20.12 (2021): 1038-1047. 3. Metcalfe, B. W., et al. "First demonstration of velocity selective recording from the pig vagus using a nerve cuff shows respiration afferents." Biomedical Engineering Letters 8 (2018): 127-136.

Acknowledgements:

Learning Objectives: 1. Develop an experimental protocol for the detection of seizure biomarkers on the VN. 2. Develop a signal processing method to determine presence of seizure biomarkers on the VN. 3. Study the properties of seizure biomarkers on the VN.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

223

Poster on Board
POSTER ON BOARD: AS04AC. BRAIN - INVASIVE: EPILEPSY
13-05-2024 08:00 - 19:00

DEEP BRAIN STIMULATION FOR EPILEPSY: META-ANALYSIS OF OUTCOMES AND CONNECTOMIC UNDERPINNINGS

Artur Vetkas, MD, Alexandre Boutet, MD, Jürgen Germann, PhD, Mojgan Hodaie, MD, Suneil Kalia, MD, Andres Lozano, MD
Toronto Western Hospital - University of Toronto, Neurosurgery, Toronto, Canada

Introduction: The primary aim of the systematic review and meta-analysis is to summarize recent advancements in epilepsy deep brain stimulation (DBS), compare trial results, and assess its clinical utility in drug-resistant epielpsy (DRE). The secondary goal is to identify neural networks linked to DBS targets for epilepsy and explore their potential as new biomarkers for neuromodulation.

Materials / Methods: Two independent authors conducted a systematic literature search, resulting in 44 articles for a meta-analysis involving 527 patients across three brain regions: anterior thalamic nucleus (ANT), centromedian thalamic nucleus (CMT), and hippocampus. Functional connectivity maps from 1000 normative fMRI scans were analyzed to identify brain areas linked to seizure outcomes. Overlaps in connectivity among ANT, CMT, hippocampus, and other epilepsy targets were studied. MRI-derived measures were also used to assess neuroanatomical differences (n=15) and longitudinal changes (n=7) in long-term ANT DBS using deformation-based morphometry (DBM) analyses.

Results: The mean seizure reduction after stimulation of the ANT, CMT, and hippocampus in our meta-analysis was 60.8%, 73.4%, and 67.8%, respectively. DBS is an effective and safe therapy in patients with DRE. Cortical nodes identified in the normative epilepsy DBS network were in the anterior and psterior cingulate, medial frontal and sensorimotor cortices, frontal operculum and bilateral insulae. Subcortical nodes of the network were in the basal ganglia, mesencephalon, basal forebrain, and cerebellum. The ANT was identified as a central hub in the network with the highest betweenness and closeness values. The caudate nucleus and mammillothalamic tract also displayed high centrality values. The anterior cingulate cortex was identified as an important cortical hub associated with the effect of DBS in epilepsy. Two cortical clusters identified in the epilepsy DBS network included regions corresponding to physiological resting state networks, mainly the default mode and salience networks. The DBM analysis revealed volumetric changes in multiple cortical regions corresponding to the normative network of neuromodulation in epilepsy. Additionally, a smaller preoperative volume of the amygdala was associated with better response to DBS. The DBS neural network shared hubs with known epileptic networks and brain regions involved in seizure propagation and generalization.

Discussion: Recent studies confirm the satisfactory results of the ANT DBS in DRE and responsive neural stimulation of the hippocampus.

Conclusions: We described a brain network common to epilepsy neuromodulation based on normative functional connectivity. The cortico-subcortical network underpins the mechanisms of seizure generation and propagation, and effects of neuromodulation. In the future, DBS treatment could be tailored to individual patients and disease-specific networks.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. Describe the neural network associated with clinically important deep brain stimulation (DBS) targets for epilepsy (anterior thalamic nucleus (ANT), centromedian thalamic nucleus (CMT), hippocampus (HC) based on resting state functional connectivity maps, and outcomes of the meta-analysis of DBS in epilepsy. The mean seizure reduction after stimulation of the ANT, CMT, and hippocampus in our meta-analysis was 60.8%, 73.4%, and 67.8%, respectively. The functional networks of the DBS targets (ANT, CMT, HC) have an overlap with patterns of connectivity associated with less studied epilepsy DBS targets and epilepsy pathophysiology. This suggests that there is a common cortico-subcortical network shared by these targets, which may be responsible for the antiseizure action of DBS. 2. Examine how the functional networks of key DBS targets relate to each other, epilepsy pathophysiology, and canonical resting state networks. The study identified a novel brain network associated with DBS targets used for epilepsy by analyzing seed-to-voxel functional connectivity maps from resting state fMRI scans. Cortical nodes in this "epilepsy DBS network" included the anterior and posterior cingulate, medial frontal and sensorimotor cortex, frontal operculum, and bilateral insulae. Subcortical nodes included the basal ganglia, mesencephalon, basal forebrain, and cerebellum. 3. Analyze the relationship between regions in the identified epilepsy DBS network using graph analysis of functional connectivity. Graph analysis revealed ANT and anterior cingulate cortex as a central hub. The network overlapped with known epileptic networks and regions involved in seizure propagation/generalization. It also overlapped with the default mode and salience networks. The results were supported by previous patient fMRI studies and deformation based morphometry analysis of patients undergoing DBS of ANT.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

224

Poster on Board
POSTER ON BOARD: AS04AD. BRAIN - INVASIVE: NEUROREHABILITATION
13-05-2024 08:00 - 19:00

HOW LONG DOES DEEP BRAIN STIMULATION GIVE PATIENTS BENEFIT? A SCOPING REVIEW

Julie Pilitsis, MD, PhD[1], Esin Bulut, MSc[2], Alya Elbualy, N/A[2], Cheyenne Kalman, BS[2], Ryan Mayer, BS[2], Nicholas Kato, BS[2], Rodrigo Salmeron De Toledo Aguiar, MD[2]
[1]Charles E. Schmidt College of Medicine, Florida Atlantic University, Boca raton, United States of America, [2]Florida Atlantic University, Boca Raton, United States of America

Introduction: Since the advent of deep brain stimulation (DBS) in 1987, one prevailing question has been- how long will patients benefit? Here we performed a scoping review to define longevity of the therapy in different disease states and longevity of device components and techniques to augment battery life.

Materials / Methods: The authors performed a MEDLINE search inclusive of articles from 1987 to June 2023 including human and modeling studies written in English. For longevity of therapy studies, only studies with a mean follow up of 3 years or more were included. Using the Rayyan platform, two reviewers (J.P. and R.M.) performed a title screen. Of the 731 articles, 205 were selected by title screen and 109 from abstract review. Ultimately after references from the manuscripts identified were assessed a total of 133 articles were reviewed. The research questions we explore are: 1) how long do device components last? and 2) how long does DBS therapy last in Parkinson's Disease (PD) (a), essential tremor (ET) (b), dystonia (c), and other disorders (d)?

Results: We demonstrate that patients with PD, ET and dystonia maintain considerable long-term benefit in motor scores 7 to 10 years after implant, though the percentage improvement decreases over time. STIM OFF scores in PD and ET show worsening, consistent with disease progression. Battery life varies by the disease treated and the programming settings used. Higher amplitudes and longer pulse widths are associated with shorter duration while cycling and turning the device off (in ET) is associated with longer battery life.

Discussion: Here we are able to provide data to health care teams caring for DBS patients on what to expect from their devices as their disease progresses and describe techniques to minimize battery revision/recharging.

Conclusions: Outcomes data after 10 years of therapy is a gap in the literature.

Supplemental Data:

References: none

Acknowledgements:

Learning Objectives: 1) How long do device components last 2) How long does DBS therapy last in Parkinson's Disease 3)How long does DBS therapy last in Other disorders such as: Essential Tremor, Dystonia, and etc.

Financial Disclosures: Dr. Pilitsis receives grant support from Medtronic, Boston Scientific, Abbott, NIH 2R01CA166379, NIH R01EB030324, and NIH U44NS115111. She is the medical advisor for Aim Medical Robotics and has stock equity. RTA receives fellowship support from Medtronic, Abbott and Boston Scientific.

Disclosure: No significant relationships.

225

Poster on Board
POSTER ON BOARD: AS04AE. BRAIN - INVASIVE: PAIN
13-05-2024 08:00 - 19:00

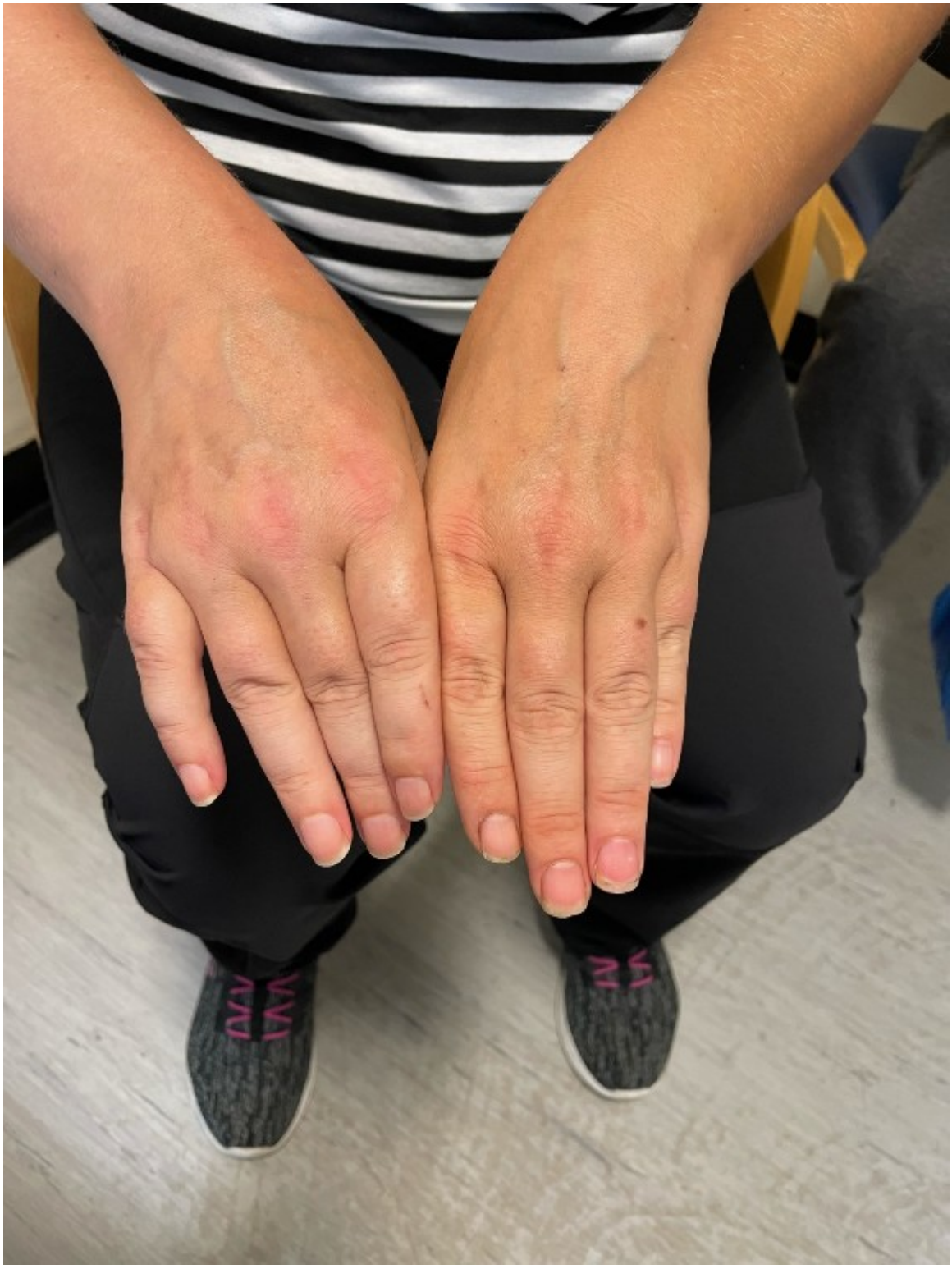
CERVICAL SCS FOR MANAGEMENT OF CENTRAL NEUROPATHIC PAIN FOLLOWING GLIOBLASTOMA RESECTION

Sheila Black, MB ChB[1], Hollie Watson, RN[2]
[1]Leeds teaching hospitals NHS trust, Pain Management, Leeds, United Kingdom, [2]Leeds Teaching Hospitals NHS Trust, Pain Management Department, Leeds General Infirmary, Leeds, United Kingdom

Introduction: Glioblastoma multiforme is an aggressive, fast-growing brain tumour which invades nearby brain tissue. Occuring mainly in the cerebral hemispheres, especially the frontal and parietal lobes, is it a devastating brain tumour resulting in death within 6 months if untreated. The average survival is 12-18 months, with 25% surviving more than one year, and less than 5% surviving more than 5 years. Treatment involves surgical resection/debulking, chemotherapy and radiotherapy. Following curative treatment, patients can be left with debilitating sequelae, including permanent neurological deficit, sensory disturbance, and persistant central neuropathic pain. Treatment of the central neuropathic pain can be resistant to treatment with conventional antineuropathic agents, and options for neuromodulation would significantly improve the quality of life for this group of cancer survivors.

Materials / Methods: The authors present the case of a 36 year old female who suffered glioblastoma multiforme, undergoing 3 surgical resections to debulk the tumour, 30 fractions of radiotherapy and 3 cycles of PCV chemotherapy. She achieved >90% resection, and has confirmed stable disease. However, she suffers expressive aphasia, and persistent central neuropathic pain involving right arm. Conventional medical management with antineuropathic agents were not helpful, and so spinal cord stimulation was considered. Medical advice warned that due to the central nature of the pain, then neuromodulation at cervical spinal cord level may not be helpful in her case, though it was felt by the multidisciplinary team appropriate to conduct a 2 week temporary trial. A percutaneous trial was undertaken with on-tabel paearsthesia mapping which confirmed coverage of entire painful right arm.

Results: The trial was successful, with significantly reduced neuropathic pain in whole right arm. Patient was able to lift her arm above her head, which was previously impossible due to weakness. The skin in arm which had been pale was returned to pink, comparable to her other hand. She was visibly more content, and was able to converse with her husband in her native language.



Discussion: The authors report success in managing central neuropathic pain using percutaneous neuromodulation techniques. This opens possibilities of pain relief to those patients who would have been denied more invasive neuromodulation therapies such as deep brain stimulation. This implies a central mode of action which ascends to cover neural pathways in the cerebral hemispheres, using placement of cervical spinal stimulating electrodes.

Conclusions: This case report demonstrates successful management of central neuropathic pain following surgery and chemoradiotherapy to frontal glioblastoma, by means of percutaneous placement of cerivcla spinal cord stimulator.

Supplemental Data:

References: 1. Thakkar et al, Glioblastoma multiforme. Americal Association of Neurological surgery. Glioblastoma Multiforme – Symptoms, Diagnosis and Treatment Options (aans.org) Accessed 31/10/2023.

Acknowledgements:

Learning Objectives: 1. Explore the management of glioblastoma multiforme and central neuropathic pain. 2. Demonstrate positive trial of percutaenous SCS and assessment of outcomes. 3. Explore the theoretical explanations for managing central neuropathic pain, originating in the cerebral hemispheres by means of spinal cord epidural electrode.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

226

Poster on Board
POSTER ON BOARD: AS04AE. BRAIN - INVASIVE: PAIN
13-05-2024 08:00 - 19:00

MOTOR CORTEX STIMULATION AND FUNCTIONAL CONNECTIVITY; A FEASIBILITY STUDY

Jeremy Hanemaaijer, BSc (Hons)[1], Amir Divanbeighi Zand, BA BM BCh[2], John Eraifej, MB ChB[2,3], Alexander Green, PhD FRCS(SN)[2,3], Erkan Kurt, MD[1]
[1]Radboud University Medical Center, Neurosurgery, Nijmegen, Netherlands, [2]University of Oxford, Nuffield Department Of Surgical Sciences, Oxford, United Kingdom, [3]University of Oxford, Nuffield Department Of Clinical Neurosciences (ndcn), Medical Sciences Division, Oxford, United Kingdom

Introduction: Since the 1990s Motor Cortex Stimulation (MCS) is a last-resort neurosurgical therapy to treat intractable neuropathic pain [1]. Despite the experience of over 30 years, the inconsistent results of MCS divided the opinion on the utility of this therapy. This is mainly contributed to the incomplete understood mechanisms of action in MCS, discrepancies of the procedure, as well as the poor methodology employed in several clinical studies [2]. Therefore, a feasibility study is conducted to investigate the functional connectivity between the location of the electrode and several brain regions.

Materials / Methods: Two patients who underwent MCS were included in this study. One patient was classified as a responder (pain reduction of ≥30% on the Visual Analogue Scale), the other patient was a non-responder. Neuroanatomic resting-state functional connectivity was quantified between, MNI-transformed *"areas of activation"* and pre-specified regions defined by the AAL V3 Atlas [3]. The following AAL regions were included: *the anterior cingulate cortex (pregenual, subgenual, supracallosal), rectus gyrus, orbitofrontal cortex (anterior, lateral, medial, posterior), periaqueductal grey, ventral anterior nucleus of the thalamus, ventral lateral nucleus of the thalamus and ventral posterolateral nucleus of the thalamus*.

Results: There was a notable difference observed in functional connectivity between the responder and non-responder. In particular, the difference in functional connectivity between the *"areas of activation"* and two specific brain regions was observed, namely the anterior cingulate cortex supracallosal and the thalamic nuclei. The primary contrast arises from the location of cathodal stimulation on the motor cortex, resulting in the strongest functional connectivity with the aforementioned brain regions. This observation indicates that the cathodal electrode in the non-responder may be placed too far from the surface of the motor

cortex.

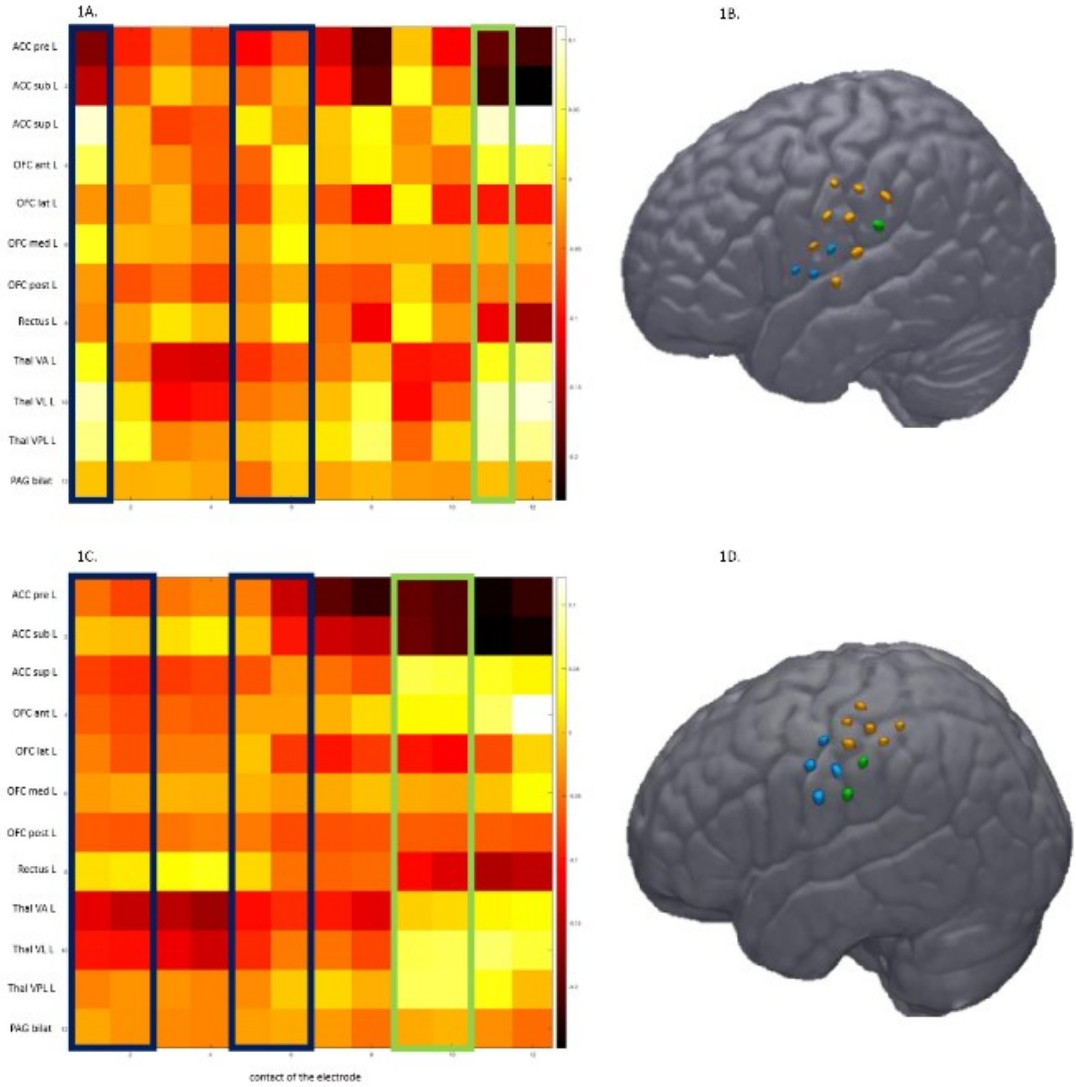


Figure 1: functional connectivity between electrode configuration "best moment" and different brain regions in a responder vs non-responder.
Blue = Cathode (- pole); Green = anode (+ pole)
***Responder**: Figure 1A & 1B; **Non-responder**: Figure 1C & 1D*
ACC_pre_L = anterior cingulate cortex pregenual left; ACC_sub_L = anterior cingulate cortex subgenual left; ACC_sup_L = anterior cingulate cortex supracallosal left; OFC_ant_L = anterior orbital gyrus left; OFC_lat_L = lateral orbital gyrus left; OFC_med_L = medial orbital gyrus left; OFC_post_L = posterior orbital gyrus left; Rectus_L = gyrus rectus left; Thal_VA_L = ventral anterior nucleus thalamus left; Thal_VL_L = ventral lateral nucleus thalamus left; Thal_VPL_L = ventral posterolateral nucleus thalamus left; PAG_bilat = periaqueductal grey matter bilateral

Discussion: These results suggest a possible association between the placement of the electrode epidurally and functional connectivity differences between responders and non-responders of this last-resort neurosurgical therapy. This study demonstrates the feasibility of electrode reconstruction, image co-registration and connectivity quantification using a normative functional connectome. Due to the inclusion of two individual cases in this feasibility study, statistical analysis between the two cases was not valuable.

Conclusions: The outcome of this study shows that it is feasible and valuable to investigate functional connectivity between the *"areas of activation"* and several brain regions in MCS patients. In addition, this study indicates that probably appropriate positioning of the MCS electrode is necessary to induce pain relief in intractable neuropathic pain patients.

Supplemental Data:

References: 1.Tsubokawa T, Katayama Y, Yamamoto T, Hirayama T, Koyama S. Chronic motor cortex stimulation for the treatment of central pain. Acta Neurochir Suppl (Wien). 1991;52:137-9. doi:

10.1007/978-3-7091-9160-6_37. PMID: 1792954. 2.Kurt E, Henssen DJHA, Steegers M, Staal M, Beese U, Maarrawi J, Pirotte B, Garcia-Larrea L, Rasche D, Vesper J, Holsheimer J, Duyvendak W, Herregodts P, van Dongen R, Moens M. Motor Cortex Stimulation in Patients Suffering from Chronic Neuropathic Pain: Summary of Expert Meeting and Premeeting Questionnaire, Combined with Literature Review. World Neurosurg. 2017 Dec;108:254-263. doi: 10.1016/j.wneu.2017.08.168. Epub 2017 Sep 4. PMID: 28882715. 3.Rolls ET, Huang CC, Lin CP, Feng J, Joliot M. Automated anatomical labelling atlas 3. Neuroimage. 2020 Feb 1;206:116189. doi: 10.1016/j.neuroimage.2019.116189. Epub 2019 Sep 12. PMID: 31521825.

Acknowledgements:

Learning Objectives: 1. It is valuable to investigate the correlation between the location of the electrode and the clinical outcome. 2. It is feasible to use electrode reconstruction, image co-registration and connectivity quantification using a normative functional connectome in MCS patients. 3. Functional connectivity could potentially contribute to new insights into the underlying mechanisms of action in MCS.

Financial Disclosures: 'No significant relationships'

Disclosure: No significant relationships.

227

Poster on Board
POSTER ON BOARD: AS04BB. BRAIN - NON-INVASIVE STIMULATION: PSYCHIATRIC DISORDERS
13-05-2024 08:00 - 19:00

PREDICTION OF EFFECTIVENESS AND EARLY STOPPING OF TREATMENT USING FUNCTIONAL NEAR-INFRARED SPECTROSCOPY SIMULTANEOUSLY RECORDED DURING HOME-BASED TRANSCRANIAL PHOTOBIOMODULATION THERAPY IN OLDER ADULTS WITH COGNITIVE DECLINE

Minyoung Chun, MS student[1], Kyeonggu Lee, phD candidate[1], Seung-Hwan Lee, PhD[2], Chang-Hwan Im, PhD[1]
[1]Hanyang university, Seoul, Korea, Republic of, [2]Inje university, Goyang, Korea, Republic of

Introduction: Transcranial photobiomodulation (tPBM) has shown a potential to improve cognitive function in older adults with cognitive decline [1,2]. However, a part of old adults with cognitive decline has demonstrated a lack of response to tPBM [3]. In this regard, to enhance the cost-effectiveness of tPBM therapy, we attempted to screen out tPBM non-responders in the early stage by using graph-theoretical indices of the prefrontal functional connectivity network estimated with functional near-infrared spectroscopy (fNIRS) signals simultaneously recorded during tPBM for 12 weeks.

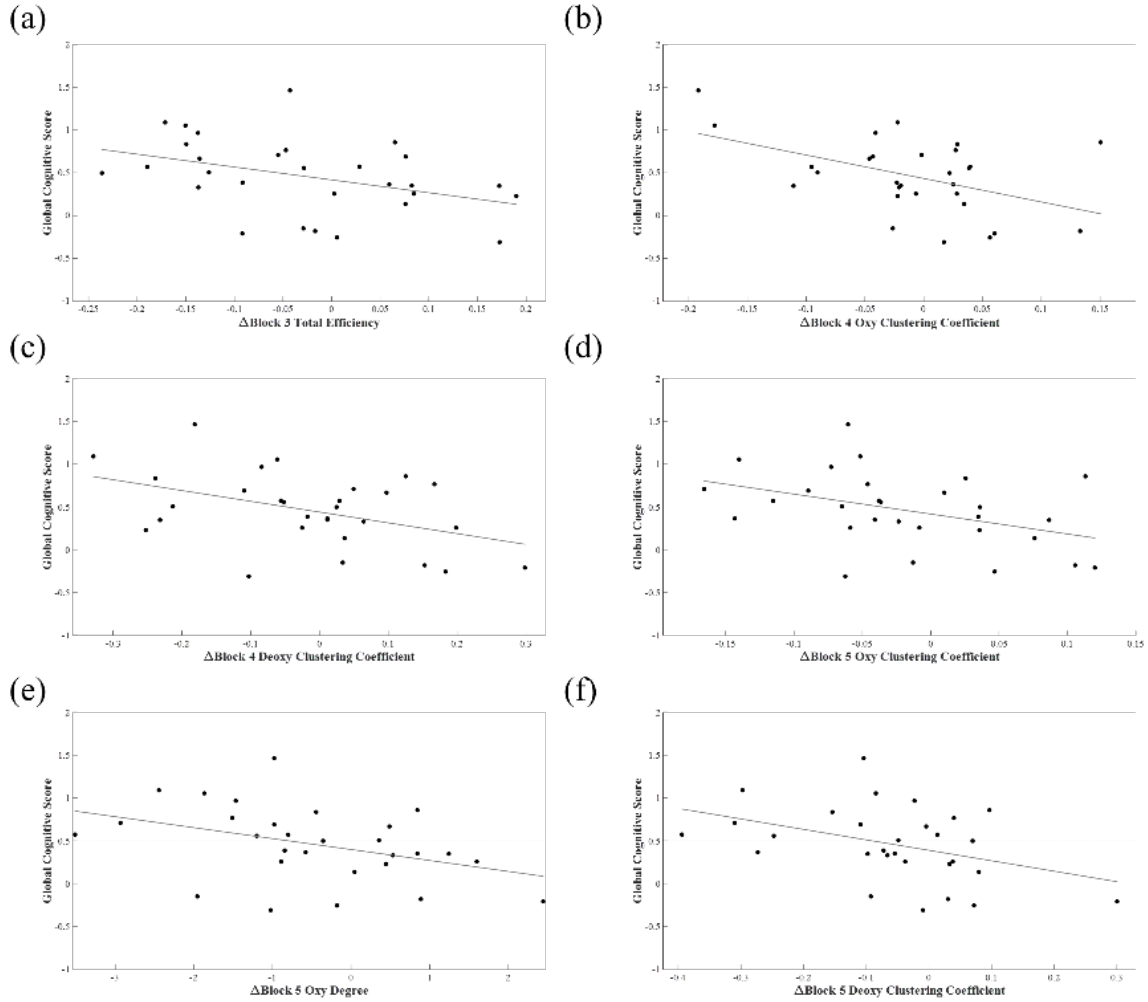
Materials / Methods: The data from 29 participants were used for analysis. Fifteen trials were randomly selected among the initial 20 sessions of tPBM therapy. Subsequently, the 15 trials were sequentially allocated to five blocks. Each graph-theoretical index of each block was analyzed by Pearson correlation coefficient with the global cognitive score (GCS) which represents the change in cognitive function between baseline and post-stimulation. With these graph-theoretical indices, a simple linear regression was performed for the early prediction of non-responders. Those whose regression results were below the threshold of 0.35 were classified as non-responders of tPBM therapy.

Results: The efficiency change of total-hemoglobin change (ΔHbT) in block 3, the clustering coefficient change of oxy-hemoglobin change (ΔHbO) and deoxy-hemoglobin change (ΔHbR) in block 4, and the clustering coefficient change of ΔHbO and ΔHbR and the degree change of ΔHbO in block 5 had a significant negative correlation with GCS. In each of the blocks, specifically block 3, block 4, and block 5, nine, three, and one participant, respectively, were classified as non-responders. It was found that two individuals who actually responded to the tPBM therapy were erroneously categorized as non-responders. Consequently, 11 out of 13 participants postulated as non-responders revealed to be non-responders after the tPBM sessions.

Discussion: The novel method for predicting the effectiveness of tPBM therapy and the early stopping of treatment using fNIRS has shown promise. In the future, it will be necessary to incorporate additional data to enhance the generalizability of our findings.

Conclusions: The present study demonstrated that the graph-theoretical index of prefrontal functional connectivity using fNIRS signals could be a potential biomarker for assessing the effectiveness of tPBM therapy.

Supplemental Data:



References: [1] Vargas, E., et al., *Beneficial neurocognitive effects of transcranial laser in older adults.* Lasers Med Sci, 2017. **32**(5): p. 1153-1162. [2] Chan, A.S., et al., *Photobiomodulation Enhances Memory Processing in Older Adults with Mild Cognitive Impairment: A Functional Near-Infrared Spectroscopy Study.* J Alzheimers Dis, 2021. **83**(4): p. 1471-1480. [3] Staudt, M.D., et al., *Evolution in the Treatment of Psychiatric Disorders: From Psychosurgery to Psychopharmacology to Neuromodulation.* Front Neurosci, 2019. **13**: p. 108.

Acknowledgements: This work was supported by the Korea Medical Device Development Fund grant funded by the Korea government (the Ministry of Science and ICT, the Ministry of Trade, Industry and Energy, the Ministry of Health & Welfare, Republic of Korea, the Ministry of Food and Drug Safety) (Project Number: 202013B10)

Learning Objectives: 1. Demonstration of the effectiveness of tPBM therapy using diverse cognitive tasks. 2. The cost-effectiveness strategy for tPBM therapy in older adults with cognitive decline. 3. Proposal of the biomarkers of identifying non-responders of tPBM therapy using fNIRS.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

228

Poster on Board
POSTER ON BOARD: AS04BB. BRAIN - NON-INVASIVE STIMULATION: PSYCHIATRIC DISORDERS
13-05-2024 08:00 - 19:00

TRANSCRANIAL MAGNETIC STIMULATION VERSUS IMPULSIVITY: LITERATURE REVIEW

Ivete Ferrraz, MSc, Mario Ferraz Filho, BSc (Hons), Amanda Ferraris, MD
Neuromood - TMS, Neuromodulation, Curitiba, Brazil

Introduction: Transcranial Magnetic Stimulation is a non-invasive brain stimulation (NIBS) method that has been widely studied and may be one of the keys to the treatment of impulsivity, a symptom that is part of several disorders in psychiatry. However, there are only few studies with a specific focus on impulsivity, so this review was carried out, with articles that bring rTMS to treat some disorders that have impulsivity as a common symptom.

Materials / Methods: The literature research was performed between the Years of 2013 and 2023,following these databases: PUBMED, SCIELO, GOOGLE SCHOLAR e WEB OF SCIENCE with the following Keywords: Transcranial Magnetic Stimulation, neuromodulation, impulsiveness, suicide, obsessive compulsive disorder, NIBS and decision making. Systematic reviews, case studies and case reports were excluded from the analysis.

Results: The articles presentes varied protocols for the use of TMS, but all 21 articles included use TMS to treat or to study psychiatric disorders in which impulsivity is part of the symptom, such as suicidal desire, Bordeline personality disorder (BPD), Generalized Anxiety Disorder (GAD) and compulsive disorders as gambling disorder (GD), Substanse Use Disorder (SUD) and Impulse Control Disorder (ICD).

Discussion: The articles presentes varied protocols for the use of TMS, but all 21 articles included use TMS to treat or to study psychiatric disorders in which impulsivity is part of the symptom, such as suicidal desire, Bordeline personality disorder (BPD), Generalized Anxiety Disorder (GAD) and compulsive disorders as gambling disorder (GD), Substanse Use Disorder (SUD) and Impulse Control Disorder (ICD).

Conclusions: This review shows a tendency for the use of TMS in symptoms of impulsivity, since more than Half of the articles bring a good repercussion of its use in relation to impulsivity, despite the diversity of protocols.

Supplemental Data:

References: Cirillo G, Di Pino G, Capone F, Ranieri F, Florio L, Todisco V, Tedeschi G, Funke K, Di Lazzaro V. Neurobiological after-effects of non-invasive brain stimulation. Brain Stimul. 2017 Jan-Feb;10(1):1-18. doi: 10.1016/j.brs.2016.11.009. Epub 2016 Nov 17. PMID: 27931886. Brevet-Aeby C, Brunelin J, Iceta S, Padovan C, Poulet E. Prefrontal cortex and impulsivity: Interest of noninvasive brain stimulation. Neurosci Biobehav Rev. 2016 Dec;71:112-134. doi: 10.1016/j.neubiorev.2016.08.028. Epub 2016 Aug 30. PMID: 27590833. De Vidovich GZ, Muffatti R, Monaco J, Caramia N, Broglia D, Caverzasi E, Barale F, D'Angelo E. Repetitive TMS on Left Cerebellum Affects Impulsivity in Borderline Personality Disorder: A Pilot Study. Front Hum Neurosci. 2016 Dec 5;10:582. doi: 10.3389/fnhum.2016.00582. PMID: 27994543; PMCID: PMC5136542. Lefaucheur JP. Transcranial magnetic stimulation. Handb Clin Neurol. 2019;160:559-580. doi: 10.1016/B978-0-444-64032-1.00037-0. PMID: 31277876. Cocchi L, Zalesky A. Personalized Transcranial Magnetic Stimulation in Psychiatry. Biol Psychiatry Cogn Neurosci Neuroimaging. 2018 Sep;3(9):731-741. doi: 10.1016/j.bpsc.2018.01.008. Epub 2018 Mar 20. PMID: 29571586. Chamberlain SR, Stochl J, Redden SA, Grant JE. Latent traits of impulsivity and compulsivity: toward dimensional psychiatry. Psychol Med. 2018 Apr;48(5):810-821. doi: 10.1017/S0033291717002185. Epub 2017 Aug 14. PMID: 28805173;

PMCID: PMC5699644. Riley EN, Combs JL, Jordan CE, Smith GT. Negative Urgency and Lack of Perseverance: Identification of Differential Pathways of Onset and Maintenance Risk in the Longitudinal Prediction of Nonsuicidal Self-Injury. Behav Ther. 2015 Jul;46(4):439-48. doi: 10.1016/j.beth.2015.03.002. Epub 2015 Mar 11. PMID: 26163709; PMCID: PMC4801770. Rømer Thomsen K, Callesen MB, Hesse M, Kvamme TL, Pedersen MM, Pedersen MU, Voon V. Impulsivity traits and addiction-related behaviors in youth. J Behav Addict. 2018 Jun 1;7(2):317-330. doi: 10.1556/2006.7.2018.22. Epub 2018 Apr 12. PMID: 29642723; PMCID: PMC6174598. Bari A, Robbins TW. Inhibition and impulsivity: behavioral and neural basis of response control. Prog Neurobiol. 2013 Sep;108:44-79. doi: 10.1016/j.pneurobio.2013.06.005. Epub 2013 Jul 13. PMID: 23856628. Siafis S, Tzachanis D, Samara M, Papazisis G. Antipsychotic Drugs: From Receptor-binding Profiles to Metabolic Side Effects. Curr Neuropharmacol. 2018;16(8):1210-1223. doi: 10.2174/1570159X15666170630163616. PMID: 28676017; PMCID: PMC6187748. Divac N, Prostran M, Jakovcevski I, Cerovac N. Second-generation antipsychotics and extrapyramidal adverse effects. Biomed Res Int. 2014;2014:656370. doi: 10.1155/2014/656370. Epub 2014 Jun 3. PMID: 24995318; PMCID: PMC4065707. Yang CC, Völlm B, Khalifa N. The Effects of rTMS on Impulsivity in Normal Adults: a Systematic Review and Meta-Analysis. Neuropsychol Rev. 2018 Sep;28(3):377-392. doi: 10.1007/s11065-018-9376-6. Epub 2018 May 5. PMID: 29730846. Yang CC, Khalifa N, Völlm B. Excitatory repetitive transcranial magnetic stimulation applied to the right inferior frontal gyrus has no effect on motor or cognitive impulsivity in healthy adults. Behav Brain Res. 2018 Jul 16;347:1-7. doi: 10.1016/j.bbr.2018.02.047. Epub 2018 Mar 2. PMID: 29505803. Schluter RS, van Holst RJ, Goudriaan AE. Effects of Ten Sessions of High Frequency Repetitive Transcranial Magnetic Stimulation (HF-rTMS) Add-on Treatment on Impulsivity in Alcohol Use Disorder. Front Neurosci. 2019 Dec 4;13:1257. doi: 10.3389/fnins.2019.01257. PMID: 31866805; PMCID: PMC6904338. Jung J, Bungert A, Bowtell R, Jackson SR. Modulating Brain Networks With Transcranial Magnetic Stimulation Over the Primary Motor Cortex: A Concurrent TMS/fMRI Study. Front Hum Neurosci. 2020 Feb 14;14:31. doi: 10.3389/fnhum.2020.00031. PMID: 32116612; PMCID: PMC7033446. Galhardoni R, Correia GS, Araujo H, Yeng LT, Fernandes DT, Kaziyama HH, Marcolin MA, Bouhassira D, Teixeira MJ, de Andrade DC. Repetitive transcranial magnetic stimulation in chronic pain: a review of the literature. Arch Phys Med Rehabil. 2015 Apr;96(4 Suppl):S156-72. doi: 10.1016/j.apmr.2014.11.010. Epub 2014 Nov 28. PMID: 25437106. Hallett M. Transcranial magnetic stimulation: a primer. Neuron. 2007 Jul 19;55(2):187-99. doi: 10.1016/j.neuron.2007.06.026. PMID: 17640522. Wang J, Deng XP, Wu YY, Li XL, Feng ZJ, Wang HX, Jing Y, Zhao N, Zang YF, Zhang J. High-Frequency rTMS of the Motor Cortex Modulates Cerebellar and Widespread Activity as Revealed by SVM. Front Neurosci. 2020 Mar 19;14:186. doi: 10.3389/fnins.2020.00186. PMID: 32265624; PMCID: PMC7096733. Voss P, Thomas ME, Cisneros-Franco JM, de Villers-Sidani É. Dynamic Brains and the Changing Rules of Neuroplasticity: Implications for Learning and Recovery. Front Psychol. 2017 Oct 4;8:1657. doi: 10.3389/fpsyg.2017.01657. PMID: 29085312; PMCID: PMC5649212. Cossu G, Rinaldi R, Colosimo C. The rise and fall of impulse control behavior disorders. Parkinsonism Relat Disord. 2018 Jan;46 Suppl 1:S24-S29. doi: 10.1016/j.parkreldis.2017.07.030. Epub 2017 Aug 1. PMID: 28818561. Grant JE, Chamberlain SR. Expanding the definition of addiction: DSM-5 vs. ICD-11. CNS Spectr. 2016 Aug;21(4):300-3. doi: 10.1017/S1092852916000183. Epub 2016 May 6. PMID: 27151528; PMCID: PMC5328289. Fonseca NKOD, Molle RD, Costa MA, Gonçalves FG, Silva AC, Rodrigues Y, Price M, Silveira PP, Manfro GG. Impulsivity influences food intake in women with generalized anxiety disorder. Braz J Psychiatry. 2020 Aug;42(4):382-388. doi: 10.1590/1516-4446-2019-0556. Epub 2020 Feb 14. PMID: 32074229; PMCID: PMC7430399. Xia L, Gu R, Zhang D, Luo Y. Anxious Individuals Are Impulsive Decision-Makers in the Delay Discounting Task: An ERP Study. Front Behav Neurosci. 2017 Jan 24;11:5. doi: 10.3389/fnbeh.2017.00005. PMID: 28174528; PMCID: PMC5258725. Jakuszkowiak-Wojten K, Landowski J, Wiglusz MS, Cubała WJ. Impulsivity in anxiety disorders. A critical review. Psychiatr Danub. 2015 Sep;27 Suppl 1:S452-5. PMID: 26417814. Çörekçioğlu S, Cesur E, Devrim Balaban Ö. Relationship between impulsivity, comorbid anxiety and neurocognitive functions in bipolar disorder. Int J Psychiatry Clin Pract. 2021 Mar;25(1):62-72. doi: 10.1080/13651501.2020.1833040. Epub 2020 Oct 16. PMID: 33063587. Lijffijt M, Lane SD, Moeller FG, Steinberg JL, Swann AC. Trait impulsivity and increased pre-attentional sensitivity to intense stimuli in bipolar disorder and controls. J Psychiatr Res. 2015 Jan;60:73-80. doi: 10.1016/j.jpsychires.2014.10.004. Epub 2014 Oct 12. PMID: 25455512. Grande I, Berk M, Birmaher B, Vieta E. Bipolar disorder. Lancet. 2016 Apr 9;387(10027):1561-1572. doi: 10.1016/S0140-6736(15)00241-X. Epub 2015 Sep 18. PMID:

26388529. Swann AC, Dougherty DM, Pazzaglia PJ, Pham M, Steinberg JL, Moeller FG. Increased impulsivity associated with severity of suicide attempt history in patients with bipolar disorder. Am J Psychiatry. 2005 Sep;162(9):1680-7. doi: 10.1176/appi.ajp.162.9.1680. PMID: 16135628. Swann AC, Lijffijt M, Lane SD, Kjome KL, Steinberg JL, Moeller FG. Criminal conviction, impulsivity, and course of illness in bipolar disorder. Bipolar Disord. 2011 Mar;13(2):173-81. doi: 10.1111/j.1399-5618.2011.00900.x. PMID: 21443571; PMCID: PMC3151155. Chapman AL. Borderline personality disorder and emotion dysregulation. Dev Psychopathol. 2019 Aug;31(3):1143-1156. doi: 10.1017/S0954579419000658. Epub 2019 Jun 6. PMID: 31169118. Videler AC, Hutsebaut J, Schulkens JEM, Sobczak S, van Alphen SPJ. A Life Span Perspective on Borderline Personality Disorder. Curr Psychiatry Rep. 2019 Jun 4;21(7):51. doi: 10.1007/s11920-019-1040-1. PMID: 31161404; PMCID: PMC6546651. McHugh C, Balaratnasingam S. Impulsivity in personality disorders: current views and future directions. Curr Opin Psychiatry. 2018 Jan;31(1):63-68. doi: 10.1097/YCO.0000000000000383. PMID: 29120916. Lazaratou H, Palaiologou A, Anagnostopoulos D. [Impulsivity as an immediate factor between addictive disorders and Attention Deficit-Hyperactivity Disorder]. Psychiatriki. 2017 Apr-Jun;28(2):156-164. Greek, Modern. doi: 10.22365/jpsych.2017.282.156. PMID: 28686562. Fairchild G. Shared or Distinct Alterations in Brain Structure in Disorders Across the Impulsivity-Compulsivity Spectrum: What Can We Learn From Cross-Disorder Comparisons of ADHD, ASD, and OCD? Am J Psychiatry. 2020 Sep 1;177(9):799-801. doi: 10.1176/appi.ajp.2020.20071031. PMID: 32867517. Gouveia FV, Germann J, Devenyi GA, Morais RMCB, Santos APM, Fonoff ET, Hamani C, Brentani H, Chakravarty MM, Martinez RCR. Refractoriness of aggressive behaviour to pharmacological treatment: cortical thickness analysis in autism spectrum disorder. BJPsych Open. 2020 Aug 7;6(5):e85. doi: 10.1192/bjo.2020.71. PMID: 32762791; PMCID: PMC7453794. Blair RJ. The Neurobiology of Impulsive Aggression. J Child Adolesc Psychopharmacol. 2016 Feb;26(1):4-9. doi: 10.1089/cap.2015.0088. Epub 2015 Oct 14. PMID: 26465707; PMCID: PMC4779272. Auerbach RP, Stewart JG, Johnson SL. Impulsivity and Suicidality in Adolescent Inpatients. J Abnorm Child Psychol. 2017 Jan;45(1):91-103. doi: 10.1007/s10802-016-0146-8. PMID: 27025937; PMCID: PMC5045310. Giupponi G, Giordano G, Maniscalco I, Erbuto D, Berardelli I, Conca A, Lester D, Girardi P, Pompili M. Suicide risk in attention-deficit/hyperactivity disorder. Psychiatr Danub. 2018 Mar;30(1):2-10. doi: 10.24869/psyd.2018.2. PMID: 29546852. Lockwood J, Daley D, Townsend E, Sayal K. Impulsivity and self-harm in adolescence: a systematic review. Eur Child Adolesc Psychiatry. 2017 Apr;26(4):387-402. doi: 10.1007/s00787-016-0915-5. Epub 2016 Nov 5. PMID: 27815757; PMCID: PMC5364241. Swann AC, Lijffijt M, O'Brien B, Mathew SJ. Impulsivity and Suicidal Behavior. Curr Top Behav Neurosci. 2020;47:179-195. doi: 10.1007/7854_2020_144. PMID: 32472429. Sarkisian KL, Van Hulle CA, Hill Goldsmith H. Brooding, Inattention, and Impulsivity as Predictors of Adolescent Suicidal Ideation. J Abnorm Child Psychol. 2019 Feb;47(2):333-344. doi: 10.1007/s10802-018-0435-5. PMID: 29808397; PMCID: PMC6265119. Hadzic A, Spangenberg L, Hallensleben N, Forkmann T, Rath D, Strauß M, Kersting A, Glaesmer H. The association of trait impulsivity and suicidal ideation and its fluctuation in the context of the Interpersonal Theory of Suicide. Compr Psychiatry. 2019 Dec 26;98:152158. doi: 10.1016/j.comppsych.2019.152158. Epub ahead of print. PMID: 32004858. George MS, Raman R, Benedek DM, Pelic CG, Grammer GG, Stokes KT, Schmidt M, Spiegel C, Dealmeida N, Beaver KL, Borckardt JJ, Sun X, Jain S, Stein MB. A two-site pilot randomized 3 day trial of high dose left prefrontal repetitive transcranial magnetic stimulation (rTMS) for suicidal inpatients. Brain Stimul. 2014 May-Jun;7(3):421-31. doi: 10.1016/j.brs.2014.03.006. Epub 2014 Mar 19. PMID: 24731434. Abdelnaim MA, Langguth B, Deppe M, Mohonko A, Kreuzer PM, Poeppl TB, Hebel T, Schecklmann M. Anti-Suicidal Efficacy of Repetitive Transcranial Magnetic Stimulation in Depressive Patients: A Retrospective Analysis of a Large Sample. Front Psychiatry. 2020 Jan 8;10:929. doi: 10.3389/fpsyt.2019.00929. PMID: 31969842; PMCID: PMC6960193. Li X, Hartwell KJ, Owens M, Lematty T, Borckardt JJ, Hanlon CA, Brady KT, George MS. Repetitive transcranial magnetic stimulation of the dorsolateral prefrontal cortex reduces nicotine cue craving. Biol Psychiatry. 2013 Apr 15;73(8):714-20. doi: 10.1016/j.biopsych.2013.01.003. Epub 2013 Feb 26. PMID: 23485014; PMCID: PMC3615051. Yuan J, Liu W, Liang Q, Cao X, Lucas MV, Yuan TF. Effect of Low-Frequency Repetitive Transcranial Magnetic Stimulation on Impulse Inhibition in Abstinent Patients With Methamphetamine Addiction: A Randomized Clinical Trial. JAMA Netw Open. 2020 Mar 2;3(3):e200910. doi: 10.1001/jamanetworkopen.2020.0910. PMID: 32167568; PMCID: PMC7070234. Sheffer CE, Mennemeier M, Landes RD, Bickel WK, Brackman S, Dornhoffer J, Kimbrell T, Brown G. Neuromodulation of delay discounting, the reflection effect,

and cigarette consumption. J Subst Abuse Treat. 2013 Aug;45(2):206-14. doi: 10.1016/j.jsat.2013.01.012. Epub 2013 Mar 18. PMID: 23518286; PMCID: PMC3690153. Del Felice A, Bellamoli E, Formaggio E, Manganotti P, Masiero S, Cuoghi G, Rimondo C, Genetti B, Sperotto M, Corso F, Brunetto G, Bricolo F, Gomma M, Serpelloni G. Neurophysiological, psychological and behavioural correlates of rTMS treatment in alcohol dependence. Drug Alcohol Depend. 2016 Jan 1;158:147-53. doi: 10.1016/j.drugalcdep.2015.11.018. Epub 2015 Nov 22. PMID: 26679060. Pettorruso M, Martinotti G, Montemitro C, De Risio L, Spagnolo PA, Gallimberti L, Fanella F, Bonci A, Di Giannantonio M; Brainswitch Study Group. Multiple Sessions of High-Frequency Repetitive Transcranial Magnetic Stimulation as a Potential Treatment for Gambling Addiction: A 3-Month, Feasibility Study. Eur Addict Res. 2020;26(1):52-56. doi: 10.1159/000504169. Epub 2019 Oct 30. PMID: 31665732. Schluter RS, van Holst RJ, Goudriaan AE. Effects of Ten Sessions of High Frequency Repetitive Transcranial Magnetic Stimulation (HF-rTMS) Add-on Treatment on Impulsivity in Alcohol Use Disorder. Front Neurosci. 2019 Dec 4;13:1257. doi: 10.3389/fnins.2019.01257. PMID: 31866805; PMCID: PMC6904338. Croarkin PE, Nakonezny PA, Deng ZD, Romanowicz M, Voort JLV, Camsari DD, Schak KM, Port JD, Lewis CP. High-frequency repetitive TMS for suicidal ideation in adolescents with depression. J Affect Disord. 2018 Oct 15;239:282-290. doi: 10.1016/j.jad.2018.06.048. Epub 2018 Jul 18. PMID: 30031247; PMCID: PMC6431788. Ozcan S, Gica S, Gulec H. Suicidal behavior in treatment resistant major depressive disorder patients treated with transmagnetic stimulation(TMS) and its relationship with cognitive functions. Psychiatry Res. 2020 Feb 19;286:112873. doi: 10.1016/j.psychres.2020.112873. Epub ahead of print. PMID: 32114209. Pan F, Shen Z, Jiao J, Chen J, Li S, Lu J, Duan J, Wei N, Shang D, Hu S, Xu Y, Huang M. Neuronavigation-Guided rTMS for the Treatment of Depressive Patients With Suicidal Ideation: A Double-Blind, Randomized, Sham-Controlled Trial. Clin Pharmacol Ther. 2020 Oct;108(4):826-832. doi: 10.1002/cpt.1858. Epub 2020 Jun 4. PMID: 32319673. Cailhol L, Roussignol B, Klein R, Bousquet B, Simonetta-Moreau M, Schmitt L, Thalamas C, Tap G, Birmes P. Borderline personality disorder and rTMS: a pilot trial. Psychiatry Res. 2014 Apr 30;216(1):155-7. doi: 10.1016/j.psychres.2014.01.030. Epub 2014 Jan 30. PMID: 24503285. Calderón-Moctezuma AR, Reyes-López JV, Rodríguez-Valdés R, Barbosa-Luna M, Ricardo-Garcell J, Espino-Cortés M, Hernández-Chan N, García-Noguez L, Roque-Roque G, Trejo-Cruz G, Cañizares-Gómez S, Hernández-Montiel H. Improvement in borderline personality disorder symptomatology after repetitive transcranial magnetic stimulation of the dorsomedial prefrontal cortex: preliminary results. Braz J Psychiatry. 2021 Feb 1;43(1):65-69. doi: 10.1590/1516-4446-2019-0591. PMID: 32876128; PMCID: PMC7861182. Reyes-López J, Ricardo-Garcell J, Armas-Castañeda G, García-Anaya M, Arango-De Montis I, González-Olvera JJ, Pellicer F. Clinical improvement in patients with borderline personality disorder after treatment with repetitive transcranial magnetic stimulation: preliminary results. Braz J Psychiatry. 2018 Jan-Mar;40(1):97-104. doi: 10.1590/1516-4446-2016-2112. Epub 2017 Jun 12. PMID: 28614492; PMCID: PMC6899410. Diefenbach GJ, Bragdon LB, Zertuche L, Hyatt CJ, Hallion LS, Tolin DF, Goethe JW, Assaf M. Repetitive transcranial magnetic stimulation for generalised anxiety disorder: a pilot randomised, double-blind, sham-controlled trial. Br J Psychiatry. 2016 Sep;209(3):222-8. doi: 10.1192/bjp.bp.115.168203. Epub 2016 May 19. PMID: 27198484. Cho SS, Koshimori Y, Aminian K, Obeso I, Rusjan P, Lang AE, Daskalakis ZJ, Houle S, Strafella AP. Investing in the future: stimulation of the medial prefrontal cortex reduces discounting of delayed rewards. Neuropsychopharmacology. 2015 Feb;40(3):546-53. doi: 10.1038/npp.2014.211. Epub 2014 Aug 29. PMID: 25168685; PMCID: PMC4289950. Herz DM, Christensen MS, Bruggemann N, Hulme OJ, Ridderinkhof KR, Madsen KH, Siebner HR. Motivational tuning of fronto-subthalamic connectivity facilitates control of action impulses. J Neurosci. 2014 Feb 26;34(9):3210-7. doi: 10.1523/JNEUROSCI.4081-13.2014. PMID: 24573279; PMCID: PMC6795302.

Acknowledgements: There was no other support besides de Neuromood Lab.

Learning Objectives: Objectives:1. To evaluate the efficacy and safety of the use of Transcranial Magnetic Stimulation in the psychiatric symptom of impulsivity. 2. Objectives: to compare the efficacy of the use of transcranial magnetic stimulation in impulsivity among different psychiatric disorders.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

229

Poster on Board
POSTER ON BOARD: AS04BD. BRAIN - NON-INVASIVE STIMULATION: NEUROREHABILITATION
13-05-2024 08:00 - 19:00

VARIATION OF CORTICOSPINAL EXCITABILITY DURING KINESTHETIC ILLUSION INDUCED BY MUSCULOTENDINOUS VIBRATION

Lydiane Lauzier, MSc[1], Marie-Pier Perron, BSc (Hons)[1], Laurence Munger, BSc (Hons)[1], Émilie Bouchard, MSc[1], Jacques Abboud, PhD[2], François Nougarou, PhD[3], Louis-David Beaulieu, PhD[4]
[1]UQAC, Science De La Santé, Chicoutimi, Canada, [2]UQTR, Sciences De L'activité Physique, Trois-Rivières, Canada, [3]UQTR, Génie électrique Et Informatique, Trois-Rivières, Canada, [4]Université Chicoutimi, Unité D'enseignement En Physiothérapie, Chicoutimi, Canada

Introduction: Musculotendinous vibration (VIB) is a peripheral neurostimulation method known to elicit kinesthetic illusions (KI) in absence of visual feedback [1]. This method strongly stimulates muscle spindles of the vibrated muscle, therefore sending proprioceptive information perceived as an illusory feeling of movement coherent with the stretching of the muscle [2]. VIB-induced KI has been recently proposed as an innovative diagnostic and therapeutic approach with somatosensory and motor deficits [4-6]. The aim was to investigate corticospinal excitability with transcranial magnetic stimulation (TMS) at different time points during VIB-induced KI.

Materials / Methods: Twenty healthy participants were recruited and VIB was applied over wrist flexor tendons (80 Hz, 10s, 1 mm amplitude) [15] by a custom-made vibratory device. Standardized Kinesthetic Illusions Procedure (SKIP) was followed to standardize procedure and to qualitatively measure the perceived illusory movement [15]. Electrodes were placed over extensor digitorium communis (EDC) muscle to record electromyographic signals. Motor evoked potential (MEP) amplitude and latency were calculated to assess corticospinal excitability. Single-pulsed TMS was delivered in four conditions (10 trials/condition) in random order of conditions between participants and sides (dominant or non-dominant) consisting of different timings between vibration start and TMS delivery: baseline without vibration, TMS delivered 1s (t1), 5s (t5) and 10s (t10) after vibration start. A within-subject analysis of variance (ANOVA) was applied using factors Stimulation timings and side.

Results: ANOVA found a significant effect of timings on MEP amplitudes ($p=0.035$). Pair-wise comparisons showed that MEP amplitudes were significatively lower in t1 compared to t5 ($p=0.025$) and t10 ($p=0.003$). No difference was found between baseline and t1-t5-10 data. KI perceptions were stable across each condition and in the expected direction of wrist extension according to SKIP scores.

Discussion: Results suggest a time-specific modulation of corticospinal excitability in muscles antagonistic to those vibrated, i.e. muscles involved in the perceived movement. An early decrease of excitability was observed at 1s followed by a stabilization of values near baseline at subsequent time-points. At 1s, the illusion is not yet perceived or not strong enough to up-regulate corticospinal networks coherent with the proprioceptive input. Spinal mechanisms, as reciprocal inhibition, could also contribute to lower the corticospinal drive of non-vibrated muscles in short period before the illusion emerges.

Conclusions: This study suggests that the time course of VIB-induced corticospinal effects evolves dynamically over time. Testing supplementary time points during VIB and using neurophysiological investigations specific to spinal and cortical networks would help improving our comprehension of underlying mechanisms.

Supplemental Data:

References: 1. Calvin-Figuière, S., et al., *Antagonist motor responses correlate with kinesthetic illusions induced by tendon vibration.* Experimental Brain Research, 1999. **124**(3): p. 342-350. 2. Roll,

J.P. and J.P. Vedel, *Kinaesthetic role of muscle afferents in man, studied by tendon vibration and microneurography.* Exp Brain Res, 1982. **47**(2): p. 177-90. 3. Roll, J.P., J.P. Vedel, and E. Ribot, *Alteration of proprioceptive messages induced by tendon vibration in man: a microneurographic study.* Exp Brain Res, 1989. **76**(1): p. 213-22. 4. Conrad, M.O., R.A. Scheidt, and B.D. Schmit, *Effects of wrist tendon vibration on arm tracking in people poststroke.* J Neurophysiol, 2011. **106**(3): p. 1480-8. 5. Poenaru, D., et al., *Local Application of Vibration in Motor Rehabilitation - Scientific and Practical Considerations.* Maedica (Bucur), 2016. **11**(3): p. 227-231. 6. Souron, R., et al., *Acute and chronic neuromuscular adaptations to local vibration training.* Eur J Appl Physiol, 2017. **117**(10): p. 1939-1964. 7. Romaiguere, P., et al., *Motor and parietal cortical areas both underlie kinaesthesia.* Brain Res Cogn Brain Res, 2003. **16**(1): p. 74-82. 8. Naito, E., et al., *Human limb-specific and non-limb-specific brain representations during kinesthetic illusory movements of the upper and lower extremities.* Eur J Neurosci, 2007. **25**(11): p. 3476-87. 9. Siggelkow, S., et al., *Modulation of motor evoked potentials by muscle vibration: the role of vibration frequency.* Muscle Nerve, 1999. **22**(11): p. 1544-8. 10. Rosenkranz, K. and J.C. Rothwell, *Differential effect of muscle vibration on intracortical inhibitory circuits in humans.* J Physiol, 2003. **551**(Pt 2): p. 649-60. 11. Mancheva, K., et al., *Vibration-Induced Kinesthetic Illusions and Corticospinal Excitability Changes.* J Mot Behav, 2017. **49**(3): p. 299-305. 12. Calvin-Figuiere, S., et al., *Antagonist motor responses correlate with kinesthetic illusions induced by tendon vibration.* Exp Brain Res, 1999. **124**(3): p. 342-50. 13. Lapole, T., et al., *Achilles tendon vibration-induced changes in plantar flexor corticospinal excitability.*Exp Brain Res, 2015. **233**(2): p. 441-8. 14. Seizova-Cajic, T., et al., *Proprioceptive movement illusions due to prolonged stimulation: reversals and aftereffects.* PloS one, 2007. **2**(10): p. e1037. 15. Beaulieu, L.D., et al., *A new method to elicit and measure movement illusions in stroke by means of muscle tendon vibration: the Standardized Kinesthetic Illusion Procedure (SKIP).* Somatosens Mot Res, 2020. **37**(1): p. 28-36. 16. Groppa, S., et al., *A practical guide to diagnostic transcranial magnetic stimulation: report of an IFCN committee.* Clin Neurophysiol, 2012. **123**(5): p. 858-82. 17. Rossini, P.M., et al., *Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: Basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee.* Clin Neurophysiol, 2015. **126**(6): p. 1071-1107. 18. Awiszus, F. and J. Borckardt, *TMS Motor Threshold Assessment Tool (MTAT 2.0).* 2010. 19. Eklund, G. and K.E. Hagbarth, *Normal variability of tonic vibration reflexes in man.* Exp Neurol, 1966. **16**(1): p. 80-92. 20. Rosenkranz, K., et al., *Focal reduction of intracortical inhibition in the motor cortex by selective proprioceptive stimulation.* Exp Brain Res, 2003. **149**(1): p. 9-16. 21. Talis, V.L., I.A. Solopova, and O.V. Kazennikov, *Changes in corticospinal excitability in the reactions of forearm muscles in humans to vibration.* Neurosci Behav Physiol, 2010. **40**(1): p. 21-8. 22. Kossev, A., et al., *Muscle vibration: different effects on transcranial magnetic and electrical stimulation.*Muscle Nerve, 1999. **22**(7): p. 946-8. 23. Naito, E., T. Morita, and K. Amemiya, *Body representations in the human brain revealed by kinesthetic illusions and their essential contributions to motor control and corporeal awareness.* Neurosci Res, 2016. **104**: p. 16-30. 24. Beaulieu, L.D., et al., *After-effects of peripheral neurostimulation on brain plasticity and ankle function in chronic stroke: The role of afferents recruited.* Neurophysiol Clin, 2017. **47**(4): p. 275-291. 25. Dilena, A., et al., *What is the effect of bodily illusions on corticomotoneuronal excitability? A systematic review.* PLoS One, 2019. **14**(8): p. e0219754. 26. Marconi, B., et al., *Long-term effects on cortical excitability and motor recovery induced by repeated muscle vibration in chronic stroke patients.* Neurorehabil Neural Repair, 2011. **25**(1): p. 48-60.

Acknowledgements:

Learning Objectives: 1. Corticospinal excitability modulation of the muscle perceiving the illusory movement is time-specific. 2. Kinesthetic illusion varies during a 10s vibration interval. 3. Spinal mechanisms could contribute to an early decrease in corticospinal excitability before the kinesthetic illusion is perceived.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

230

Poster on Board
POSTER ON BOARD: AS04BE. BRAIN - NON-INVASIVE STIMULATION: PAIN
13-05-2024 08:00 - 19:00

ELUCIDATING THE MECHANISM AND OPTIMIZING PARAMETERS OF TRANSCUTANEOUS AURICULAR NEUROSTIMULATION (TAN) FOR CHRONIC PAIN

Bashar Badran, PhD, Xiaolong Peng, PhD, Falon Sutton, BSc (Hons), Brenna Baker-Vogel, B.S., John Robinson, BSc (Hons), Marion Wood, BSc (Hons), Dillon Connolly, BSc (Hons), Emeline Spake, BSc (Hons), Andrew Manett, MD, Ethan Ashley, MD, E Short, MD
Medical University of South Carolina, Psychiatry And Behavioral Sciences, Charleston, United States of America

Introduction: Neuromodulation approaches have emerged as promising nonpharmacological pain interventions, offering safe and effective analgesia as well as mitigation of opioid withdrawal syndrome. Of interest is transcutaneous auricular neurostimulation (tAN) which delivers electricity to the vagal and trigeminal nerves and is therapeutically indicated for pain during opioid withdrawal. Yet, the mechanisms of action remain poorly understood. In two ongoing, five-year clinical trials, we explore the anti-pain effects of stimulating the trigeminal nerve (TN) and the auricular branch of the vagus nerve (ABVN) in healthy individuals both independently and synergistically, against sham. In the first trial, we deliver stimulation simultaneously with an opioid blockade to understand if endogenous opioid mediate pain relief. In a parallel study, stimulation is delivered within the MRI scanner to understand various parametric effects on direct brain activation.

Materials / Methods: 136 healthy adults will attend two identical experimental visits at least one week apart during which they received stimulation to one of four stimulation areas (TN, ABVN, Combo, or Sham) while also receiving either naloxone (0.15mg/kg) or saline (matched volume) intravenously. The stimulation condition stayed constant for both visits, and the only variable that changed was the drug given. We measured thermal thresholds with quantitative sensory thresholds (QST) before and after stimulation. This analysis investigates the anti-pain effects of either TN, ABVN, Combo, or Sham stimulation under blinded drug conditions assigned Y and Z in the first.

Results: To date we have enrolled n=47 (mean age ± SD = 32.5 ±11.32 years, n=31 female), and in this analysis we present blinded data from the first n=12 participants. All active stimulation conditions induced anti-pain effects by increasing pain thresholds, whereas sham stimulation demonstrated no anti-pain effects. Anti-pain effects in active conditions were dependent on drug condition, where under drug condition “Y” anti-pain effects were blunted, compared to drug “Z”. Largest effects on pain were demonstrated in the TN group compared to other stimulation conditions [(mean threshold change post-pre stimulation, °C) Sensory, Drug Y: -0.07, Drug Z: 1.54; Pain, Drug Y: -1.23 Drug Z:-0.41; Tolerance, Drug Y: -1.39, Drug Z: 0.69].

Discussion: tAN is a promising new neuromodulation technique that could provide benefit for individuals with chronic pain.

Conclusions: It is still early to determine whether these anti-pain effects are caused by the release of endogenous opioids, although we are hopeful that upon completion of this trial in 2027, we will have sufficient evidence to determine the optimal stimulation placement and underlying mechanism.

Supplemental Data:

References:

Acknowledgements: Funding for this work was provided by the NIH Heal Inititative Project Number: RM1NS128787

Learning Objectives: Transcutaneous auricular neruostimulation (tAN) may provude anti-pain benefits. Using a naloxone blockade is a method to determine the invovlement of endogenous opioids underlying tAN mechanism. Double-blinded data suggests there may be a drug interaction that attenuates tAN anti-pain effects.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

231

Poster on Board
POSTER ON BOARD: AS04BE. BRAIN - NON-INVASIVE STIMULATION: PAIN
13-05-2024 08:00 - 19:00

FEASIBILITY OF TRANSCRANIAL DIRECT CURRENT STIMULATION, NECK EXERCISE, AND COMBINED TREATMENT FOR INDIVIDUALS WITH POST-TRAUMATIC HEADACHE

Aaron Parr, PT[1], Bahar Shahidi, PhD[2], David Berry, PhD[2], Katrina Monroe, PhD[3]
[1]San Diego State University Public Health, Public Health, San Diego, United States of America, [2]University of California San Diego, Orthopaedic Surgery, La Jolla, United States of America, [3]San Diego State University, School Of Exercise And Nutritional Sciences, Doctor Of Physical Therapy Program, San Diego, United States of America

Introduction: Persistent post-traumatic headache (PTH) is a prevalent and disabling condition following mild traumatic brain injury. Transcranial direct current stimulation (tDCS) and therapeutic neck exercise (TNE) have been shown to improve clinical outcomes of nontraumatic headache, yet have not been investigated in PTH. We aimed to assess the safety, acceptability, and preliminary efficacy of a telehealth intervention using tDCS, TNE, or tDCS+TNE for the management of PTH.

Materials / Methods: In an open-label feasibility study, consecutive participants with PTH were assigned to tDCS (n=4), TNE (n=5), or tDCS+TNE (n=5). tDCS groups received 20-min of 2-mA anodal stimulation over the left primary motor cortex 3 times per week for 6 weeks. TNE groups performed craniocervical and scapulothoracic strengthening with or without tDCS for an equivalent treatment duration. Adverse events, study retention, and treatment adherence rates assessed safety and acceptability of the intervention, respectively. Preliminary efficacy was assessed by comparing perceived satisfaction and improvement between groups using Global Rating of Change (GRC) scales. Group x time (pre/post-intervention) effect sizes were calculated for headache and neck pain intensity using PROMIS scales.

Results: Adverse events were no greater than mild to moderate in severity and resolved within three sessions. Study retention rates were 83% for tDCS+TNE, 100% for tDCS, and 50% for TNE. For those who completed the study, adherence rates were 100% for all but one participant who completed 72% of assigned TNE treatments. Median GRC scores for tDCS+TNE participants were extremely satisfied (1.0 [IQR 1-3]) and very much improved (1.0 [IQR 1-3]). In contrast, TNE participants reported being very satisfied 2.0 [IQR 1-4] and much improved 2.0 [IQR 1-3] and tDCS indicated being satisfied 3.0 [IQR 1-4] with minimal to no improvement in symptoms 3.5 [IQR 2-4]. Large effect sizes were found for improvements in headache (η^2=0.233) and neck pain (η^2=0.190) intensity.

Discussion: All treatments were safe and well tolerated by individuals with PTH, but retention was highest for tDCS interventions. Perceived satisfaction, overall improvement, and treatment effects sizes were greatest following treatment with tDCS+TNE. These findings are consistent with evidence that tDCS is most effective when applied over active brain circuits, such as when the motor cortex is engaged by exercise.

Conclusions: tDCS and TNE appear safe and acceptable when used alone or in combination for PTH management. Combined treatment with tDCS+TNE demonstrates the greatest preliminary efficacy and warrants further investigation.

Supplemental Data:

References: Reference: 1) Bini, P., et al. "The Effectiveness of Manual and Exercise Therapy on Headache Intensity and Frequency among Patients with Cervicogenic Headache: A Systematic Review and Meta-Analysis." Chiropr Man Therap 30.1 (2022): 49. Print. 2) Cai, G., et al. "A Systematic Review and Meta-Analysis on the Efficacy of Repeated Transcranial Direct Current Stimulation for Migraine." J Pain Res 14 (2021): 1171-83. Print. 3) Mavroudis, I., et al. "Post-Traumatic Headache: A Review of Prevalence, Clinical Features, Risk Factors, and Treatment

Strategies." J Clin Med 12.13 (2023). 4) Park, Seung Kyu et al. “Effects of cranio-cervical flexion with transcranial direct current stimulation on muscle activity and neck functions in patients with cervicogenic headache.” *Journal of physical therapy science* vol. 31,1 (2019): 24-28. doi:10.1589/jpts.31.24 5) Woldeamanuel, Y. W., and A. B. D. Oliveira. "What Is the Efficacy of Aerobic Exercise Versus Strength Training in the Treatment of Migraine? A Systematic Review and Network Meta-Analysis of Clinical Trials." J Headache Pain 23.1 (2022): 134. Print.

Acknowledgements: Supported by NIH Grant R21NS109852 and VA San Diego Health Care Center of Excellence in Stress and Mental Health Pilot Award

Learning Objectives: 1) Attendees will be able to describe the use of transcranial direct current stimulation (tDCS), therapeutic neck exercise (TNE), and their combination to treat post-traumatic headache (PTH). 2) Attendees will be able to discuss evidence supporting the feasibility and acceptability of combining tDCS with TNE for the treatment of PTH. 3) Attendees will be able to discuss evidence supporting the preliminary efficacy of combining tDCS with TNE for the treatment of PTH.

Financial Disclosures: 'No significant relationships'

Disclosure: No significant relationships.

232

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

DESIGN AND IMPLEMENTATION OF A PROACTIVE REMOTE MONITORING ALGORITHM IN CHRONIC PAIN PATIENTS

Aamna Ahsan, BSc[1], Dorna Mansouri, MD[1], Caleb Pettit, BSc[1], Sreetharan Thankathuraipandian, MSc[1], Soroush Dehghan, MSc[1], Anne Christopher, MD[2], David Page, PhD[1]
[1]Abbott Laboratories, Neuromodulation, Plano, United States of America, [2]St. Louis Pain Consultants, Pain, Chesterfield, United States of America

Introduction: Remote monitoring has fast emerged as an integral digital tool, with the Covid-19 pandemic further highlighting the need for remote management [1]. Manual monitoring and patient follow up by clinics may limit efficient long term patient care. Various automated data analytics methods exist [2], however, there is a gap in automated remote management methods for chronic pain patients. To this end, we designed and tested a remote monitoring change detection algorithm to trigger human outreach to chronic pain patients during their follow-up after receiving Spinal Cord Stimulation (SCS) therapy.

Materials / Methods: Patients were given a digital survey application and a wearable sensor for daily use. The algorithm monitored the data daily and used edge detection along with probability analytics to determine a new change point. Once a potential data point was identified, predetermined, patient-personalized thresholding and statistical analysis were conducted to identify if the potential change point was significant. Only a statistically significance data point was identified as a new change point. The new change point then triggered a system alert via an automatic email sent to staff in an email message, prompting proactive patient outreach via a phone call.

Results: Initially, the algorithm was used on offline retrospective patient data to detect multiple change points. Subsequently, the algorithm was deployed for real-time use in a prospective SCS study that is currently ongoing. The algorithm has successfully triggered numerous outreach phone calls, based on changes in patient step count, sleep, and missing data. One of the triggered outreach phone calls resulted in identifying an untreated pain location resulting in referral back to the pain physician and subsequent corrective treatment action. The study is currently ongoing, with more results expected.

Discussion: Remote monitoring coupled with proactive outreach is a powerful tool that can improve the longitudinal management of patients. As the demand for remote monitoring grows in healthcare [3], clinic staff may become overwhelmed with the amount of data produced by a large pool of patients over long-term follow-up time periods. Automated data analytics algorithms will become essential for identifying at-risk patients and help focus clinical staff efforts.

Conclusions: The remote monitoring algorithm described in this abstract has been successfully used to proactively manage chronic pain patients during long-term follow-up after receiving SCS therapy. We hypothesize that use of this proactive data–driven monitoring algorithm will improve response time to patient events and ultimately improve therapy outcomes and patient and clinician satisfaction.

Supplemental Data:

References: [1] Vermani, S. (2023). Smart Healthcare: Future Applications & Challenges. 2023 10th International Conference on Computing for Sustainable Global Development (INDIACom), Computing for Sustainable Global Development (INDIACom), 2023 10th International Conference On, 131–135. [2] Aminikhanghahi, S., & Cook, D. (2017). A survey of methods for time series change point detection. Knowledge & Information Systems, 51(2), 339–367. https://doi-org.ez03.infotrieve.com/10.1007/s10115-016-0987-z [3] Staats, P., Deer, T. R., Hunter, C., Li, S., Dickerson, D., Petersen, E., Kapural, L., Durbhakula, S., Gilligan, C., Slavin, K. V., Pope, J.,

Amirdelfan, K., Poree, L., Naidu, R., & Levy, R. M. (2023). Remote Management of Spinal Cord Stimulation Devices for Chronic Pain: Expert Recommendations on Best Practices for Proper Utilization and Future Considerations. Neuromodulation: Technology at the Neural Interface, 26(7), 1295–1308. https://doi-org.ez03.infotrieve.com/10.1016/j.neurom.2023.07.003

Acknowledgements: The support of Abbott Laboratories for this project is gratefully acknowledged.

Learning Objectives: 1. Learners will be able to demonstrate understanding of current limitations in remote monitoring methods. 2. Learners will be able to explain how change detections are identified by the remote monitoring system 3. Learners will be able to distinguish key steps that contibute to change detection and proactive triggers by the system being implemented.

Financial Disclosures: Presenting Author: AA is a company employee of Abbott Laboratories. Co-author: AC, is a consultant/Advisory Board member for Abbott Laboratories. Co-authors DM, CP, ST, SD, DP are company employees of Abbott Laboratories.

Disclosure: Employee of Sponsor (Abbott Laboratories) sponsoring the research mentioned in the abstract.

233

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

REMOTE MANAGEMENT OF SPINAL CORD STIMULATION REDUCES PATIENT TRAVEL TIME AND COST BURDEN: 12-MONTH OUTCOMES FROM A PROSPECTIVE MULTICENTER STUDY

Marc Russo, MBBS[1], James Yu, MD[2], Kasra Amirdelfan, MD[3], Leonardo Kapural, MD[4], Paul Verrills, MBBS[5]
[1]Hunter Pain Specialists, Broadmeadow, Australia, [2]Sydney Spine and Pain, Hurstville, Australia, [3]Boomerang Healthcare, Pain Management, Walnut Creek, United States of America, [4]Carolinas Pain Institute, Winston-Salem, United States of America, [5]Monash House Private Hospital, Metro Pain Group, Clayton, Australia

Introduction: Most spinal cord stimulation (SCS) systems require frequent in-person visits for reprogramming. These can lead to extended wait times to optimize pain management[1] and increased travel-related time/cost for patients.[2] Recent technological advances, however, enable remote SCS device management, which may reduce patient burden and increase healthcare efficiencies.[3] BENEFIT-03 (NCT04683718) is, to our knowledge, the world's first long-term study of an SCS system with remote programming and automatic daily transmission of objective device monitoring data. Here, we report benefits of proactive daily monitoring and remote programming for participants and clinicians in BENEFIT-03.

Materials / Methods: BENEFIT-03 is a prospective, single-arm, multicenter study ongoing in Australia with Human Research Ethics Committee approval in consenting participants with chronic low back and/or leg pain. Post-implant follow-up consists of in-office visits (3, 6, 12, and 24 months) and remote visits initiated by participants, investigators, proactive triggers (based on automatic daily device monitoring), or patient-reported outcomes. Primary endpoints are responder rate (at least 50% overall pain relief, VAS) and freedom from device-related complications at 6 months. Additional outcomes include questionnaires assessing participant and clinician experiences, healthcare utilization, and travel burden.

Results: As of this March 2024 interim analysis, 25 of 31 implanted participants had completed the 12-month follow-up and had data available for analysis. Participants reported reductions in time/cost burdens: 96% agreed/strongly agreed that remote stimulator adjustments saved money (by reducing travel for office visits) and 92% agreed/strongly agreed remote follow-up provided more time for daily activities (by avoiding in-office reprogramming). Consistent with these benefits, 96% agreed/strongly agreed they would choose a device with remote capabilities. Clinicians reported that 96% of participants benefited from remote device management and clinic staff burdens were reduced in management of 72% of participants. Furthermore, clinicians estimated that remote management saved the top quarter of participants a mean of 8.0 visits from implant to month 12 (population mean: 3.0 visits saved). Saved visits avoided substantial travel time and cost, as participants reported mean round-trip travel of 291.8 km from home to clinic.

Discussion: Nearly all participants would choose a system with remote capabilities. Clinicians reported remote management benefited participants and reduced clinic staff burden.

Conclusions: These results demonstrate proactive remote device management reduced participant in-office visit burden for SCS reprogramming, resulting in time and monetary savings.

Supplemental Data: None

References: 1. Amirdelfan K, Antony A, Levy R, et al. Patient Burdens Associated with Spinal Cord Stimulation: Impact of Wait Times to Address Device-Related Issues in a Real-World Cohort with Chronic Back and Leg Pain [WIP abstract P-136]. *Pain Pract*. 2022;22(S1): 25-27. 2. Han Y, Lu Y, Wang D, et al. The Use of Remote Programming for Spinal Cord Stimulation for Patients With Chronic

Pain During the COVID-19 Outbreak in China. *Neuromodulation*. 2021;24(3):441-447. 3. Staats P, Deer TR, Hunter C, et al. Remote Management of Spinal Cord Stimulation Devices for Chronic Pain: Expert Recommendations on Best Practices for Proper Utilization and Future Considerations. *Neuromodulation*. 2023;26(7):1295-1308.

Acknowledgements: BIOTRONIK sponsors the study and funded writing/editorial support.

Learning Objectives: 1. To identify patient burdens (e.g., travel-related cost/time) that can potentially be reduced via remote SCS device management 2. To discuss both participant- and clinician-reported benefits of remote device management in BENEFIT-03, including reductions in travel-related cost burden and in-clinic visits 3. To describe SCS system preferences among BENEFIT-03 participants, nearly all of whom would choose an SCS system with remote capabilities

Financial Disclosures: Marc Russo: SPR Therapeutics, historical stockholder <1%; Saluda Medical, stock options <0.5%; and Presidio Medical, stock options <0.5%. **James Yu:** Abbott, consultant; Nevro, consultant, research; Medtronic, consultant, research; Boston Scientific, consultant, research; Saluda, research; Biotronik, research; and Nalu, research. **Kasra Amirdelfan:** Medtronic, consultant; Boston Scientific, consultant; Nevro, consultant; Biotronik, consultant; and Nalu, consultant, stock options. **Leonardo Kapural:** Nevro, consultant, research; Abbott, consultant; Medtronic, consultant, research; Nalu, consultant; Saluda, consultant, research; Biotronik, consultant, research; Gimer Medical, research; Neuros, research; and SPR Therapeutics, research. **Paul Verrills:** Presidio, consultant, research, $500 – $5,000; Biotronik, consultant, research, $1 - $500; Saluda, consultant, $5,000 - $20,000; and Nalu, consultant, $1 – $500.

Disclosure: Jacob Hicks is an employee at Biotronik Inc.

234

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

REAL-WORLD OUTCOMES WITH SINGLE-STAGE ECAP CONTROLLED CLOSED-LOOP SCS: A SINGLE-CENTRE CASE-SERIES.

Philippa Armstrong, MB ChB, Peter Hall, MB ChB, Amy Britten, RN, Karthik Dhandapani, MBBS, Sophie Atkins, RN
York and Scarborough Teaching Hospitals, Anaesthetics, York, United Kingdom

Introduction: Spinal cord stimulation (SCS) presents an effective treatment for neuropathic pain refractory to medical management (1). In the past a screening trial needed to be conducted before a final implant of SCS in every case in the UK (2). Recent findings have suggested that at-home trials of SCS delivered no clinical advantage to patients in terms of long-term improvement of pain intensity or quality of life (3). As a result, all-in-one implantation is an alternative in the UK.
This single-centre case-series collects real-world long-term outcomes on pain relief in chronic pain patients who underwent a single-stage evoked compound action potential (ECAP)-controlled closed-loop SCS system implant.

Materials / Methods: This ongoing single-centre real-world experience collects data of patients that underwent a single-stage all-in-one permanent implantation of the ECAP-controlled closed-loop system. Pain intensity was assessed using the numeric rating scale (NRS; 0: no pain, 10: extremely severe pain) before permanent implant of the device and at 6 weeks, 6-, 12-, and 18-months post implant. Objective device data were collected at each follow-visit. Collection and analysis of data are currently ongoing. Interim results are presented below. Higher patient numbers and results on quality of life will be presented during INS meeting.

Results: A total of nine patients underwent an all-in-one single-stage permanent implantation of the ECAP-controlled closed-loop system. Most of the patients had a diagnosis of chronic intractable pain of the trunk and/or limbs due to a PSPS type 2 with predominant pain in the legs. On average patients suffered for 7.8 years from their chronic pain condition. There were 3 females and 6 males included in the analysis. Mean (± SEM) baseline NRS score was 9.33 (± 0.167) and decreased to 3.36 (± 0.564) after 12-months and 2.75 (± 0.479) after 18-months (Fig. 1A). Patient used the therapy 91.17 % (median) of the time and spent 94.58 % of the time in closed-loop. Pain relief improved overtime from 56.71 % at 6-weeks post permanent implant to 70.00 % after 18-months of ECAP-controlled closed-loop SCS therapy (Fig. 1B).

Discussion: Our results confirm sustainable pain relief in patients suffering from chronic pain who underwent a single-stage ECAP-controlled closed-loop SCS system implant. Data collection is ongoing and additional data are needed to support the findings.

Conclusions: Our results confirm sustainable pain relief in patients suffering from chronic pain who underwent a single-stage ECAP-controlled closed-loop SCS system implant. Data collection is ongoing and additional data are needed to support the findings.

Supplemental Data:

References: Caylor J, Reddy R, Yin S, et al.. Spinal cord stimulation in chronic pain: evidence and theory for mechanisms of action. Bioelectron Med. 2019;5(1):12. Smith BH, et al. Health and quality of life associated with chronic pain of predominantly neuropathic origin in the community. Clin J Pain. 2007;23(2): 143–9. Eldabe S, et al. Does a Screening Trial for Spinal Cord Stimulation in Patients with Chronic Pain of Neuropathic Origin have Clinical Utility and Cost-Effectiveness? (TRIAL-STIM Study): study protocol for a randomised controlled trial. Neurosurgery. 2023 jan 1;92(1):75-82.

Acknowledgements:

Learning Objectives: All-in-one implantation of ECAP-controlled closed-loop SCS results in stable pain relief over time in real world patients. ECAP-controlled closed-loop SCS therapy leads to an increasing pain relief over time up to 24-months.

Financial Disclosures: Philippa MC Armstrong; Saluda; Speaker at Sense meeting London May 2023; travel accomodation and speaker preparation and presentation time reimbursement Philippa MC Armstrong; Saluda; Speaker at eINS Hamburg 2023; travel accomodation and speaker preparation and presentation time reimbursement Peter A Hall; Saluda; Delegate at Sense Meeting London May 2023; travel and accomodation reimbursement Karthikeyan Dhandapani; Saluda; Delegate at eINS Hamburg 2023; travel and accomodation reimbursement

Disclosure: No significant relationships.

235

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

SPINAL CORD STIMULATION FOR CHRONIC PELVIC PAIN

Anna Balzer, MD[1], Itay Goor-Aryeh, [2], Vadim Tashlykov, [3]
[1]Sheba Tel- HaShomer Medical Centre., Pain Clinic, xxx, Israel, [2]Sheba Tel- HaShomer Medical Centre, Pain Clinic, xxx, Israel, [3]Salomon MC, Assuta Ashdod, Pain Clinic, xxx, Israel

Introduction: Chronic pelvic pain (CPP) in females – pain in pelvic floor which is continuous for at least 6 months prior to observation. Two to ten percent of all gynecologic outpatient clinic consultations are due to CPP, in which 60% of patients cannot identify factors associated to the pain. Untreated CPP may result in long-term disability, depression, and personality changes. We present a case report of a young patient with CPP due to endometriosis, who we treated with neurostimulation in the Sheba MC, Ramat Gan, Israel.

Materials / Methods: *Participant*

A twenty-five-year-old nulliparous single woman, was referred to the Sheba Pain Clinic in 2021 by the Gynecology Unit for the treatment of intense pelvic and leg pain. The pain started one and a half year prior to consultation. Despite normal neurologic status the patient stopped working in 2022 secondary to pain.
On initial evaluation she had scores: functional independence measurement=108/126, muscle testing= 3-4/5, VAS (pain measure) = 10/10 in rest, 6-minute walk=350m, 5-times sit to stand=10.3s. Following the pain clinic evaluation, attempts with neuroaxial and local injections were not successful. Physiotherapeutic procedures caused to the pain worsening. Medications, including Pregabalin, weak opioids, and non-opioid central analgesics did not provide significant pain reduction.

Procedure
One year after the patient's first pain clinic evaluation, she underwent trial spinal cord stimulator implantation. One 8-contact electrode was implanted with entry level T12-L1, and stimulation zone T8. During the one-week trial period, the pain had a significant decrease in both lower back and leg, with partial coverage of pelvic floor. The patient proceeded to permanent implantation with two 16-contact leads. One of the electrodes was implanted at the same level as trial lead, and the second was inserted in retrograde, with entry level L1-L2, and the tip at level S1.

Results: Follow up evaluation was done at 1 month and 6 months after the procedure. Currently, the patient has normal neurological status, she is completely independent (basic and instrumentally), works full time and drives. She is in a romantic relationship. Her pain went down from 10 to 3 points (VAS) when exercising. She manages to walk long distances without breaks. The pain medication was reduced.

Discussion: Neuromodulation should be considered as a relevant option for treatment of not only neuropathic but also mixed complicated pain. Appropriate patient selection is a key factor in neuromodulation effectiveness. The goal of the treatment should be not restricted to reduce the pain, but to increase quality of life and functionality as well.

Conclusions:

Supplemental Data:

References:

Acknowledgements:

Learning Objectives:

Financial Disclosures: There are no financial conflicts of interest to disclose

Disclosure: No significant relationships.

236

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

DRESSING TECHNIQUE FOR USE IN SPINAL CORD STIMULATION TRIAL

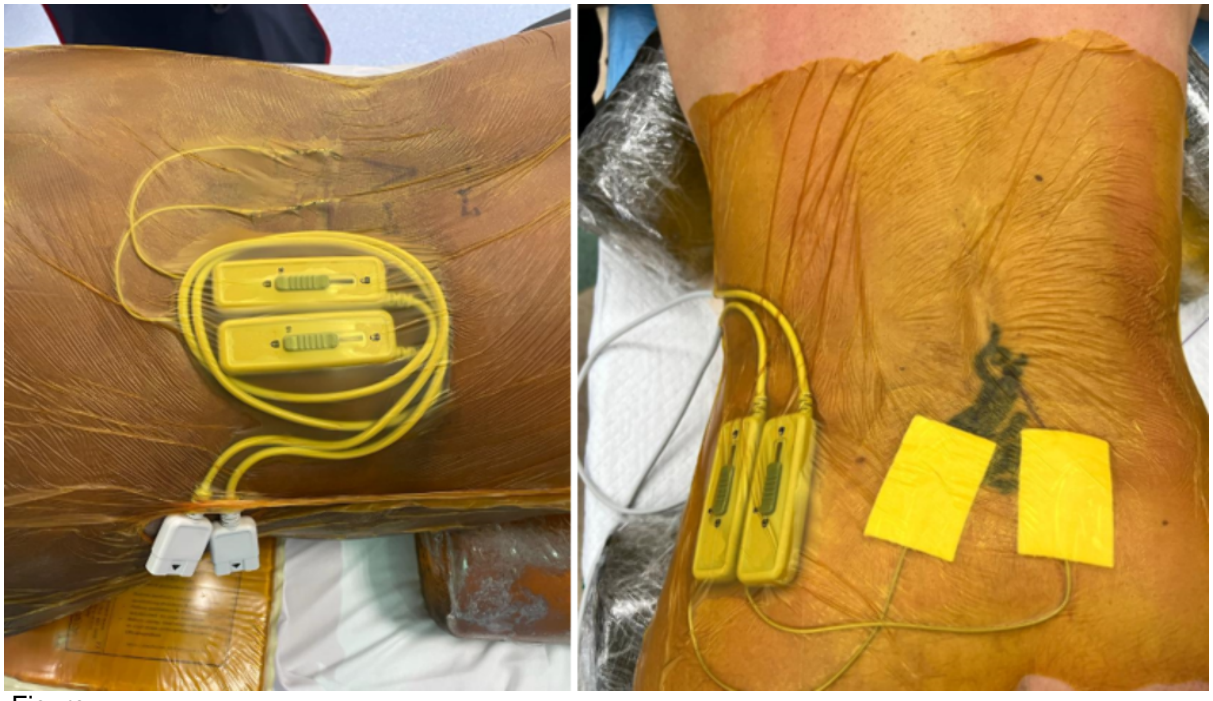
Laura Barros, MD[1], Catarina Lins, MD[2]
[1]Department of Pain, Hospital São Luiz de Osaco- SP, OSASCO, Brazil, [2]Pain Center, University of São Paulo School of Medicine, São Paulo – SP, SAO PAULO, Brazil

Introduction: Before qualifying for a permanent spinal cord stimulation (SCS) system implantation, patients need to undergo a successful SCS trial (1) . There exist various methodologies to conduct an SCS trial, but the prevalent approach involves the fluoroscopic placement of percutaneous trial leads for a span of 5-7 days (2). Following this duration, these trial leads are extracted. The primary objective of this trial phase is to ascertain the efficacy of the SCS in alleviating pain and to pinpoint the specific location on the spinal cord yielding the optimal pain relief for the patient.

Materials / Methods: Introduce a dressing model that can be used during the trial period of percutaneous spinal cord electrode implantation.

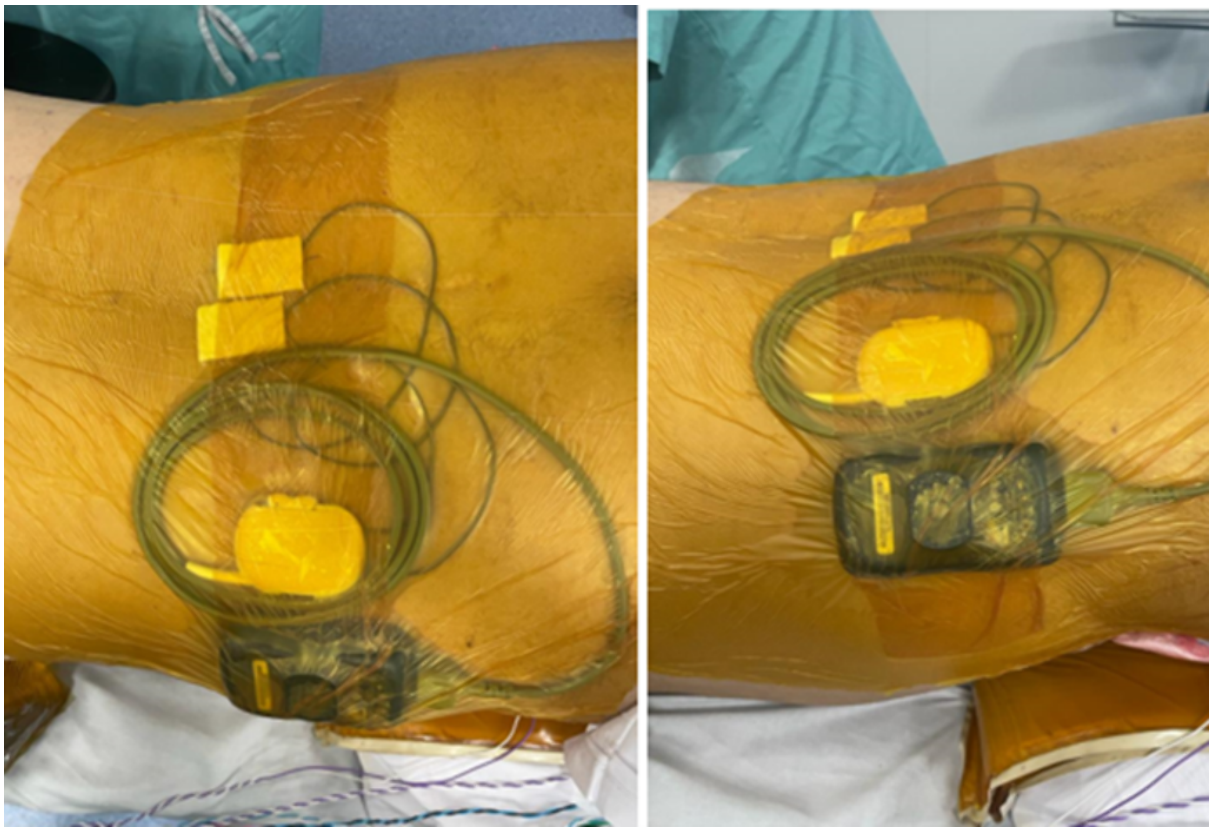
Results: According to our protocol, this period lasts 10 days, during which the patient stays at home. It involves the application of a sterile dressing traditionally used in surgical procedures. The connection cables to the electrodes are also incorporated into it.

Discussion: One of the major advantages of augmentative (neuromodulation) procedures such as spinal cord stimulation (SCS) is the availability of a trial which emulates the definitive procedure exactly (3). This dressing model was developed to secure the test implant, allowing the patient greater freedom to carry out their activities during the test period. Figure 1



Figure

2



Conclusions: This dressing model allows the patient to stay at home during their test period and provides greater freedom for the patient to carry out their daily activities, offering a more realistic assessment of improvement after the implant.

Supplemental Data:

References: 1. Osborne MD, Ghazi SM, Palmer SC, Boone KM, Sletten CD, Nottmeier EW. Spinal cord stimulator--trial lead migration study. Pain Med. 2011 Feb;12(2):204-8. doi: 10.1111/j.1526-4637.2010.01019.x. Epub 2010 Dec 10. PMID: 21143759. 2. Haider N, Ligham D, Quave B, Harum KE, Garcia EA, Gilmore CA, Miller N, Moore GA, Bains A, Lechleiter K, Jain R. Spinal Cord Stimulation (SCS) Trial Outcomes After Conversion to a Multiple Waveform SCS System. Neuromodulation. 2018 Jul;21(5):504-507. doi: 10.1111/ner.12783. Epub 2018 Jun 11. PMID: 29889356. 3. North RB. SCS Trial Duration. Neuromodulation. 2003 Jan;6(1):4-5. doi: 10.1046/j.1525-1403.2003.03010.x. PMID: 22150907

Acknowledgements:

Learning Objectives: DEMONSTRATE DRESSING TO PERFORM THE MEDULLARY ELECTRODE TEST PERIOD IN A NON-HOSPITAL ENVIRONMENT.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

237

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

PATIENTS WITH COMPLEX REGIONAL PAIN SYNDROME TREATED WITH DORSAL ROOT GANGLION STIMULATION: A LONG-TERM RETROSPECTIVE PSYCHOSOCIAL EVALUATION IN BELGIAN PAIN CENTERS

Bart Billet, MD[1], Jonas Verzele, MD[2], Martine Puylaert, MD[3], Sofie Denkens, MD[4], Mayken Gorissen, MD[5], Bram Blomme, PhD[6], Tony Van Havenbergh, MD, PhD[7], Mark Plazier, MD[8], Jean-Pierre Van Buyten, MD, PhD[9]
[1]AZ Delta, Roeselare, Belgium, [2]AZ Sint-Elisabeth, Zottegem, Belgium, [3]Ziekenhuis Oost-Limburg, Multidisciplinary Pain Centre, Genk, Belgium, [4]Heilig Hart Ziekenhuis, Lier, Belgium, [5]AZ Sint-Jan, Brugge, Brugge, Belgium, [6]Abbott, Zaventem, Belgium, [7]ZAS Hospitals, Neurosurgery, Antwerp, Belgium, [8]Jessa Hospital, Neurosurgery, Hasselt, Belgium, [9]AZ Vitaz, Multidisciplinary Pain Center, Sint-Niklaas, Belgium

Introduction: Dorsal root ganglion neurostimulation (DRG-S) has resulted in higher responder rates for pain relief compared to spinal cord stimulation (SCS) in patients with chronic complex regional pain syndrome (CRPS) types 1 and 2.[1] Although the pivotal Accurate trial and other studies have shown improvements in mood, catastrophizing states, and depression,[1-4] there is a lack of data on the long-term psychosocial consequences of DRG-S in this difficult-to-treat patient population. The aim of this abstract is to present a comprehensive evaluation of changes in cognition, behavior, and self-reliance in CRPS patients treated with DRG-S, in addition to standard safety and effectiveness assessments, in pain clinics in Belgium.

Materials / Methods: Data will be collected from 8 tertiary multidisciplinary pain centers, retrospectively sourced from clinical records and a national web-based application (Neuro-Pain Platform). All patients with CRPS, diagnosed based on the Budapest criteria, who underwent a trial of the DRG-S system were included in the retrospective chart review. All patients provided written informed consent for DRG-S implantation and follow-up every 6 months. Ethical approval for the retrospective analysis was obtained from local ethics committees. The Illness Attitude Scale (IAS), Symptom Checklist-90 (SCL-90), and Pain Coping Inventory (PCI) questionnaires assess multiple aspects of the patient's psychopathology. The Pain Disability Index (PDI) measures the extent to which aspects of a patient's life are disrupted by chronic pain. The Katz scale assesses the patient's ability to independently perform activities of daily living. Pain intensity and sleep quality were recorded using a numerical rating scale (NRS). Device- and procedure-related adverse events are presented.

Results: Data from 80 trialed and 70 implanted patients were included in the interim analyses. The mean age (SD) at baseline was 47.4 (14.8) years; 79% were women. Of these patients, 90% had CRPS-related single-site knee or foot pain. 47.1%, 44.3%, 7.1%, and 1.4% received: one, two, three, and four DRG-S leads, respectively, with >85% covering L3-L5. At baseline, IAS assessment showed that only 16.4% met the threshold for serious health anxiety, but patients reported extensive treatment experience and their complaints hindered work, concentration, and enjoyment. At the end of the DRG-S trial (EoT), >80% of patients were completely independent in dressing, toileting, and feeding. About 40% still needed help with bathing and transfer. NRS pain scores decreased from 8.2 (1.1) at baseline to 2.3 (1.6) at the EoT and to 3.3 (1.8), 3.9 (2.1), 4.0 (2.1), 4.1 (2.1) and 3.5 (1.9) at 6, 12, 18, 24, and 30 months, respectively. Sleep quality improved from an NRS score of 3.3 to approximately 7.0 at 6 months, maintained through 30 months follow-up. The total score on the SCL-90 (measure of psycho-neuroticism) decreased from 162.3 (55.3) at baseline to 120.0 (37.3), 140.6 (42.8), and 124.7 (59.6) at EoT, 6 and 12 months and patients reported improvements for all nine SCL-90 subscales. At follow-up timepoints, DRG-S patients improved in passive pain coping (resting, retreating, and worrying), but not in active pain coping (distraction, pain transformation, and reducing demands). 74%-58% of patients were below the clinical cutoff for chronic pain (≥39) on the PDI after 6 to 24 months of DRG-S treatment. The most common adverse event was pocket pain (13.8% of patients), followed by dural tear and hematoma (both 5.0%).

Discussion: CRPS, a severely debilitating chronic pain condition, causes stressors that lead to cognitive and psychological deficits and loss of independence. DRG-S can target discrete anatomical regions of pain and treat dermatomes difficult to manage with SCS, providing therapy tailored to the distinct pathology of CRPS. In this retrospective analysis, DRG-S treatment for CRPS not only led to improvements in pain and sleep but also to less psychological/physical dysfunction. Patients tend to be independent in activities of daily living, their pain limits them less in performing these activities, and they rely less on passive pain coping strategies.

Conclusions: This retrospective analysis shows that appropriately selected CRPS patients treated with DRG-S result in significant long-term improvements in pain, sleep, and in multiple aspects of the patient's psychopathology.

Supplemental Data:

References: 1. Deer T, Levy R, Kramer J, et al. Dorsal root ganglion stimulation yielded higher treatment success rate for complex regional pain syndrome and causalgia at 3 and 12 months: a randomized comparative trial. Pain 2017; 158(4): 669–681 2. Liem L, Russo M, Huygen F, et al. One-year outcomes of spinal cord stimulation of the dorsal root ganglion in the treatment of chronic neuropathic pain. Neuromodulation 2015;18(1):41-8 3. Morgalla MH, Bolat A, Fortunato M, Lepski G, Chander BS. Dorsal Root Ganglion Stimulation Used for the Treatment of Chronic Neuropathic Pain in the Groin: A Single-Center Study With Long-Term Prospective Results in 34 Cases. Neuromodulation 2017;20(8):753-760. 4. Morgalla MH, Fortunato M, Lepski G, Chander BS. Dorsal Root Ganglion Stimulation (DRGS) for the Treatment of Chronic Neuropathic Pain: A Single-Center Study with Long-Term Prospective Results in 62 Cases. Pain Physician 2018;21(4):E377-E387.

Acknowledgements: The support of Abbott for this project is gratefully acknowledged.

Learning Objectives: 1. Assess multiple aspects of the psychopathology of a chronic CRPS patient after dorsal root ganglion (DRG) stimulation

2. Understand the change in the impact of pain on a chronic CRPS patient's life and their ability to perform daily activities after DRG stimulation

3. Evaluate the safety and effectiveness of DRG stimulation in pain clinics in Belgium

Financial Disclosures: B Billet is a consultant for Nevro Corp, Abbott, and Saluda

B Blomme is an employee of Abbott

T van Havenbergh is a consultant for Abbott

M Plazier is consultant for Abbott, Medtronic, Boston Scientific, and Salvia. Has received scientific grants from Abbott and Medtronic

JP Van Buyten is a consultant for Medtronic, Abbott, Nevro, Mainstay Medical, and Boston Scientific

J Verzele, M Puylaert, S Denkens, and M Gorissen declare no significant relationships. #Complex Regional Pain Syndrome, Dorsal Root Ganglion Stimulation, Psychosocial Evaluation, Belgium

Disclosure: I am an employee of Abbott

238

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

HOLISTIC OUTCOMES WITH ECAP-CONTROLLED CLOSED-LOOP SCS: INTERIM AZ DELTA EXPERIENCE

Bart Billet, MD[1], Ruben De Vos, MD[2], Karel Hanssens, MD[2]
[1]AZ Delta, Anesthesiology, Roeselare, Belgium, [2]AZ Delta, Roeselare, Belgium

Introduction: Chronic pain is a multidimensional disease characterized by impairments in several health-related domains (1). Herein, we characterized the holistic treatment response of a real-world chronic pain population utilizing evoked-compound action potential (ECAP)-controlled closed-loop spinal cord stimulation (CL-SCS) and explored its association with objective neurophysiological measurements.

Materials / Methods: An analysis of subjects implanted for 6 months (n=11) with CL-SCS at one investigational site in an ongoing, prospective, multicentre EU post-market study (NCT#04627974) is presented. Objective device data including median system utilization, ECAP dose and time stimulating above the ECAP threshold, as well as patient-reported outcome measures were collected. Holistic treatment response, as defined by clinically meaningful improvements (literature defined MCIDs) in baseline dysfunctional (non-normative) PROMIS-29 domains of physical function and sleep disturbance, VAS primary pain region percentage reduction, POMS total mood disturbance score, and EQ-5D-5L were assessed. From the holistic domains, a cumulative responder score is calculated (addition of all MCIDs)

Results: The device was utilized 97.1% of the time by patients, at 95.0% of time above ECAP threshold, and ab ECAP dose of 16.8 µV.1. Patients showed an average improvement of greater than one MCID in each holistic domain (mean MCIDs at 6 months: PROMIS-29 Physical Function: 1.6; PROMIS-29 Sleep: 2.3; VAS primary region: 2.0; POMS: 1.8; EQ-5D: 4.6). The mean cumulative responder score was 11.6 MCIDs (standard deviation 4.8).

Discussion: A treatment effect equivalent to an average of 2.5 MCIDs per domain (range, 1.6 to 4.6) was observed at 6 months. The potential of holistic treatment response and cumulative MCIDs in assessing long-term SCS treatment response instead of pain reduction should be considered in future studies.

Conclusions: The ECAP-controlled CL-SCS consistently elicited a prescribed neural response. Consistent neural activation and confirmed patient adherence contribute to a meaningful, holistic treatment response.

Supplemental Data: Learning Objectives: 1. To evaluate the holistic treatment response in patients suffering from chronic pain receiving ECAP-controlled CL-SCS therapy at a single center. 2. To measure neural activation and accuracy, it provides a transparent evaluation of SCS therapy.

References: Levy RM, et al. Holistic Treatment Response: An International Expert Panel Definition and Criteria for a New Paradigm in the Assessment of Clinical Outcomes of Spinal Cord Stimulation. Neuromodulation 2023; online ahead of print.

Acknowledgements:

Learning Objectives: 1. To evaluate the holistic treatment response in patients suffering from chronic pain receiving ECAP-controlled CL-SCS therapy at a single center. 2. To measure neural activation and accuracy, it provides a transparent evaluation of SCS therapy. 3. Evaluate consistency of stimulation.

Financial Disclosures: Bart Billet: ABBOTT consultancy, educational services. Bart Billet: Saluda consultancy, educational services Bart Billet: Salvia-Bioelectronics consultancy, educational services Bart Billet: Medtronic consultancy, educational services - NO stock options

Disclosure: No significant relationships.

239

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

NEUROMODULATION FOR CANCER-RELATED PAIN - A CASE SERIES.

Sheila Black, MB ChB[1], Beatrice Bretherton, BSc (Hons), PhD[2]
[1]Leeds teaching hospitals NHS trust, Pain Management, Leeds, United Kingdom, [2]Leeds Teaching Hospitals NHS Trust, Pain Management Department, Leeds, United Kingdom

Introduction: Cancer and treatment for cancer can leave many patients with problematic neuropathic pain, which can be resistant to treatment. In cancer survivors, long-term neuromodulation in the form of spinal cord stimulation (SCS) or peripheral nerve stimulation (PNS) can be considered. The authors describe 25 cases of neuromodulation used to manage cancer related neuropathic pain in a tertiary cancer centre.

Materials / Methods: All patients were referred by oncology services and seen in dedicated cancer pain clinic. All patients completed local neuromodulation pathway, including consultant and CNS assessment, psychology if required, and MDT approval.

Results: 25 cases of SCS/PNS for treatment of chronic neuropathic pain in cancer survivors described: **Pain resulting from cancer disease:** Muscle tumours: Fibromatosis of deltoid, peripheral nerve stimulator to left brachial plexus; Fibromatosis deep loin, SCS T8/9; Sarcoma (multiply recurrent) requiring hindquarter amputation with L5 pain, SCS T10/11. Nerve tumours: Cervical ependymoma C5-T1, PNS to left brachial plexus; Neurofibroma C5 SCS C2/3; Neurofibromatosis type II, L5 pain, SCS T10/11 Bone tumours: Myeloma, L5 root compression, SCS T8-10; Myeloma L1-3 fusion, SCS T9/10; Metastatic prostate cancer with bone mets L3, SCS T8/9. **Pain following treatment of cancer:** Surgery: SCS for Post-thoracotomy pain from oesophageal cancer age 35; Ovarian cancer hysterectomy oophorectomy with pelvic pain, SCS T8 and L1; Breast Ca excision, SCS T2/3. Radiotherapy: Sacral radiotherapy to SCC anal verge with buttock/sciatic pain, SCS T8-10; Vulval Ca, left hemipelvectomy and vulval radiotherapy, SCS T11/12; Radiation neuritis following SCC mandible, brachial plexus PNS; SCC vagina, high dose pelvic radiotherapy, SCS T12/L1; Anal Ca, chemoradiotherapy with pelvic pain, SCS T11/12. Chemotherapy: CIPN both legs following chemo for acute myeloid leukaemia, SCS T10/11; CIPN following chemo for mediastinal germ cell tumour, bilateral hands and feet, SCS cervical and thoracic. **Pain from other origin, complicated by cancer management:** Neuropathic AKA stump pain following femoral pseudoaneurysm, complicated by radical radiotherapy for SCC glottis, SCS T9/10-

Discussion: Prompt referral from oncology services facilitated assessment of patient suitability. Established neuromodulation pathway remains essential, including MDT assessment, discussion and approval. Weekly rapid-access out-patient clinic and weekly cancer pain day-case theatre lists facilitated timely conduct of SCS trial and full implants.

Conclusions: This case series demonstrates that cancer survivors can suffer chronic neuropathic pain, either from cancer disease and treatment for cancer, which can be appropriately treated with neuromodulation.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. Explore the neuropathic pain conditions which can result from cancer, its treatment and metastatic sequelae. 2. Demonstrate that effective pain relief can be achieved with neurodulation, both with spinal cord stimulation and peripheral nerve stimulation. 3. Explore the

potential use of neuromodulation both in cancer survivors and those with stable or progressive cancer disease states.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

240

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

DIAGNOSTIC CONUNDRUM - MECHANICAL BACK PAIN WITH MULTIFIDUS DYSFUNCTION OR NEUROPATHIC NON-SURGICAL BACK PAIN

Sheila Black, MB ChB, Harry Soar, MBChB FRCA EDPM
Leeds teaching hospitals NHS trust, Pain Management, Leeds, United Kingdom

Introduction: Axial low back pain is a comon condition, often managed with physiotherapy, exercise programs, simple analgesics and lifestyle modifications. Growing interest in the use of spinal cord stimulation for non-surgical back pain has opened up this therapy to a larger cohort of patients, but care should be taken in correctly idenitfying those who would most benefit from this moderately-invasive therapy. On the other hand, use of restorative muscle stimulation for those with mechanical back pain may pose an alternative therapeutic option, though again, much research is needed to identify those who would be most likely to respond.

Materials / Methods: The authors present the case of a 41 year old female who was referred to pain clinic with low back pain, with little relief from conventional medical and physical therapies. She proceeded to have full implant of high frequency spinal cord stimulation, but failed to recieve any benefit from it for a year, despite repeat attempts at reprogramming. Axial back pain continued, and a trial of diagnostic lumbar medial branch blocks was performed. These were extremely helpful, indicating a positive MBB trial, and patient proceeded to have radiofrequency rhizolysis, which again, unfortunately, did not prove to be helpful . MRI scan was undertaken, which showed wasting and fatty infiltration of the multifidus muscles bilaterally, and so multifidus stimulation was considered.

Results: During a simltaneous procedure, the redundant spinal cord stimulator was explanted and multifidus stimulator was implanted. Following commencement of the multifidus stimulation regime, the patient noticed significant reduction in low back pain, though full results and pain scores will be available for the final submission of the abstract for the conference in May 24.

Discussion: This case illustrates the diagnostic difficulty in identifying the most appropriate treatment for axial low back pain. On one hand, recent studies suggest that there is a significant neuropathic component, and this can be managed with spinal cord stimulation[1]. However, if mechanical components predominate, then restorative multifidus stimulation may be more effective[2]. The invasiveness of both therapies are similar, involving placement of spinal electrodes which are tunnelled to subcutaneous placement of IPG battery. More research is needed into this non-surgical back pain cohort to identify predicative features to aid the clinician to choosing the most approprite therapy.

Conclusions: The authors present the case of a patient with axial low back pain, who responded better to multifidus muscle stimulation compared with high frequency spinal cord stimulation

References: 1. Kapural et al, Treatment of nonsurgical refractory back pain with high-frequency spinal cord stimulation at 10 kHz: 12-month results of a pragmatic, multicenter, randomized controlled trial. J Neurosurg Spine. 2022 Feb 11:1-12. 2. Gilligan et al. Long-Term Outcomes of Restorative Neurostimulation in Patients With Refractory Chronic Low Back Pain Secondary to Multifidus Dysfunction: Two-Year Results of the ReActiv8-B Pivotal Trial. Neuromodulation. 2023 Jan;26(1):87-97.

Acknowledgements:

Learning Objectives: 1. Explore the assessment process for patients with axial low back pain, to identify cardical features of mechanical and neuropathic pain. 2. Discuss the benefits of both spinal cord stimulation and multifidus restoration therapy and the differences in practice. 3. Explore the

options for screening and identifying these cohorts to optimise the decision making for these therapies.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

241

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

IMPROVEMENT IN HEALTH-RELATED QUALITY OF LIFE WITH SPINAL CORD STIMULATION IN COMPLEX REGIONAL PAIN SYNDROME: A SINGLE-CENTRE, RETROSPECTIVE STUDY

Mazen Khabbass, MBBS[1], Mohammad Saleki, MB ChB[1], Beatrice Bretherton, BSc (Hons), PhD[1,2], Ganesan Baranidharan, FRCA[1,3]
[1]Leeds Teaching Hospitals NHS Trust, Pain Management Department, Leeds, United Kingdom, [2]University of Leeds, School Of Biomedical Sciences, Faculty Of Biological Sciences, Leeds, United Kingdom, [3]University of Leeds, School Of Medicine, Faculty Of Medicine And Health, Leeds, United Kingdom

Introduction: Complex regional pain syndrome (CRPS) can profoundly affect many aspects of everyday life. Spinal cord stimulation (SCS) is a potential therapeutic option with evidence showing promising effects (1). This retrospective, single-site evaluation explored health-related quality of life (HRQoL) in individuals with CRPS treated with SCS in our Pain Service.

Materials / Methods: All patients aged ≥18 years with CRPS with a fully implanted SCS between June 2013 and January 2023 were identified. Gender, age, chronic pain diagnosis, SCS system, pre-implant and follow-up scores for HRQoL (EQ-5D-3L index score), average pain, worst pain and the influence of pain on aspects of everyday life [all numerical rating scale, NRS], and the occurrence and reasons for revisions and explants were collected. Initially, HRQoL over time was visualised, then Wilcoxon Signed-Rank Tests explored differences between pre-implant and the most recent follow-up visit. Counts and percentages were generated for HRQoL and pain response rates. An intention-to-treat approach was adopted.

Results: The final cohort comprised 88 patients (49 females), with a mean (standard deviation) follow-up duration of 33.83 (16.92) months. All patients (n=77) had HRQoL scores lower than the population norm of 0.82 (2) at pre-implant. Visualisation of scores for each patient across all follow-ups showed that HRQoL largely improved (see Figure 1a). HRQoL scores were significantly improved at the most recent follow-up compared to pre-implant (see Figure 1b) and 52% showed ≥0.074 improvement. Despite these positive effects on HRQoL, relatively low pain response rates were observed: 34% reported a reduction ≥30% in average pain NRS and the pain remission rate (average pain score ≤3 NRS) was
14%.

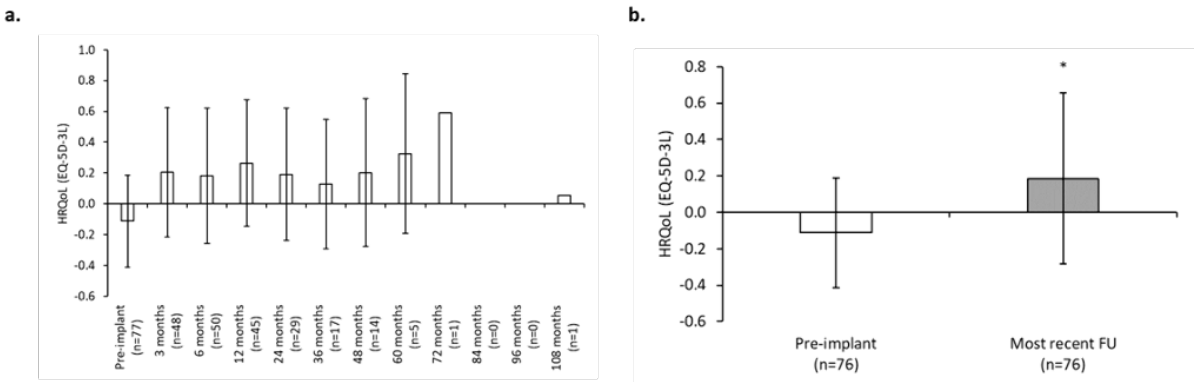


Figure 1: HRQoL in all patients at each visit (a) and at pre-implant and the most recent follow-up (b). * = significantly different to pre-implant. Data presented as mean ± 1 SD. 40 patients (45%) had a surgical revision. Ten patients (11%) had their system fully explanted due to insufficient pain relief (n=9), infection (n=2) and requiring an MRI (n=1).

Discussion: Patients had statistically and clinically meaningful improvements in HRQoL despite pain response and remission rates that were lower than those reported in the literature (3). This therefore suggests that HRQoL is a key outcome in ascertaining the overall outcome of SCS in CRPS.

Conclusions: With further research exploring the long-term effects of SCS in prospective, randomised, controlled clinical trials, its efficacy in difficult-to-treat CRPS may be established.

Supplemental Data:

References: 1. Mekhail N, Deer TR, Poree L, Staats PS, Burton AW, Connolly AT, et al. Cost-effectiveness of dorsal root ganglion stimulation or spinal cord stimulation for complex regional pain syndrome. Neuromodulation Technol Neural Interface [Internet]. 2021 Jun;24(4):708–18. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1094715921000015 2. Szende A, Janssen B, Cabasés J. Self-Reported Population Health: An International Perspective based on EQ-5D [Internet]. Szende A, Janssen B, Cabases J, editors. Self-Reported Population Health: An International Perspective Based on EQ-5D. Dordrecht: Springer Netherlands; 2014. Available from: http://link.springer.com/10.1007/978-94-007-7596-1 3. Gill JS, Asgerally A, Simopoulos TT. High-frequency spinal cord stimulation at 10 kHz for the treatment of complex regional pain syndrome: A case series of patients with or without previous spinal cord stimulator implantation. Pain Pract [Internet]. 2019 Mar;19(3):289–94. Available from: https://onlinelibrary.wiley.com/doi/10.1111/papr.12739

Acknowledgements: No support was received for this work.

Learning Objectives: Readers will learn new information on: 1. The importance of longitudinal data collection in neuromodulation, particularly in patients with CRPS treated with SCS. This is crucial as longer-term outcomes for this therapy in patient groups can be examined, inform future practice and have pathways to impact to benefit patients. 2. The importance of quantifying and exploring the impact of neuromodulation on HRQoL (i.e., limiting the reliance on pain scores to determine treatment success). 3. Potential next steps to build on the findings of this single-centre, retrospective study.

Financial Disclosures: BB has provided consultancy to Abbott and Platform 14. GB has a consulting agreement with Saluda, Nevro Corp, Abbott, Medtronic, Boston Scientific, Stryker and Mainstay Medical. GB had educational and research grants from Nevro Corp, Abbott and Boston Scientific. GB is on the advisory board for Abbott and Nalu Medical. The remaining authors report no conflicts of interest.

Disclosure: No significant relationships.

242

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

WHAT IMPACT HAS THE COVID-19 PANDEMIC HAD ON OUTCOMES FOR SPINAL CORD STIMULATION IN THE TREATMENT OF CHRONIC PAIN? A SINGLE-CENTRE, RETROSPECTIVE AUDIT

Andrea Byfield, BSc (Hons)[1], Christopher Gillman-Wells, [1], Beatrice Bretherton, BSc (Hons), PhD[1,2], Ganesan Baranidharan, FRCA[1,3]
[1]Leeds Teaching Hospitals NHS Trust, Pain Management Department, Leeds, United Kingdom, [2]University of Leeds, School Of Biomedical Sciences, Faculty Of Biological Sciences, Leeds, United Kingdom, [3]University of Leeds, School Of Medicine, Faculty Of Medicine And Health, Leeds, United Kingdom

Introduction: For staff and patient safety during the COVID-19 pandemic, there was a shift in medical practice towards the adoption of telemedicine (1). In the Leeds Teaching Hospitals NHS Trust, the spinal cord stimulation (SCS) pathway changed during the pandemic where most patient follow-up visits changed from face-to-face to telephone or video. This retrospective, single-site audit explored the extent to which the changes in our SCS pathway impacted outcomes, including health-related quality of life (HRQoL), average pain, worst pain, global impression of change, rates of revisions and full system explants.

Materials / Methods: All patients aged ≥18 years that had an SCS system implanted between July 2020 and December 2021 were identified. Gender, age, chronic pain diagnosis, SCS system, pre-implant and follow-up scores for HRQoL (EQ-5D-3L index score), average pain, worst pain and the influence of pain on aspects of everyday life [all numerical rating scale, NRS], follow-up appointment modality (telephone, video, face-to-face), and the occurrence and reasons for revisions and explants were collected. The data will be analysed using an intention-to-treat approach.

Results: One hundred and sixty-six patients (Table 1) in this period, with the majority operated on for back and leg pain and both pre and post-OP data for 141 patients. The mean average NRS scale from 7.17(1.51) dropped to 4.40 (2.2), and the worst NRS from 8.96(1.09) to 6.89(2.58). EQ-5D-5L improved from -0.08(0.37) to 0.34 (0.42). 29 (17.475) of the 166 patients underwent revision surgery (Table 2), with IPG site pain (14) being the most typical cause for revision. Four patients out of the 166 (2.41%) explanted as of March 2024 (1 Medical investigation, 2 poor relief, 1 infection). We also collected the number of face-to-face visits for programming till September 2024(Table 4).

		Females	**Males**
Demographics Details	Females (n) / Males (n)	90	76
	Age (mean (SD), years	56 (13)	
IPG Site location	Chest Wall	26	30
	Buttock	62	39
	Flank	2	1
	Hip	0	1
Diagnosis	Visceral pain	8	4
	Back and leg pain	56	52
	Neck and arm pain	7	5
	Pelvic pain	5	0
	Peripheral neuropathy	7	7
	CRPS	6	6
	Other Pain	1	2

Table 1 – provides a summary of the characteristics of the samples of 166 patients, where only age is presented as a mean and all other values corresponded to the number of patients. IPG = Implantable Pulse Generator, CRPS = Complex Regional Pain Syndrome and SD = Standard Deviation.

Table 2: Revision Surgery

Revision reason	Count
Lead Migration	1
IPG Site Altered	14
Replacement of lead or system	6
additional lead	1
Poor pain relief	4
Infection	1

Table 4: Programming visits

Number of appointments for programming	**Patient Count**	**Percentage**
0	46	32%
1	40	28%
2	33	23%
3	15	10%
4	9	6%

Discussion: The results of both outcome measures, NRS, EQ5D, and the complication rate, were comparable to the publications pre-COVID (Table 5). We collated the results of 387 patients from our pre-COVID publications. We conclude that the introduced changes have not affected our patient-reported outcome with fewer face-to-face appointments. It is the first time we have seen a report on a number of programming visits.

Table 5: PROMS Comparison

	Pre COVID (n=387)	Post COVID (n= 141)
Pre-OP EQ-5D-5L	-0.02	-0.08
Post OP EQ-5D-5L	0.25	0.34
Pre-OP Avg NRS	7.3	7.17
Post OP Avg NRS	4.99	4.39
Pre-OP Worst NRS	8.84	8.96
Post OP Worst NRS	6.83	6.89

Conclusions: We have adopted most of the post-COVID changes in our routine neuromodulation pathway.

Supplemental Data:

References: 1. Al-Jabir A, Kerwan A, Nicola M, Alsafi Z, Khan M, Sohrabi C, et al. Impact of the Coronavirus (COVID-19) pandemic on surgical practice - Part 1. Int J Surg [Internet]. 2020 Jul;79:168–79. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1743919120304052

Acknowledgements: No support was received for this work.

Learning Objectives: Readers will learn new information on: 1. How our Pain Service adapted the SCS pathway during the COVID-19 pandemic and how this differed to the SCS pathway prior to the pandemic. 2. The extent to which the changes in our Pain Service's SCS pathway impacted patient outcomes. This is important to assess because it will inform SCS pathways going forwards. 3. Potential next steps to build on the findings of this single-centre, retrospective audit.

Financial Disclosures: BB has provided consultancy to Abbott and Platform 14. GB has a consulting agreement with Saluda, Nevro Corp, Abbott, Medtronic, Boston Scientific, Stryker and Mainstay Medical. GB had educational and research grants from Nevro Corp, Abbott and Boston Scientific. GB is on the advisory board for Abbott and Nalu Medical. The remaining authors report no conflicts of interest.

Disclosure: No significant relationships.

243

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

EFFECTS OF SPINAL CORD STIMULATION IN PATIENTS WITH SMALL FIBER NEUROPATHY FROM MULTIPLE ETIOLOGIES

M. Angeles Canos-Verdecho, MD[1], Beatriz Castel, MD[1], Ara Bermejo, MD[1], Rosa Izquierdo, MD[1], Ruth Robledo, MD[1], Elisa Gallach, PhD[1], Teresa Sevilla, MD[2], Pilar Argente, MD[1], Ismael Huertas, PhD[3]
[1]University and Polytechnic Hospital La Fe, Pain Management, Anaesthesiology, Valencia, Spain, [2]University and Polytechnic Hospital La Fe, Neurology, Valencia, Spain, [3]Boston Scientific, Neuromodulation Research And Advanced Concepts (nrac), Valencia, United States of America

Introduction: Small Fiber Neuropathy (SFN) is associated with wide variety of conditions, such as immune and metabolic (e.g. diabetes) disorders, induced by toxics or drugs (e.g. chemotherapy), although often its cause remains undetermined (i.e. idiopathic). Spinal Cord Stimulation (SCS) has been shown to effectively treat diabetic SFN, however, scarce evidence is supporting its effects on other sub-types. In a multi-disciplinary effort, we sought to evaluate the effects of SCS on clinical outcomes in SFN from multiple etiologies.

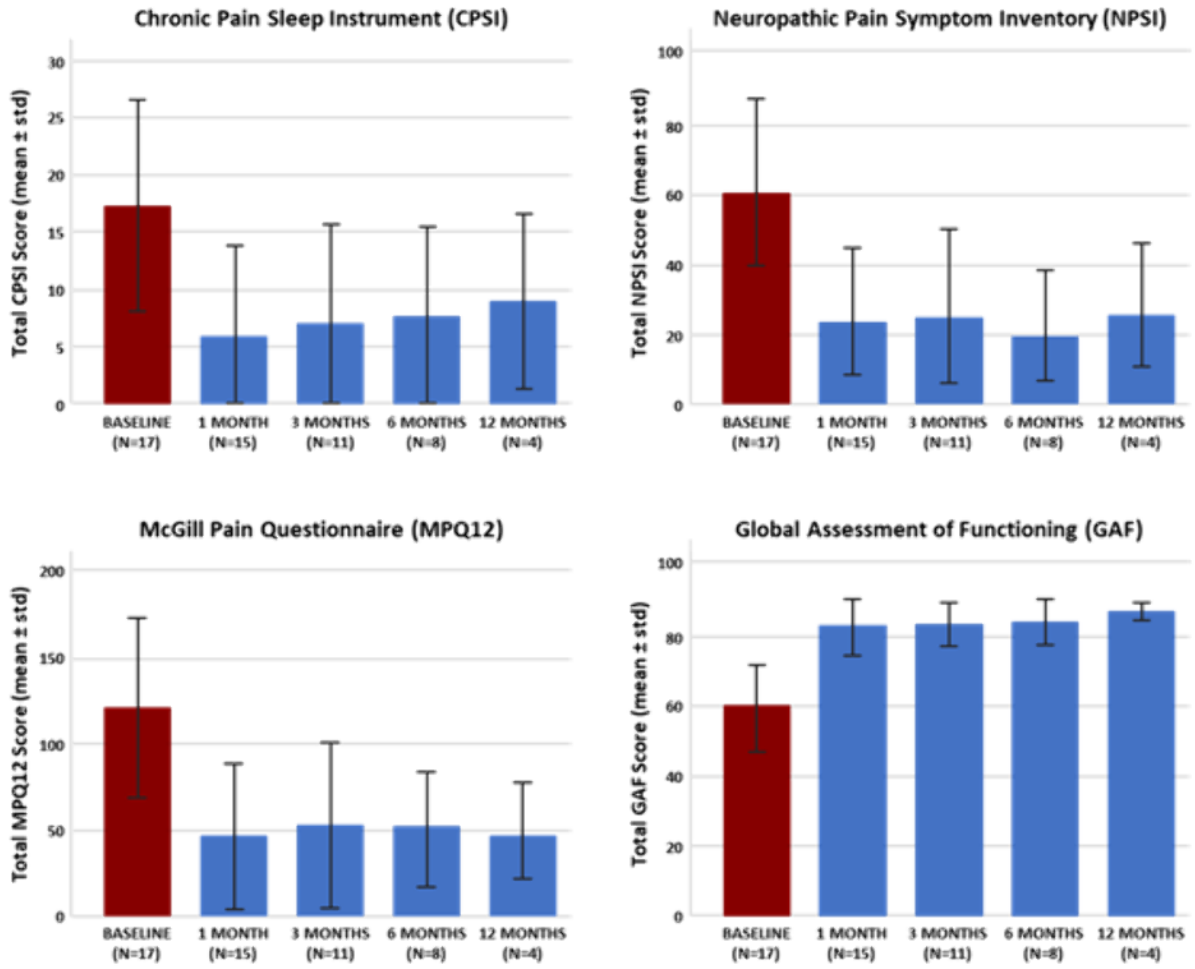
Materials / Methods: This is a single-center, prospective, observational case series including up to 30 patients from multiple SFN etiologies: idiopathic (iSFN), diabetic peripheral neuropathy (DPN), chemotherapy-induced peripheral neuropathy (CIPN), and other causes. Patients are being implanted with 4-port SCS system (WaveWriter Alpha, Boston Scientific) and percutaneous leads targeting lower and, if necessary, upper limbs. Programming is individualized based on patient preference (paresthetic or sub-paresthetic) and best response. Several assessments are conducted at baseline and 3-, 6- and 12-months post-activation, including but not limited to, pain intensity (VAS), Chronic Pain Sleep Inventory (CPSI), Quality-of-life (EQ-5D), Neuropathic Pain Symptoms Inventory (NPSI), McGill Pain Questionnaire (MPQ), Global Assessment of Functioning (GAF), and Intra-Epidermal Nerve Fiber Density (IENFD).

Results: To date, 17 patients have been enrolled: iSFN (N=6), DPN (N=5), CIPN (N=4), and others (N=2). A subset of these subjects has reached the 3- (N=11), 6- (N=8) and 12-months (N=4) visits. At last follow-up, a significant and sustained improvement in various domains has been observed, including pain intensity (VAS) from 8.9 to 2.6, sleep (CPSI) from 17.9 to 7.3, QoL (EQ-5D) from 10.4 to 5.8, neuropathic symptoms (NPSI) from 61 to 25 and (MPQ) from 120.2 to 53.8, and functioning (GAF) from 60 to 84. Most patients had low-frequency sub-perception (50-90Hz) programs. All patients had a pathological IENFD at baseline, and post-SCS results will be presented at the conference.

Discussion: Our current results support the use of SCS to effectively treat multiple types of painful SFN. SCS provides these patients pain symptoms relief, and improvement of sleep, functioning and quality of life. A larger cohort and a more complete follow-up will be presented at the conference. Potential differences across sub-types will be also investigated. The use of SCS for idiopathic and other non-rare SFN sub-types deserves more awareness among pain practitioners and referral specialists.

Conclusions: Diverse types of polyneuropathies can be effectively treated with SCS.

Supplemental Data:



References: [1] Nolano, M. et al. Contribution of Skin Biopsy in Peripheral Neuropathies. Brain Sci. 2020, 10, 989; doi:10.3390/brainsci10120989

Acknowledgements: The support of Boston Scientific for this project is gratefully acknowledged. We would like also to thank Ana Isabel Miravet for her SCS programming support.

Learning Objectives: (1) To evaluate SCS as an effective treatment for diverse types of small fiber neuropathies (SFN) (2) To evaluate potential differences in treatment approach or effects across SFN subtypes (3) To assess potential small-fiber re-growth after SCS

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

244

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

EFFECTS OF SPINAL CORD STIMULATION ON NEUROPATHIC PAIN SYMPTOMS AND SMALL-FIBER PATHOLOGY IN VARIOUS TYPES OF POLYNEUROPATHIES (IDIOPATHIC, DIABETIC, POST-CHEMO, AND OTHERS)

M. Angeles Canos-Verdecho, MD[1], Ara Bermejo, MD[1], Beatriz Castel, MD[1], Rosa Izquierdo, MD[1], Ruth Robledo, MD[1], Elisa Gallach, PhD[1], Teresa Sevilla, MD[2], Pilar Argente, MD[1], Ismael Huertas, PhD[3]
[1]University and Polytechnic Hospital La Fe, Pain Management, Anaesthesiology, Valencia, Spain, [2]University and Polytechnic Hospital La Fe, Neurology, Valencia, Spain, [3]Boston Scientific, Neuromodulation Research And Advanced Concepts (nrac), Valencia, United States of America

Introduction: Small Fiber Neuropathy (SFN) is associated with wide variety of conditions, such as immune and metabolic (e.g. diabetes) disorders, induced by toxics or drugs (e.g. chemotherapy), although often its cause remains undetermined (i.e. idiopathic)[1]. We are currently conducting a study to investigate the effects of SCS on various types of SFN. In this communication, we present sub-analyses on the profile of neuropathic pain symptoms (i.e. sensory profile) and small-fiber pathology across sub-types and the specific effects of SCS on these features.

Materials / Methods: This is a single-center, prospective, observational case-series including up to 30 patients from distinct SFN sub-types: idiopathic (iSFN), diabetic peripheral neuropathy (DPN), chemotherapy-induced peripheral neuropathy (CIPN), and other sub-types. Patients are implanted with 4-port SCS system (WaveWriter Alpha™, Boston Scientific) and percutaneous leads targeting lower and, if necessary, upper limbs. Assessments are performed pre- and post-SCS (3-, 6- and 12-months). Neuropathic pain symptoms are characterized using Neuropathic Pain Symptoms Inventory (NPSI) and McGill Pain Questionnaire (MPQ). Skin punch is performed at the proximal and distal leg to assess the Intra-Epidermal Nerve Fiber Density (IENFD).

Results: To date, 17 patients have been enrolled: iSFN (N=6), DPN (N=5), CIPN (N=4), and others (N=2). A subset have reached the 3- (N=11), 6- (N=8) and 12-months (N=4) visits. At baseline, our DPN cases presented a less severe neuropathy (NPSI=40, MPQ=80) than CIPN (NPSI=69, MPQ=151) and iSFN (NPSI=77, MPQ=136). Item analyses revealed that CIPN and iSFN had more superficial (burning) and evoked pain (hyperalgesia) than DPN. MPQ and NPSI highly correlated ($p<0.001$). SCS alleviated the neuropathy for all patients (NPSI from 61 to 25, MPQ from 120 to 53, after 3- and 6-months, $p<0.001$), although relief was higher for DPN (90%) than for CIPN (69%) and iSFN (55%). Most patients had low-frequency sub-perception (50-90Hz) programs. All cases had a pathological IENFD in both proximal (mean-count 5.8 vs. normative-count 8.5) and distal (mean-count 2.5 vs. normative-count 4.5) leg. Neuropathic pain scales did not correlate with IENFD counts. There were no IENFD differences across groups. The 12-months post-SCS IENFD readouts will be presented at the conference.

Discussion: Differences in the sensory or neuropathic profile may exist across SFN etiologies. The mechanism and the magnitude of SCS effects may also differ. Small-fiber counting does not seem associated with pain severity or SFN condition. Comprehensive assessment of these observations will be presented at the conference.

Conclusions: SCS can effectively treat multiple-cause painful SFN with diverse neuropathic pain symptoms phenotype and severity.

Supplemental Data:

References: [1] Nolano M. Contribution of Skin Biopsy in Peripheral Neuropathies. Brain Sci. 2020, 10, 989; doi:10.3390/brainsci10120989

Acknowledgements: The support of Boston Scientific for this project is gratefully acknowledged. We would like to thank Ana Isabel Miravet for her support in SCS programming.

Learning Objectives: (1) To assess the neuropathic pain symptoms profile of diverse types of small fiber neuropathies (SFN) (2) To assess potential prognostic features for successful SCS in this patient population (3) To evaluate the impact of SCS on symptoms and small-fiber density of these distinct sub-types of SFN

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

245

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

DORSAL ROOT GANGLION STIMULATION OUTCOMES FOR TREATMENT OF MECHANICAL KNEE PAIN AMONG PATIENTS WITH OSTEOARTHRITIS OF THE KNEE

Tariq Yousef, MD[1], Kenneth Chapman, MD[2,3,4], Ajax Yang, MD[1], Noud Van Helmond, MD, PhD[1], Julia Montag, BSc (Hons)[1]
[1]THE SPINE AND PAIN INSTITUTE OF NEW YORK, New York, United States of America, [2]Spine and Pain Institute of New York, New York, United States of America, [3]NYU Langone Medical Center, Anesthesiology/pain Medicine, New York, United States of America, [4]Zucker School of Medicine at Hofstra Northwell, Department Of Anesthesiology, Manhassat, United States of America

Introduction: DRG stimulation (DRG-S) is a form of neuromodulation used to treat CRPS type I or II (causalgia) of the groin and lower extremities. In addition to better pain relief, benefits include lower energy use, better dermatomal coverage, and potentially less loss of efficacy. DRG-S has also shown promise in treating mixed pain syndromes such as post joint replacement pain and axial low back pain, suggesting it may be able to treat nociceptive, or mechanical pain in addition to neuropathic pain. Supported in a rodent model of osteoarthritis (OA) of the knee, where DRG-S alleviated pain-related behavior in rats. This investigator-sponsored, single-site, open-label, controlled Investigational Device Exemption (IDE) pilot study will evaluate outcomes of patients trialed and implanted with the ProclaimTM DRG System to treat mechanical knee pain secondary to OA.

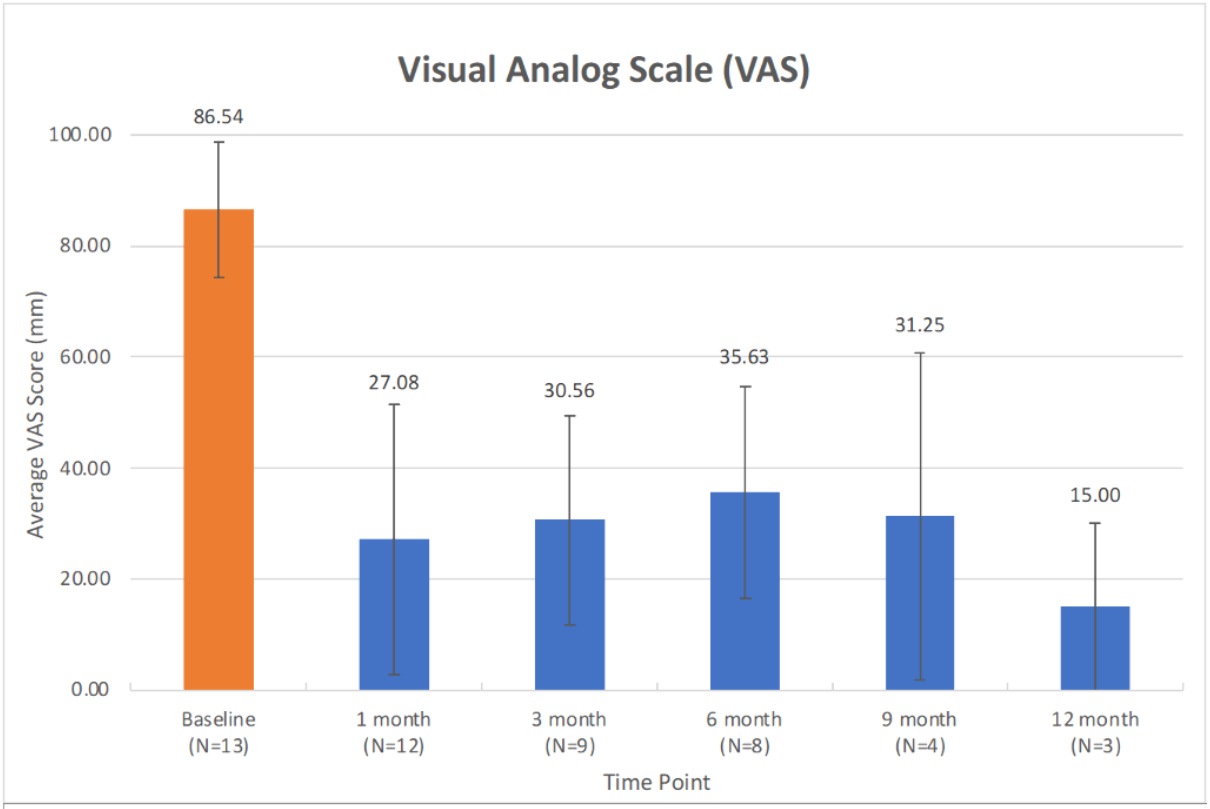
Materials / Methods: Eligible patients will be trialed with DRG-S with planned muti-level lead placement and program settings at sub-threshold stimulation tailored to cover painful area, using very low frequency parameters (4Hz), with or without intermittent cycling parameters (1 min on, 1 min off). Successful responders will be implanted and followed for a year. We will study pain relief and a comprehensive evaluation of function, mobility, and quality of life based on patient reported outcome measures, video analysis of gait and mobility, health device monitoring, serum biomarkers, and radiologic findings.

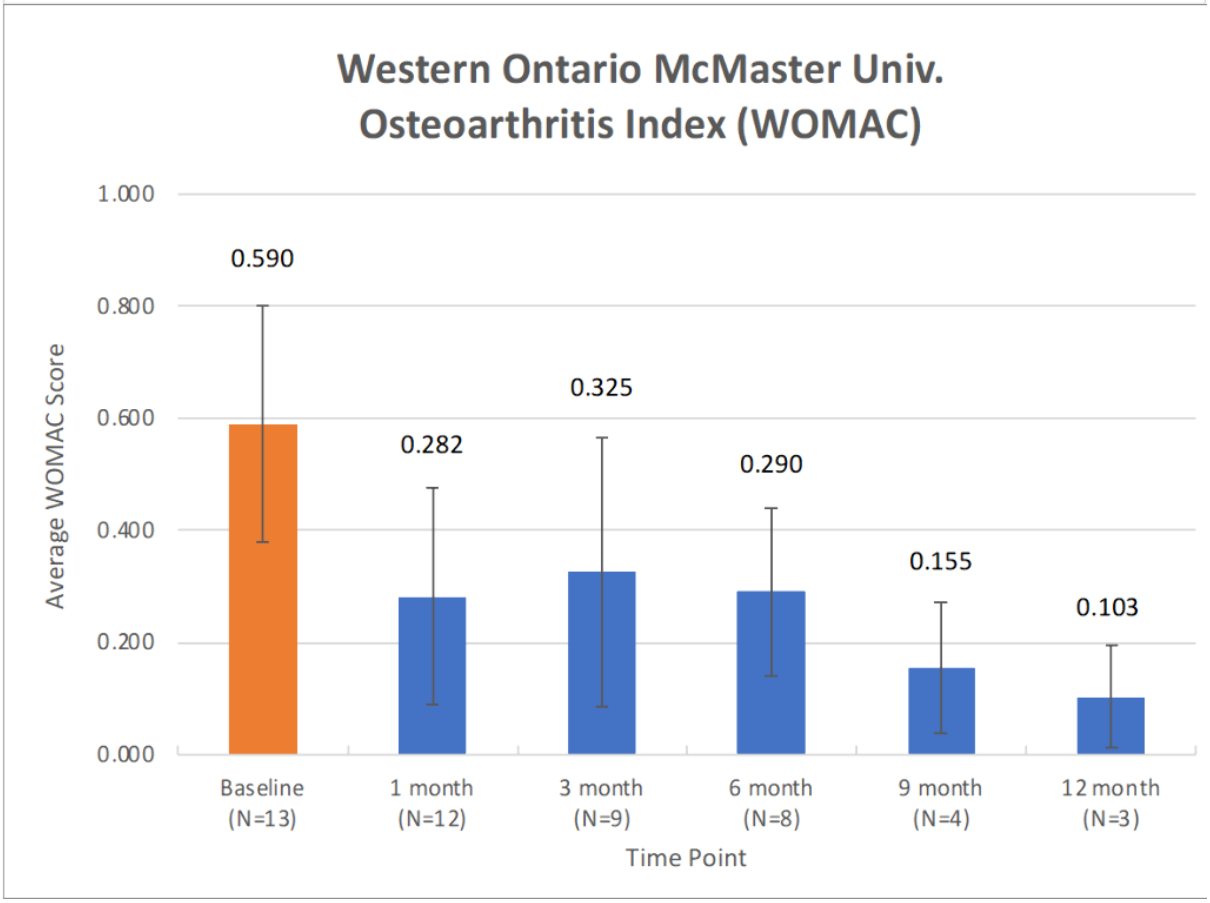
Results: At present, 22 patients completed 1-week DRG-S trials, with 20/22 (91%) being successful (>50% pain relief) responders. Five successful trial patients declined to proceed to implant, and 2 patients are scheduled for implant at time of publication. Thirteen patients received permanent implants. Nine patients reached the primary endpoint of 3 months with 100% (9/9) success rate. There has been significant improvement in all collected patient reported outcomes at end of one week trial and post-implant follow up visits compared to baseline, with sustained improvements out to **12 months**.

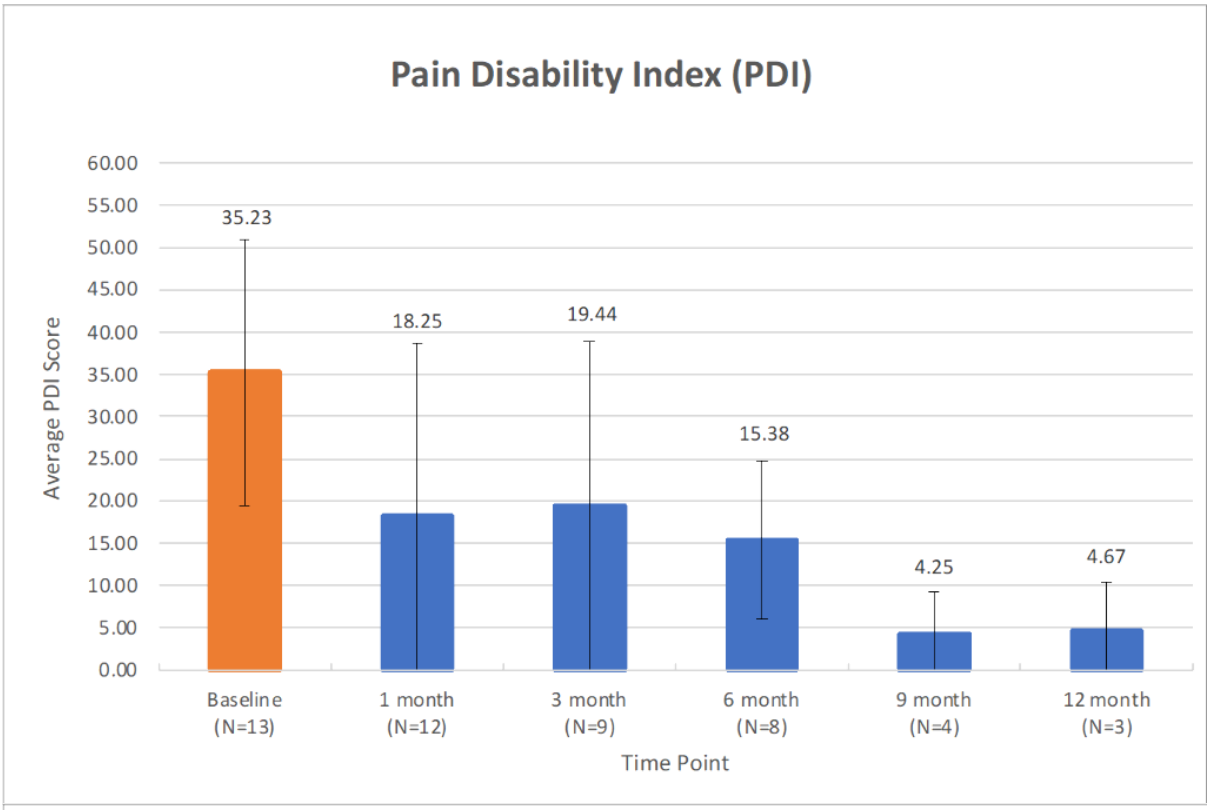
Discussion: Preliminary results have been promising, with a high responder rate and positive outcome measures thus far. In addition to PROMs, we will correlate outcomes with objective measures as described in the methods section.

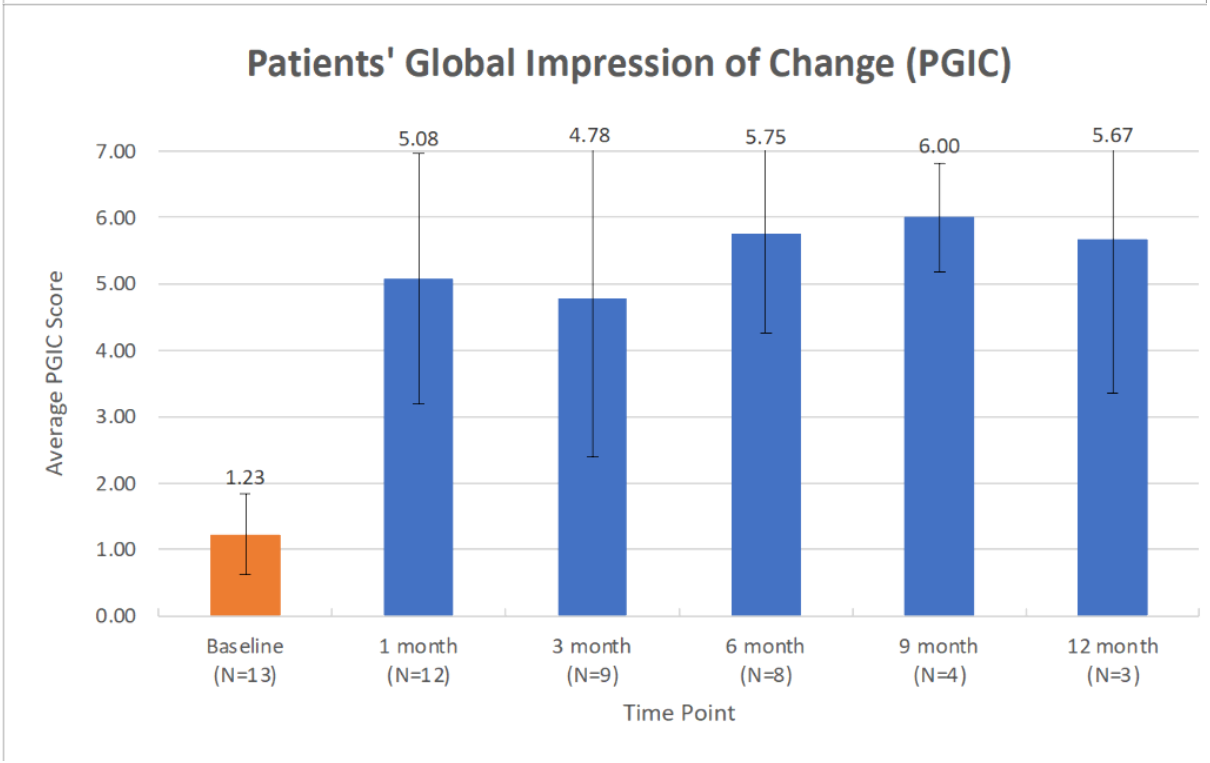
Conclusions: This IDE pilot study is the first to investigate the utility of DRG-S to treat nociceptive / mechanical knee pain due to OA. Eligible patients will be trialed with DRG-S over the next 9-12 months with the goal of enrolling 20 successful responders who will receive a permanent device implant. The completion of the study is expected to be in the fall of 2024.

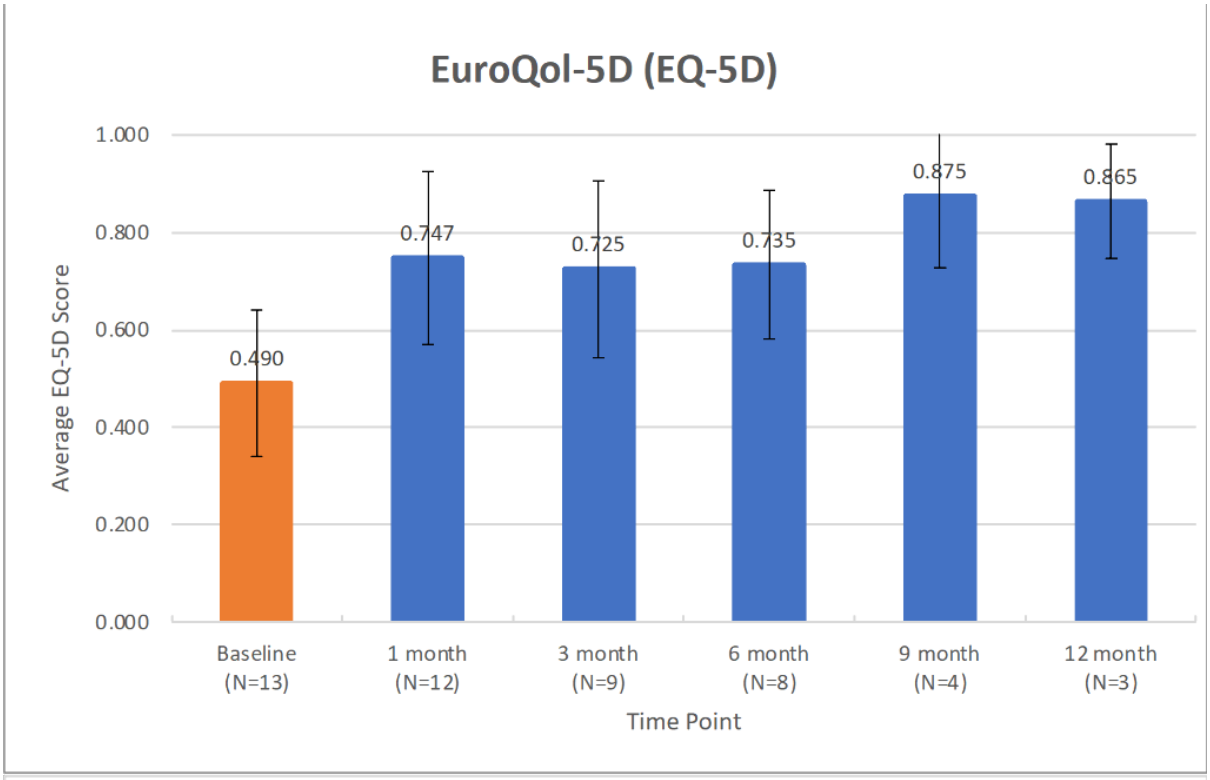
Supplemental Data: Figures: Mean Patient Reported Outcome Measures Comparing Baseline to End of Trial and Post Implant study
timepoints.

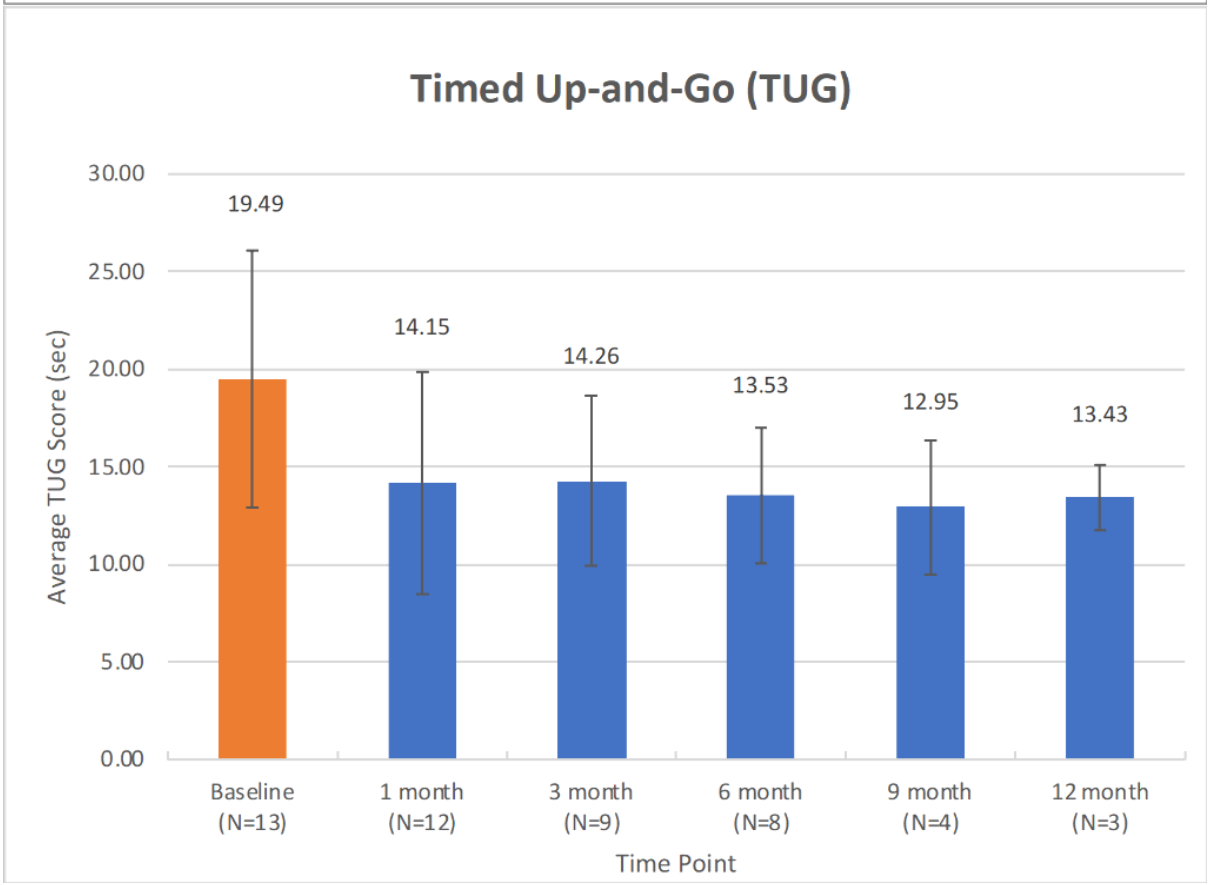

Visual Analog Scale (VAS)
Average VAS Score (mm)
100.00
80.00
60.00
40.00
20.00
0.00
86.54
27.08
30.56
35.63
31.25
15.00
Baseline (N=13)
1 month (N=12)
3 month (N=9)
6 month (N=8)
9 month (N=4)
12 month (N=3)
Time Point


Western Ontario McMaster Univ. Osteoarthritis Index (WOMAC)
Average WOMAC Score
1.000
0.800
0.600
0.400
0.200
0.000
0.590
0.282
0.325
0.290
0.155
0.103
Baseline (N=13)
1 month (N=12)
3 month (N=9)
6 month (N=8)
9 month (N=4)
12 month (N=3)
Time Point


Pain Disability Index (PDI)
Average PDI Score
60.00
55.00
50.00
45.00
40.00
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
35.23
18.25
19.44
15.38
4.25
4.67
Baseline (N=13)
1 month (N=12)
3 month (N=9)
6 month (N=8)
9 month (N=4)
12 month (N=3)
Time Point


Patients' Global Impression of Change (PGIC)
Average PGIC Score
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
1.23
5.08
4.78
5.75
6.00
5.67
Baseline (N=13)
1 month (N=12)
3 month (N=9)
6 month (N=8)
9 month (N=4)
12 month (N=3)
Time Point





References: 1. Chapman et al. T12 Dorsal Root Ganglion Stimulation to Treat Chronic Low Back Pain: A Case Series. Neuromodulation Technol Neural Interface [Internet]. 2020 Feb 6;23(2):203–12. http://www.ncbi.nlm.nih.gov/pubmed/31588662 2. Kallewaard et al. A Prospective Study of Dorsal Root Ganglion Stimulation for Non-Operated Discogenic Low Back Pain. Neuromodulation Technol Neural Interface. 2019 Mar 1; http://www.ncbi.nlm.nih.gov/pubmed/308219013. 3. Yu et al. (2020).

Dorsal Root Ganglion Stimulation Alleviates Pain-related Behaviors in Rats with Nerve Injury and Osteoarthritis. Anesthesiology, 133(2), 408–425. https://doi.org/10.1097/ALN.0000000000003348

Acknowledgements: The support of Abbott Neuromodulation for this project is gratefully acknowledged.

Learning Objectives: 1. Define inclusion/criteria and primary and secondary outcome measures for this Investigator Sponsored Investgational Device Exemption (IDE) study using DRG Stimulation to treat arthritic joint pain of the knee. 2. Update data results of ongoing IDE study NCT05103527 analyzing DRG-S treatment outcomes for mechanical knee pain due to osteoarthritis. 3. Highlight the potential utility of electrical stimulation neuromodulation for arthritic nociceptive/mechanical pain.

Financial Disclosures: This study was made possible by an unrestricted study grant from Abbott Neuromodulation, who also provided equipment and devices for the sole purpose of this study.

Disclosure: No significant relationships.

246

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

PHYSIOLOGICAL AND FUNCTIONAL OUTCOME METRICS OF DORSAL ROOT GANGLION STIMULATION FOR TREATMENT OF MECHANICAL KNEE PAIN AMONG PATIENTS WITH OSTEOARTHRITIS OF THE KNEE

Tariq Yousef, MD[1], Kenneth Chapman, MD[2,3,4], Noud Van Helmond, MD, PhD[1], Ajax Yang, MD[1], Julia Montag, BSc (Hons)[1], Ameya Nanivadekar, PhD[5]
[1]THE SPINE AND PAIN INSTITUTE OF NEW YORK, New York, United States of America, [2]Spine and Pain Institute of New York, New York, United States of America, [3]NYU Langone Medical Center, Anesthesiology/pain Medicine, New York, United States of America, [4]Zucker School of Medicine at Hofstra Northwell, Department Of Anesthesiology, Manhassat, United States of America, [5]6901 Preston Rd, Plano, United States of America

Introduction: DRG stimulation (DRG-S) is a form of neuromodulation used to treat CRPS of the groin and lower extremities. DRG-S has also shown promise in treating mixed pain syndromes such as axial low back pain. A rodent model of osteoarthritis (OA) of the knee showed DRG-S alleviated pain-related behavior in rats, indicating it may be effective in mechanical. This investigator-sponsored, single-site, open-label, controlled Investigational Device Exemption (IDE) pilot study will evaluate outcomes of patients trialed and implanted with the ProclaimTM DRG System to treat mechanical knee pain secondary to OA.

Materials / Methods: Eligible patients will be trialed with DRG-S with planned muti-level lead placement and program settings at sub-threshold stimulation tailored to cover knee painful area. Successful responders will be implanted and followed for a year. We will study improvements in functional outcomes using video analysis of gait and mobility, along with objective measures of activity using health device monitoring. Additionally, serum samples collected at each in-clinic follow-up visit will be analyzed for known blood biomarkers of pain.

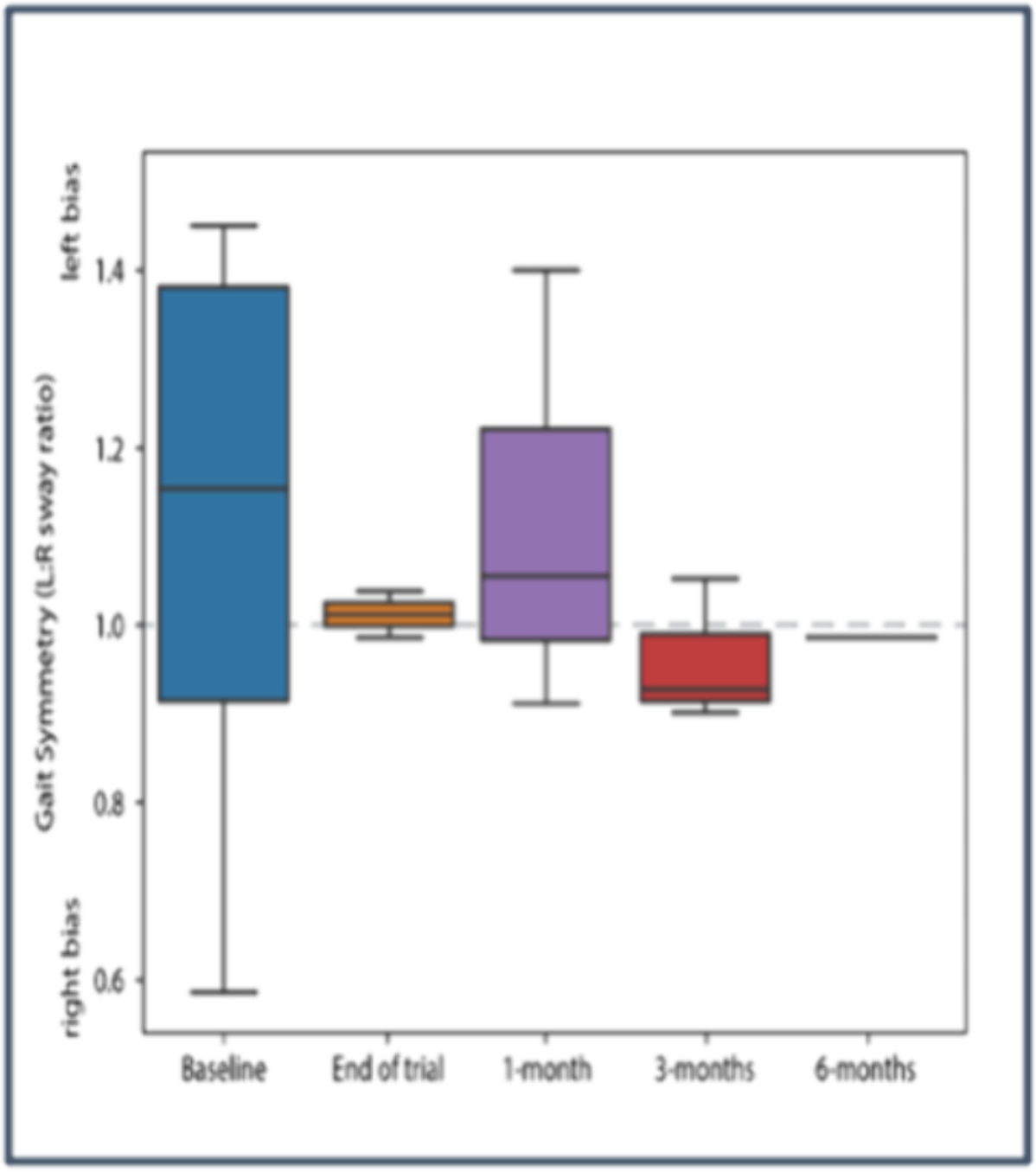
Results: At present, 22 patients completed 1-week DRG-S trials, with 20/22 (91%) being successful (>50% pain relief) responders. Five successful trial patients declined to proceed to implant, and 2 patients are scheduled for implant at time of publication. Thirteen patients received permanent implants. Nine patients reached the primary endpoint of 3 months with 100% (9/9) success rate. There has been significant improvement in all collected patient reported outcomes at end of one week trial and post-implant follow up visits compared to baseline, with sustained improvements out to **12 months**.
Video gait analysis was performed on 4 patients comparing baseline gait to post implant study points. For these 4 patients, performance on a walking task and timed up and go task were evaluated using video analysis. Patient improvements in gait symmetry were measured using OpenPose video analytics software. The asymmetry of movement in the left and right knee was calculated using landmarks extracted from the body, and the asymmetry ratio was compared between baseline and post-implant. An asymmetry ratio of 1 indicates normal left-right symmetry while walking. Across 4 subjects, there was improvement in gait symmetry between baseline (0.8 ± 0.1) and post-implant (1.0 ± 0.1) (see picture1a.png) while time to complete walking tasks decreased by 25-33% from baseline to post-implant study timepoints.

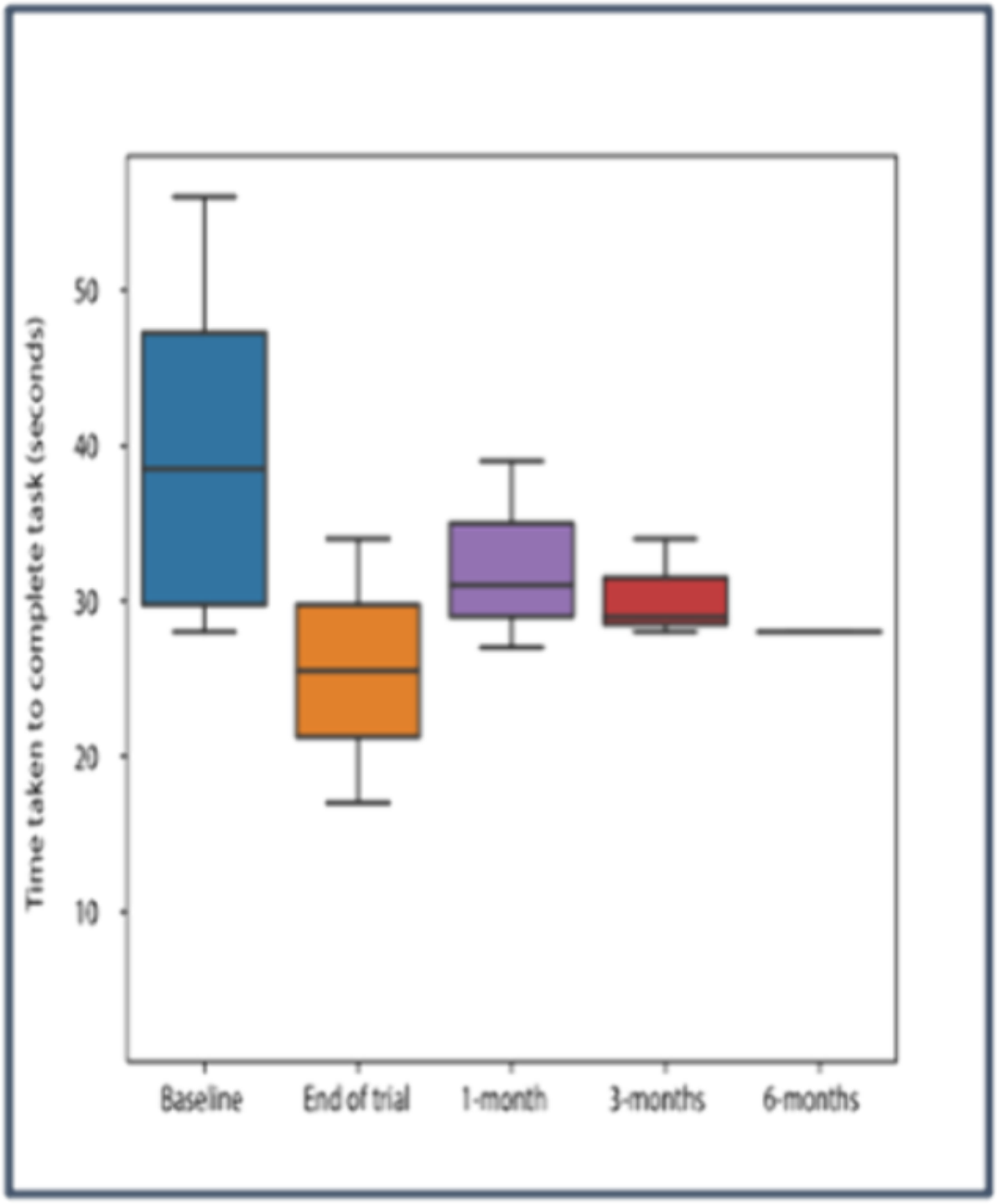
Discussion: Preliminary results have been promising, with a high responder rate and positive outcome measures thus far. Ongoing analysis is focused on correlating blood biomarkers and wearable outcomes with PROMs to build a predictive model of patient outcomes using objective metrics.

Conclusions: This IDE pilot study is the first to investigate the utility of DRG-S to treat nociceptive / mechanical knee pain due to OA. Eligible patients will be trialed with DRG-S over the next 9-12

months with the goal of enrolling 20 successful responders who will receive a permanent device implant. The completion of the study is expected to be in the fall of 2024.

Supplemental Data:





References: 1. Chapman et al. T12 Dorsal Root Ganglion Stimulation to Treat Chronic Low Back Pain: A Case Series. Neuromodulation Technol Neural Interface [Internet]. 2020 Feb 6;23(2):203–12. http://www.ncbi.nlm.nih.gov/pubmed/31588662 2. Kallewaard et al. A Prospective Study of Dorsal Root Ganglion Stimulation for Non-Operated Discogenic Low Back Pain. Neuromodulation Technol Neural Interface. 2019 Mar 1; http://www.ncbi.nlm.nih.gov/pubmed/308219013. 3. Yu et al. (2020). Dorsal Root Ganglion Stimulation Alleviates Pain-related Behaviors in Rats with Nerve Injury and Osteoarthritis. Anesthesiology, 133(2), 408–425. https://doi.org/10.1097/ALN.0000000000003348

Acknowledgements: The support of Abbott Neuromodulation for this project is gratefully acknowledged.

Learning Objectives: 1. Highlight the potential utility of electrical stimulation neuromodulation for arthritic nociceptive/mechanical pain. 2. Update data results of ongoing IDE study NCT05103527 analyzing DRG-S treatment outcomes for mechanical knee pain due to osteoarthritis. 3. Present outcome metrics focusing on objective physiologic, functional, and biologic markers.

Financial Disclosures: This study was made possible by an unrestricted study grant from Abbott Neuromodulation, who also provided equipment and devices for the sole purpose of this study. Dr. Ameya Nanivadekar is an employee of Abbott Neuromodulation.

Disclosure: Ameya Nanivadekar is an employee of Abbott Neuromodulation.

247

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

A RARE COMPLICATION OF SPINAL CORD STIMULATOR INSERTION: BILATERAL ABDUCENS NERVE PALSY.

Vanessa Jane Chow, BSc, MBBS[1], Avinash Kumar Hari Narayanan, BSc (Hons), MHChB, MRes[1], Kavita Poply, FRCA, FCARCSI, FFPMRCA[2], Vivek Mehta, MBBS, MD, FRCA, FFPMRCA[2]
[1]Royal London Hospital, Barts Health NHS Foundation Trust, Department Of Neurosurgery, London, United Kingdom, [2]St Bartholomew's Hospital London, Barts Health NHS Foundation Trust, Spinal Pain & Neuromodulation, London, United Kingdom

Introduction: Spinal cord stimulation (SCS) offers a hopeful avenue for managing enduring, unrelenting chronic pain. In the span of four decades since its inception, SCS has evolved significantly in its technological components, patient screening, and physician expertise and preparation. However, SCS surgery remains susceptible to potential complications such as lead dislocation, infections, hardware malfunctions, and neurological deficits. In this narrative, we present an unusual complication resulting from SCS insertion.

Materials / Methods: Written and verbal consent was given by the patient and a case report was carried out

Results: We present a case report concerning a 65-year-old male patient with refractory chronic pain who developed bilateral abducens nerve palsy as a rare iatrogenic complication following the implantation of a spinal cord stimulation system. After an unsuccessful trial of conservative treatments and subsequent removal of the device, corrective strabismus surgery was undertaken, leading to effective symptom control.

Discussion: Abducens nerve palsy, characterized by horizontal diplopia, abduction impairment, and esotropia, is an exceptionally rare occurrence following the placement of a spinal cord stimulation device, with only one other documented case report detailing similar findings. The suggested cause in this instance is a subclinical cerebrospinal fluid (CSF) leak resulting from an inadvertent dural puncture during the SCS insertion, ultimately leading to intracranial hypotension. Abducens nerve palsy has infrequently been reported as a complication following various CSF diversion procedures, potentially with a reduced incidence when using smaller gauge spinal needles. Notably, symptoms of CSF leak, such as postural headache and nausea, often precede the development of CNVI palsy. It is also conceivable that variations in intracranial pressure fluctuations may contribute to cranial nerve dysfunction.

Conclusions: This case presents a significant diagnostic and therapeutic challenge, primarily due to the unique clinical presentation, potential pitfalls in neuroimaging, and the scarcity of robust evidence guiding effective management. We acknowledge cranial nerve palsy as a plausible, yet tangible, complication arising from SCS surgery, with abducens nerve palsy significantly impairing the quality of life for affected patients. As the utilization of SCS continues to proliferate in clinical practice, the inevitable rise in associated iatrogenic complications underscores the pressing necessity for increased recognition and the establishment of high-quality evidence to inform successful management strategies.

Supplemental Data:

References: 1. Labaran L, Jain N, Puvanesarajah V, Jain A, Buchholz AL, Hassanzadeh H. A retrospective database review of the indications, complications, and incidence of subsequent spine surgery in 12,297 spinal cord stimulator patients. *Neuromodulation: Technology at the Neural Interface.* 2020Jul;23(5):634–8. 2. O'Donnell TJ, Buckley EG. Sixth nerve palsy. Compr Ophthalmol Update. 2006;7(5):215-224. Accessed October, 2021. 3. Wolfensberger TJ, Borruat FX. Sixth nerve

palsy following epidural spinal cord stimulation for lower limb ischaemia. *Eye (Lond)*. 2000;14 Pt 5:811-812. 4. Li G, Zhu X, Zhang Y, Zhao J, Han Z, Hou K. Cranial nerve palsy secondary to cerebrospinal fluid diversion. *Clin Neurol Neurosurg*. 2016;143:19-26. 5. Epstein NE. A review article on the diagnosis and treatment of cerebrospinal fluid fistulas and dural tears occurring during spinal surgery. *Surg Neurol Int.* 2013;4(Suppl 5):S301-S317. Published 2013 May 6.

Acknowledgements: Written consent to share his case has been given by the patient

Learning Objectives: 1. Recognizing Abducens Nerve Palsy as a potential complication of Spinal Cord Stimulator (SCS) Insertion: - Discern the distinctive clinical characteristics and presentation of bilateral abducens nerve palsy observed in patients after SCS procedures. - Develop increased awareness for atypical neurological symptoms and complications that can emerge following SCS implantation. **2. Identifying Diagnostic challenges and Treatment for Abducens Nerve Palsy in the context of SCS insertion:** - Examine the diagnostic challenges when patients present with non-typical neurological symptoms in the context of SCS insertion. - Understand the underlying mechanisms that give rise to rare complications like intracranial hypotension and pseudomeningocele and their consequent impact on treatment strategies - Explore various treatment modalities including conservative measures, surgical interventions, and rehabilitation strategies. **3. Risk Mitigation and Patient Counseling**: - Physicians should be aware of the risk factors that might predispose patients to CN palsy following SCS insertion, considering elements such as the patient's medical history and the specifics of the SCS implantation procedure. - Develop strategies for informed consent discussions with patients who are contemplating SCS therapy, highlighting the potential for uncommon complications like abducens nerve palsy - Develop a patient-centered approach to care, considering the impact of these complications on patients' independence, quality of life, and functional outcomes.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

248

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

EFFECT OF LONG-TERM REMOTE MONITORING AND OUTREACH ON PATIENT OUTCOMES IN POST IMPLANT SCS PATIENTS

Anne Christopher, MD[1], Aamna Ahsan, BSc[2], Caleb Pettit, BSc[2], Dorna Mansouri, MD[2], Sreetharan Thankathuraipandian, MSc[2], Soroush Dehghan, MSc[2], David Page, PhD[2]
[1]St. Louis Pain Consultants, Pain, Chesterfield, United States of America, [2]Abbott Laboratories, Neuromodulation, Plano, United States of America

Introduction: Post-implant follow-up of SCS patients may vary from clinic to clinic and is dependent on physician and patient preference. Many patients often require multiple clinic visits for reprogramming sessions to optimize their therapy. Unbeknownst to clinicians, some patients may be not doing well or might be on the verge of falling out of therapy unless patients or clinics initiate outreach. Long term remote monitoring can aid both patients and clinicians in monitoring and intervening with at-risk patients. This study aims to compare patient outcomes in patients receiving traditional follow-up vs. follow up triggered through remote monitoring across post-implant SCS patients.

Materials / Methods: This is a prospective, randomized adaptive study designed to enroll 20-100 patients. Participants are provided with a wearable device to measure physiological metrics and a smartphone to complete digital surveys. Patients opting to receive permanent implant are randomized to either a control arm (standard of care follow-up), or to proactive monitoring arm (proactive outreach based remote monitoring algorithm). The remote monitoring algorithm is designed to monitor patient well-being and when the algorithm detects a decline in physical activity, sleep, reported pain or missing data the algorithm will send an alert to study personnel to trigger patient outreach via a phone call.

Results: The study is currently ongoing with a total of 12 patients currently enrolled. Six patients received a permanent implant with 3 of these 6 patients randomized to the proactive monitoring arm. The remote monitoring algorithm successfully triggered multiple alerts for all 3 proactive-monitoring-arm patients including triggers for a change in patient response to physical activity, sleep or pain and missing data. The study is in progress, and ongoing results are to follow.

Discussion: Patient enrollment is still ongoing with interim analysis expected once a larger number of patients reach the post-implant period. Proactive patient outreach is hypothesized to improve patient outcomes and reduce the amount of time until effective therapy is attained. Frequent remote patient outreach may also aid in identifying synergistic healthcare needs for pain patients.

Conclusions: The study aims to assess the effectiveness of data-dependent remote management and proactive patient outreach. We hypothesize that patients receiving digitally driven remote monitoring will demonstrate improved patient outcomes. Early detection and remote monitoring technologies can enable clinicians to make informed decisions and provide patients with personalized and proactive care.

Supplemental Data:

References: None

Acknowledgements: The support of Abbott Laboratories for this project is gratefully acknowledged

Learning Objectives: 1. Learners will be able to understand current needs of long term remote monitoring in chronic pain patients for improved remote monitoring standards. 2. Learners will be able to identify the differences in patient outcomes for remote monitoring patients versus patients in

traditionals follow up. 3. Learners will be able to understand and recognize elements in the data-driven outreach method implemented in the prospective study.

Financial Disclosures: Presenting Author: AC is a Consultant/Advisory Board member for Abbott Laboratories. All co-authors AA, CP, DM, ST, SD and DP are company employees of Abbott Laboratories.

Disclosure: Submitted is employee of the Sponsor (Abbott Laboratories) that is sponsoring that study mentioned in the abstract.

249

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

CLINICAL OUTCOMES AND PREFERENCES IN PATIENTS TREATED WITH SPINAL CORD STIMULATION USING MULTIPLE WAVEFORMS

Alessandro Dario, MD[1], Immacolata Mazzetto, MD[1], Claudio Reverberi, MD[2], Genny Duse, MD[3]
[1]Neurosurgical Clinic, Varese, Italy, [2]pain unit, Oglio Po Hospital, cremona, Italy, [3]Padova Hospital, Pain Unit, padova, Italy

Introduction: The introduction of different waveforms into clinical practice has increased the clinical efficacy of Spinal Cord Stimuation (SCS) and offers the "customization" of the electrical current output in order to obtain the maximum benefit on pain and the best satisfaction of the patient. We investigated the use of Multiple Waveforms (MW) in relation to pain outcomes and patient preferences.

Materials / Methods: We studied 30 patients suffering from drug-resistant neuropathic pain: 43% of the patients presented pain in the legs, 48% of the patients in the legs and back, 9% in the upper limbs. All patients were implanted, after a successful SCS trial, with a neurostimulator characterized by multiple independent sources and the possibility of programming with different single or associated programs. The minimum follow-up was 2 years, the maximum 4 years; the study was a Randomized Controlled Trial (RCT) blinded for patients and clinicians for sub-perception modalities. The scales used for the evaluation were the Visual Analogic Scale (VAS), the SF-12 and the statistical analysis was conducted through the ANOVA test. The stimulation programs used were the tonic, the burst, the 1KHZ in single or combined mode.

Results: The pain score before was 8.3 at last follow-up (2-4 years) the pain score after SCS best program was 2.9: the improvement was statistically significant; paraesthesia alone was preferred by 37% of patients, paraesthesia associated with subperception-based (SP-SCS) waveforms in 33% of patients, and SP-SCS alone was preferred by 30% of patients. 63% of patients used multiple programs during the day to obtain the best benefit on pain.

Discussion: Using different waveforms improves the result and should already be used during the trial; the flexibility and variability of the programs maintains the efficacy of the SCS over time; the paresthesia-based stimulation (PB-SCS) still remains a valid means of neurostimulation.

Conclusions: the paresthesia-based stimulation (PB-SCS) still remains a valid means of neurostimulation.

Supplemental Data: none

References: none

Acknowledgements:

Learning Objectives: 1. find the best waveform for pain control 2. evaluate the percentage of use of paresthesia output mode 3. evaluate the complications of SCS

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

250

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

EVOKED CORTICAL RESPONSES DURING CONDITIONED PAIN MODULATION (CPM) IN A PATIENT TREATED WITH TONIC AND BURST SPINAL CORD STIMULATION (SCS), A CASE REPORT

Laurien Reinders, MSc, Frank Huygen, MD, PhD, Cecile De Vos, PhD
Erasmus Medical Centre, Center For Pain Medicine, Department Of Anesthesiology, Rotterdam, Netherlands

Introduction: Spinal Cord Stimulation (SCS) is a successful neuromodulation therapy for chronic pain patients. Traditionally, the mechanisms of action of SCS rely on the gate control theory. Nowadays, the descending pain inhibitory pathway and other supraspinal structures are thought to be involved. Conditioned pain modulation (CPM) can be used to measure the endogenous pain inhibitory capacity. In CPM a first painful stimulus (test stimulus, TS) is inhibited by applying a second painful stimulus (conditioning stimulus, CS). Here we assess how cortical responses elicited by a painful stimulus are affected by CPM in a patient who receives both tonic and burst SCS.

Materials / Methods: The patient (40 yo woman) has post spinal surgery syndrome for 5 years and SCS for 2 years. Prior to SCS she rated her pain intensity 9/10, with SCS on average 5/10. The patient had two measurement sessions (burst and tonic SCS) with a one-week interval in between. We used magneto-encephalography (275-channel CTF MEG) to record evoked cortical responses to the painful TS. TS were generated by a constant current stimulator. The CS consisted of an ice pack (-10 C) on the forearm. CPM recordings consisted of three blocks: painful TS before, during, and after application of the CS. The anterior cingulate and primary somatosensory cortices were defined as regions of interest. Averaged evoked responses for each CPM condition per SCS paradigm in each defined region were analyzed.

Results: Ratings of the painful TS were not different between burst and tonic SCS, nor before, during and after CPM. In the anterior cingulate cortex, the amplitudes at 300 ms were reduced during CPM under tonic and burst SCS. In the somatosensory cortex, under tonic SCS the amplitude at 300 ms was reduced during CPM, while under burst SCS the amplitude at 300 ms was already low and not further reduced during CPM.

Discussion: Less efficient CPM in chronic pain patients could be cause or effect of chronic pain, and it is unclear whether CPM can be restored by (effective) SCS. CPM effect is most often measured using pain ratings. In our patient CPM did not decrease the pain rating of the TS, but the amplitude reduction during CPM suggests its inhibitory effects in this patient.

Conclusions: During CPM the reduction in response in the anterior cingulate cortex was similar under both SCS paradigms, whereas in the somatosensory cortex burst SCS reduced the activity regardless of CPM and tonic SCS only during CPM.

Supplemental Data:

References: 1. Brock C et al., Brain activity in rectosigmoid pain: Unravelling conditioning pain modulatory pathways. Clinical Neurophysiology, 2012;123(4):829-837. 2. Cruccu G, Aminoff MJ, Curio G, et al. Recommendations for the clinical use of somatosensory-evoked potentials. Clinical Neurophysiology. 2008;119(8):1705-1719 3. Pickering G, Pereira B et al. Impaired modulation of pain in patients with postherpetic neuralgia. Pain Res Manage, vol.19, no.1, pp e19–e23, 2014. 4. Ramaswamy S and Wodehouse T. Conditioned pain modulation-a comprehensive review. Clinical. Neurophysiology. 2021; 51(3):197–208

Acknowledgements:

Learning Objectives: 1. In our patient, CPM did not decrease the pain rating of the painful stimulus. 2. In our patient, activity in the ACC was reduced during CPM under both tonic and burst SCS. 3. In our patient, activity in the SI was reduced during CPM only under tonic SCS.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

251

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

LONG-TERM FOLLOW-UP OF BURST SPINAL CORD STIMULATION IN PATIENTS WITH PAINFUL DIABETIC NEUROPATHY

Cecile De Vos, PhD[1], Juliette Francovich, MSc[1], Sharon Van Der Tuin, MSc, RN[2], Rian Wolters, RN[2], Mathieu Lenders, MD[2]
[1]Erasmus University Medical Center, Department Of Anesthesiology, Rotterdam, Netherlands, [2]Medisch Spectrum Twente, Enschede, Netherlands

Introduction: In many countries today, spinal cord stimulation (SCS) is a reimbursed therapy for the treatment of painful diabetic neuropathy (PDN). Over the years, several studies have demonstrated its efficacy, with 59-79% of the patients perceiving >50% pain reduction. Initially, the short- and long-term efficacy of tonic SCS for the treatment of PDN was demonstrated in two RCTs [1,2]. Subsequently, high frequency SCS was also demonstrated to be a very effective treatment [3]. However, for burst SCS, only one report on short-term effects in patients with PDN has been published so far [4]. Therefore, this study explores the long-term effects of burst SCS in patients with painful diabetic neuropathy.

Materials / Methods: 25 patients who received burst stimulation for their painful diabetic neuropathy have been followed for a minimum of one year. Clinical data is collected retrospectively, including patient characteristics, pain characteristics, quality of life, medical history, neuromodulation treatment, and stimulation parameters.

Results: Average follow-up time of the 25 patients is 4.5 years (range 1-12 years) and 12 patients have received burst stimulation treatment for over 5 years. At 1 year follow-up, 80% of the patients reported pain reduction of >50% with the burst SCS therapy. After 5 years, 75% of patients still reported pain reduction of >50% with the burst SCS therapy. Given the choice between tonic and burst SCS, the majority of patients with PDN opt for burst SCS.

Discussion: Patients who currently receive spinal cord stimulation for PDN, often have advanced stages of diabetes mellitus (DM) with severe complications. Long-term follow-up of these patients is impaired by complications related to DM, and several patients died of cardiovascular diseases during the follow-up period. Future studies need to be conducted to determine whether administering burst SCS treatment in earlier stages will yield even better results.

Conclusions: Burst spinal cord stimulation can offer an effective treatment for painful diabetic neuropathy. Despite the progressive nature of diabetic neuropathy, many patients experience sustained pain relief over the long term.

Supplemental Data:

References: 1. CC de Vos, K Meier, P Brocades Zaalberg, HJA Nijhuis, W Duyvendak, J Vesper, TP Enggaard, MWPM Lenders. Spinal cord stimulation in patients with painful diabetic neuropathy: a multicentre randomized clinical trial, *PAIN* 155:2426-2431, 2014 2. R Slangen et al. Spinal Cord Stimulation and Pain Relief in Painful Diabetic Peripheral Neuropathy: A Prospective Two-Center Randomized Controlled Trial, *Diabetes Care* 37:3016–3024, 2014 3. EA Petersen et al. Effect of High-frequency (10-kHz) Spinal Cord Stimulation in Patients With Painful Diabetic Neuropathy A Randomized Clinical Trial. *JAMA Neurology* 78:687-698, 2021 4. CC de Vos, MJ Bom, S Vanneste, MWPM Lenders, D de Ridder. Burst spinal cord stimulation evaluated in patients with failed back surgery syndrome and painful diabetic neuropathy, *Neuromodulation* 17:152–159, 2014

Acknowledgements:

Learning Objectives: 1. Favourable long-term effects of tonic SCS have been obtained in patients with painful diabetic neuropathy. 2. Burst spinal cord stimulation can offer an effective treatment for diabetic neuropathic pain. 3. Despite the progressive nature of diabetic neuropathy, many patients experience sustained pain relief through burst SCS over the long term.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

252

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

APPLYING AN E-HEALTH TOOL TO APPRAISE PATIENT SELECTION FOR SPINAL CORD STIMULATION

Stephanie Fang, BSc (Hons)[1], Michael Hart, MBBS[2], Meredith Macdonald, RN[2], Moein Tavakkoli, MD FRCA[2], Claire Copland, MA(Hons) PsychD[2], Erlick Pereira, MA(Camb) BMBCh DM(Oxf) FRCS SFH[2]
[1]St George's, University of London, SWQT, United Kingdom, [2]St George's Hospital NHS Trust, Neurosurgery, SWQT, United Kingdom

Introduction: Outcomes after Spinal Cord Stimulation (SCS) are critically dependent on patient selection. A recently developed SCS "e-Health" screening tool has been proposed to deliver patient-specific recommendations for SCS (1,2). We aimed to assess the real-world utility of this e-Health tool and objectively appraise patient selection at St George's Hospital NHS Trust.

Total patients seen in service (N = 154)
- With SCS implantation = **109**
- Failed trials = **21**
- MDT-declined patients = **24**

Patients included in the study (N = 89)
- With SCS implantation = **53**
- Failed trials = **13**
- MDT-declined patients = **23**

Exclude: (Total = 65)
- With SCS implantation = **56**
  - **1** – language barrier
  - **7** – no MRI report
  - **12** – no psychology report
  - **36** – no pain scores
- Failed trials = **8**
  - **6** – no psychology report
  - **2** – no MRI report
- MDT-declined patients = **1**

	Chronic low back / leg pain	CRPS	Neuropathic pain syndrome	Ischaemic pain syndrome
With SCS implantation	39	7	7	0
Failed trials	9	1	3	0
MDT-declined patients	14	2	7	0

Materials / Methods: A retrospective analysis of all patients that had been assessed in our service between 2018 and 2023 was performed. This included patients that had either a full SCS implantation, trial only ('failed trials'), or assessment and MDT discussion (MDT-declined). Individual patient details were then analysed in the e-Health tool, outcomes recorded, and compared to whether SCS was successful (defined as a reduction in visual analogue score (VAS) of >50% at 12 months).

Results: Overall, 154 patients were evaluated in the service, of which 56 were excluded due to incomplete data, leading to an analysed cohort of 90. Of 53 patients with SCS implantation, all were either 'recommended' (85%) or 'strongly recommended' (15%) SCS. Of these 49 (92.4%) were successful. Mean VAS reduced from 8.64 pre-operatively to 2.81 at 12 months (5.83 point reduction, 67%). The e-tool recommended SCS in all 13 patients with failed SCS trials without clear differences in the scores between them and those who proceed with SCS implantation. Of the 23 MDT-declined

patients, 13 did not meet the inclusion criteria for SCS, 2 had conditions in the exclusion criteria, leaving 8 patients potentially eligible (2 were put through the e-tool and recommended for SCS while the remaining 6 lacked either psychology or MRI reports).

Discussion: Future work should investigate how recommendations and clinical variables can predict individual patient outcomes. A more comprehensive analysis of inclusion and exclusion criteria is merited, accounting for additional factors such as patient choice, novel indications for SCS, and supporting individual decision making in potentially high-risk cases (such as high body mass index, alcohol use, or anaesthetic risk).

Conclusions: These data validate our clinical decision making and demonstrate the potential of the e-Health SCS screening tool for governance and support of new services. Further work is required to understand the reasons for trials not being successful, potentially utilising additional biomarkers.

Supplemental Data:

References: 1. Ismar Healthcare. Appropriate referral and selection for Spinal Cord Stimulation in patients with chronic pain [Internet]. UK: Ismar Healthcare [updated 2022 August; cited 2023 June 12] Available from: https://www.scstool.org/en/Home 2. Thomson, S., Huygen, F. Applicability and Validity of an e-Health Tool for the Appropriate Referral and Selection of Patients With Chronic Pain for Spinal Cord Stimulation: Results From a European Retrospective Study. Neuromodulation: Technology at the Neural Interface [Internet]. Date of publication 2020 July [cited 2023 June 13]; 23(5): 660-666. Available from: https://www.sciencedirect.com/science/article/pii/S1094715921069713

Acknowledgements:

Learning Objectives: 1. Appraise the role of e-Health assessment in recommending SCS 2. Describe contemporary outcomes in a modern, recently-established neuromodulation centre 3. Understand the role of biomarkers and clinical assessment in making individual decisions

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

253

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

PERSONALIZED SPINAL CORD STIMULATION THERAPY VIA AUTOMATED NEURAL DOSING (FAST-ACTING SUB-PERCEPTION THERAPY AUTODOSE)

Richard Ferro, MD[1], James North, MD[2], Clay Dorenkamp, DO[3], Andy Kranenburg, MD[4], Jason Poston, MD[5], Stephen Pyles, MD[6], John Schneider, MD[7], Clark Metzger, MD[8], Lilly Chen, MD[9], Kacey Auten, MSc[10], Edward Goldberg, MD[9]
[1]Multidisciplinary Pain Management, Pain Management, Okemos, United States of America, [2]Carolinas Pain Institute, Pain Management, Winston-Salem, United States of America, [3]Michigan Orthopedic Center, Pain Management, Lansing, United States of America, [4]Southern Oregon Orthopedics, Pain Management, Medford, United States of America, [5]Pain and Spine Specialists, Pain Management, Idaho Falls, United States of America, [6]Pain Treatment Centers, Pain Management, Ocala, United States of America, [7]Comprehensive Pain & Neurology Center, Pain Management, Murfreesboro, United States of America, [8]West Florida Orthopaedics, Spinal Surgery, Pensacola, United States of America, [9]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America, [10]Boston Scientific, Neuromodulation, Valencia, United States of America

Introduction: A growing compendium of published studies report positive outcomes in patients with access to multiple Spinal Cord Stimulation (SCS)-based options provided by a single device.[1-5] Individualized automation (versus traditional manual adjustment) of SCS programming and neural dosing (i.e., preset, automatic modulation of neurostimulative programming/dosing according to a desired schedule/activities/other) is yet another, more recently introduced "customizable" feature now available on some commercially-available SCS-systems. Here, we examined a group of patients who utilized low frequency-based Fast-Acting Sub-perception Therapy (FAST) programming automation (AutoDose) to better understand its use and potential for improving the real-world experience of SCS in chronic pain patients.

Materials / Methods: This is an observational, case-series of patients using an SCS system (Boston Scientific, Marlborough, MA USA) for treatment of chronic pain based on retrospective chart review. To be included, all patients must have employed FAST-SCS therapy biphasic-symmetric waveform to treat chronic pain using a FAST AutoDose (i.e., automatic electric stimulation dosing) programming schedule. FAST AutoDose programs a proactive stimulation bolus within specified intervals to streamline the patient experience and potentially reduce therapy habituation. Two sub-cohorts were identified per the following: Cohort 1) patients who utilized pre-specified FAST AutoDose programming for up to 1 to 2 weeks following initial use of standard FAST; Cohort 2) patients who, following initial device implantation, were provided with 2 or more FAST AutoDose-based programs set at different neural dose intensity levels (typically within a range of 20-70% of perception threshold) so as to automatically adjust according to preference. Pain scores and other clinical measures (per standard of care) were collected and analyzed from both cohorts.

Results: So far, 12 patients from Cohort 1 have been analyzed with an average age of 61.0-years and baseline NRS score of7.7. A 5.9-point improvement (7.7 ⇒ 1.8) was noted following utilization of FAST AutoDose programming as compared with Baseline ($p<0.0001$). All patients in Cohort 1 using FAST AutoDose reported a mean overall NRS pain score of ≤3. Data collection and analysis derived from both Cohort 1 and 2 are still on-going, and tabulated results obtained from both cohorts will be reported.

Discussion: This evaluation will thus continue to seek out greater understanding with regard to how patients employ FAST-SCS to continue to optimize longevity and outcomes.

Conclusions: Preliminary results from this multicenter, observational case-series demonstrate that FAST AutoDose may provide significant improvement in overall pain without need for manual adjustment of SCS programming.

Supplemental Data:

References: 1. Paz-Solis J, Thomson S, Jain R, Chen L, Huertas I, Doan Q. Exploration of High- and Low-Frequency Options for Subperception Spinal Cord Stimulation Using Neural Dosing Parameter Relationships: The HALO Study. Neuromodulation. 2022 Jan;25(1):94-102.
2. Wille F, Breel JS, Bakker EW, Hollmann MW. Altering Conventional to High Density Spinal Cord Stimulation: An Energy Dose- Response Relationship in N europathic Pain Therapy. Neuromodulation. 2017
Jan;20(1):71-80.
3. Duse G, Reverberi C, Dario A. Effects of Multiple Waveforms on Patient Preferences and Clinical Outcomes in Patients Treated with Spinal Cord Stimulation for Leg and/or Back Pain. Neuromodulation. 2019 Feb;22(2):200-207.
4. Kallewaard JW, Paz-Solis JF, De Negri P, et al. Real-World Outcomes Using a Spinal Cord Stimulation Device Capable of Combination Therapy for Chronic Pain: A European, Multicenter Experience. J Clin Med. 2021 Sep
10;10(18):4085.
5. Rigoard P, Ounajim A, Goudman L, et al. The Challenge of Converting "Failed Spinal Cord Stimulation Syndrome" Back to Clinical Success, Using SCS Reprogramming as Salvage Therapy, through Neurostimulation Adapters Combined with 3D-Computerized Pain Mapping Assessment: A Real-Life Retrospective Study. J Clin Med. 2022 Jan 5; 11(1):272.

Acknowledgements:

Learning Objectives: This study will seeks to assess how patients 1) utilize FAST-SCS Autodosing programming 2) pain relief outcomes per use of FAST Autodosing and 3) other clinical measures obtained (per standard of care) in patient using FAST Autodosing programming.

Financial Disclosures: Drs. Ferro and North have consulting agreements with Boston Scientific. a) Boston Scientific b) consultant c) 5-20k

Disclosure: This study is sponsored by Boston Scientific. Kacey Auten, Lilly Chen, and Edward Goldberg are employees of Boston Scientific.

254

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

REAL-WORLD EVALUATION OF A MULTIMODAL SCS-SYSTEM DESIGNED TO PROVIDE PATIENT_ SPECIFIC NEUROSTIMULATIVE THERAPY FOR CHRONIC PAIN

Clark Metzger, MD[1], Blake Hammond, PA[1], Richard Ferro, MD[2], Binit Shah, MD[3], Timothy Leier, MD[4], Robert Wilson, MD[5], William Newton, DO[6], Louis Raso, MD[7], Melinda Lawrence, MD[8], Jennifer Lee, MD[9], Sayed Wahezi, MD[10], Yu Pei, MPA[11], Edward Goldberg, MD[11]
[1]West Florida Orthopaedics, Spinal Surgery, Pensacola, United States of America, [2]Multidisciplinary Pain Management, Pain Management, Okemos, United States of America, [3]Carolinas Pain Center, Pain Management, Huntersville, United States of America, [4]Savas Health, Pain Management, Rancho Mirage, United States of America, [5]Piedmont Interventional Pain Care, Pain Management, Salisbury, United States of America, [6]Interventional Spine and Pain Center, Pain Management, Manchester, United States of America, [7]The Raso Pain Center, Pain Management, Jupiter, United States of America, [8]University Hospitals Case Medical Center, Pain Management, Cleveland, United States of America, [9]Acute and Chronic Pain Therapies, Pain Management, Bellevue, United States of America, [10]Montefiore Multidisciplinary Pain Program, Pain Management, Bronx, United States of America, [11]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: Due to the varying and subjective nature of the experience of pain and its myriad clinical presentations, providing patients selected for Spinal Cord Stimulation (SCS) with a device that is able to employ a wide range of parameters with multiple programming options is increasingly recognized as an important aspect for enabling efficient and effective treatment for chronic pain.[1-3] A recently launched, commercially-available SCS device capable of full-body MRI can provide an array of paresthesia-based and sub-perception-based neurostimulation modalities that allows for engagement with different mechanisms of action, including fast-acting sub-perception therapy (FAST), combination therapy, and other multiple waveforms/field shapes.

Materials / Methods: This is an on-going, consecutive, multi-center, real-world, observational case-series evaluation (Clinicaltrials.gov: NCT01550575) that retrospectively assesses patients with chronic pain who used a newly-available SCS System (WaveWriterAlpha™, Boston Scientific, Marlborough, MA USA) designed with full-body MRI compatibility that provides for the delivery of supra- and/or sub-perception neurostimulative programming modalities either alone or combined so as to engage multiple mechanisms. These approaches can be optimized in a patient-specific manner such as including (but not limited to) novel Fast-Acting Sub-Perception Therapy (FAST) and/or a new, customizable, sub-perception-based field shape algorithm enabling precise conformational shaping and targeting of electric fields (Contour™, Boston Scientific, Marlborough, MA USA). At baseline and at follow-up visits, pain relief outcomes are collected as well as other clinical endpoints, when available per standard of care.

Results: To date, data from a total of 201 patients (mean age 66.7-years, pre-trial = pain score 7.7 ± 1.7) have been reported so far with a mean follow-up duration time of 271 days. As assessed at last follow-up, a mean 4.9-NRS point improvement was noted ($p<0.0001$), and a 76% responder rate (i.e., ≥50% pain relief). This magnitude of NRS pain score reduction was observed across timepoints out to 3-months (mean NRS = 2.1, n = 103), 12-months (mean NRS = 2.4, n = 72), and 24-months follow-up (mean NRS = 2.5, n = 21). Among the various programming modalities available, FAST was preferred most often (63%) followed by combination therapy (23%), and standard rate (10%).

Discussion: This data continues to show that providing patients with SCS systems that are equipped with capabilities allowing for patient-specific delivery of therapeutic neurostimulation can facilitate clinically-meaningful and long-term, effective outcomes.

Conclusions: On-going data collection and evaluation from this multicenter, realworld, observational, case-series demonstrate significant improvement of chronic pain in patients with a new SCS system

capable of full-body MRI and the delivery of multiple paresthesia-based and sub-perception-based modalities.

Supplemental Data:

References: 1. Fishman MA, Antony A, Esposito M, Deer T, Levy R. The Evolution of Neuromodulation in the Treatment of Chronic Pain: Forward-Looking Perspectives. Pain Med. 2019 Jun 1;20(Suppl 1):S58-S68.
2. Sheldon B, Staudt MD, Williams L, Harland TA, Pilitsis JG. Spinal cord stimulation programming: a crash course. Neurosurg Rev. 2021 Apr;44(2):709-720.
3. Kallewaard JW, Paz-Solis JF, De Negri P, et al. Real-World Outcomes Using a Spinal Cord Stimulation Device Capable of Combination Therapy for Chronic Pain: A European, Multicenter Experience. J Clin Med. 2021 Sep 10; 10(18):4085.

Acknowledgements:

Learning Objectives: This analysis will seek to assess the following: 1) magnitude of pain score change (at specific follow-up visits and/or last follow-up) 2) programming utilization among all patients assessed 3) pain reduction specifically in FAST-SCS preferred users (at specific follow-up visits and/or last follow-up)

Financial Disclosures: Dr. Ferro has a consulting agreement with Boston Scientific. a) Boston Scientific b) consultant c) 1-5k

Disclosure: This study is sponsored by Boston Scientific. Yu Pei and Ed Goldberg are employees of Boston Scientific.

255

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

CLINICAL OUTCOMES USING FAST-SCS: RESULTS OF A MULTICENTER, OBSERVATIONAL REAL-WORLD STUDY IN THE UNITED STATES

Louis Raso, MD[1], Richard Ferro, MD[2], Clark Metzger, MD[3], Blake Hammond, PA[3], William Newton, DO[4], Yu Pei, MPA[5], Edward Goldberg, MD[5]
[1]The Raso Pain Center, Pain Management, Jupiter, United States of America, [2]Multidisciplinary Pain Management, Pain Management, Okemos, United States of America, [3]West Florida Orthopaedics, Spinal Surgery, Pensacola, United States of America, [4]Interventional Spine and Pain Center, Pain Management, Manchester, United States of America, [5]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: Fast-Acting Sub-Perception Therapy (FAST), as an approach for delivering paresthesia-free Spinal Cord Stimulation (SCS), can elicit pain relief with seconds to minutes following device activiation.[1] This characteristic is particularly notable given that all other traditional sub-perception SCS methodologies (e.g., 1-10 kHz, burst) exhibit a slow "wash-in" (i.e., time duration until maximum analgesia following initial neurostimulative device activation).[2] Here, we describe our preliminary experience using FAST-SCS and examine the associated analgesic outcomes in patients who preferentially used FAST-SCS to treat their chronic pain.

Materials / Methods: This is a multi-center, observational case-series of patients in the United States who were permanently implanted with a FAST-enabled SCS system (Wavewriter Alpha™, Boston Scientific, Marlborough, MA USA) to treat chronic pain as part of an ongoing assessment of real-world outcomes of SCS for chronic pain on the basis of retrospective chart review (Clinicaltrials.gov identifier: NCT01550575). All analyzed patients were programmed using novel FAST (i.e., biphasic-symmetric waveform at 90 Hz; pulse width: 160-260 µs). Numerical Rating Scale (NRS) pain scores at baseline and at follow-up visits were obtained.

Results: To date, 126 patients who preferentially utilized FAST-SCS for chronic pain have been assessed with a mean NRS pain score at Baseline of 7.8±1.8. Out to 3-months follow-up (n=61), a 5.5-point reduction in overall NRS pain score was observed, and 72% of patients reported an overall NRS pain score of ≤2. This magnitude of pain relief was near identically sustained in those patients who had reached their 6-month follow-up (n=22). Overall NRS pain scores at 1-, 3-, and 6-months follow-up demonstrated decreased NRS pain scores (versus Baseline) of 2.9, 2.1, and 2.1, respectively. Fifty-seven percent (72/126) of all patients assessed at their last follow-up (mean 254 days) reported an overall NRS pain score of ≤2.

Discussion: The obtained pain relief data, as described in this report of patients who preferentially utilized FAST-SCS for their chronic pain, is consistent with the results of earlier published reports.[3-5]

Conclusions: This preliminary evaluation therefore provides additional evidence that FAST-SCS is capable of inducing rapid onset analgesia that is clinically meaningful and sustainable in the real-world clinical setting.

Supplemental Data:

References: 1. Metzger CS, Hammond MB, Paz-Solis JF, Newton WJ, Thomson SJ, Pei Y, Jain R, Moffitt M, Annecchino L, Doan Q. A novel fast-acting sub-perception spinal cord stimulation therapy enables rapid onset of analgesia in patients with chronic pain. Expert Rev Med Devices. 2021 Mar;18(3):299-306.
2. Chakravarthy K, Richter H, Christo PJ, Williams K, Guan Y. Spinal Cord Stimulation for Treating Chronic Pain: Reviewing Preclinical and Clinical Data on Paresthesia-Free High-Frequency Therapy. Neuromodulation. 2018 Jan;21 (1): 10-18.

3. Bayerl S, et al. Clinical Outcomes Using New Fast-Acting Sub-Perception Therapy SCS for Chronic Pain: A European Observational Study [Abstract]. North American Neuromodulation Society, 2023.
4. Ferro R, et al. Significant Pain Relief Using an SCS System Delivering Novel, Fast-Acting Sub-Perception Therapy [Abstract]. North American Neuromodulation Society, 2023.
5. Gage E, et al. Rapid Onset of Analgesia during Trial Period Utilizing FastActing Sub-Perception Therapy SCS [Abstract]. North American Neuromodulation Society, 2023.

Acknowledgements:

Learning Objectives: To assess patients using FAST-SCS to treat chronic pain according to the following: 1) overall pain relief (NRS Score reduction) 2) responder rate 3) % of patients with overall pain score of ≤2 at follow-up visits.

Financial Disclosures: Drs. Raso, Ferro, and Newton have consulting agreements with Boston Scientific. 1) Boston Scienific 2) consultant 3) 5-20k

Disclosure: This study is sponsored by Boston Scientific. Yu Pei and Edward Goldberg are employees of Boston Scientific.

256

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

WHAT WEB-BASED INFORMATION IS AVAILABLE FOR PEOPLE WITH CHRONIC PAIN INTERESTED IN SPINAL CORD STIMULATION?

Maarten Moens, MD[1], Ann De Smedt, MD[2], Maxime Billot, PhD[3], Manuel Roulaud, MSc[3], Philippe Rigoard, MD[4], Lisa Goudman, PhD[5]
[1]Vrije Universiteit Brussel, Stimulus Research Group, Jette, Belgium, [2]Universitair Ziekenhuis Brussel, Stimulus Research Group, Jette, Belgium, [3]CHU de Poitiers, Neurosurgery Departement/prismatics Lab, Poitiers, France, [4]Poitiers University, Spinal Neurosurgery, Neuromodulation, Poitiers, France, [5]Laarbeeklaan 103, Stimulus Research Group, Jette, Belgium

Introduction: The increased availability of online medical information has encouraged chronic pain patients to seek healthcare information from multiple sources, i.e. the consultation of healthcare providers combined with web-based information. The type and quality of information that is available online is very heterogeneous. To date, there are no studies that have identified and evaluated what information is available on the web for patients with chronic pain who are interested in information about neuromodulation. Therefore, the aims of this study are to explore the type, quality, and content of online information regarding Spinal Cord Stimulation for chronic pain that is freely available online and targeted at consumers of healthcare.

Materials / Methods: The social listening tool Awario© was used to search Facebook, Twitter, YouTube, Instagram, blogs, and the web for suitable hits with “pain” and “neuromodulation” as keywords. Quality appraisal of the extracted information was performed with the DISCERN instrument. Thematic analysis through inductive coding was conducted.

Results: The initial search identified a total of 2174 entries, of which 630 entries were eventually withheld. Patient information was mainly available through YouTube hits (70.79%). Most posts were originated in the USA (82.38%). For the content of information, 66.15% of the entries discussed (at least partially) how SCS works. The risks of the treatment were only discussed in a minority of entries (24.52%). In total, 55.61% of the entries did not elaborate on the fact that there may be more than one potential treatment choice and 47.67% did not discussed the influence of SCS on overall quality of life. Regarding reliability of the information, 72.19% of the entries did not clearly describe the aims that they aimed to achieve. For 94.82% of the entries it was clear or partially clear when the information in the entry was produced. Areas of uncertainty were not discussed in the majority of entries (54.06%). Inductive coding revealed four main themes: (1) pain and the burden of pain, (2) neuromodulation as a treatment approach, (3) device related aspects and (4) patient benefits and testimonials of a treatment with SCS.

Discussion: Healthcare consumers have access to online information about SCS whereby details about the surgical procedures, the type of material, working mechanisms, risks, patient expectations, and testimonials as well as potential benefits of this therapy option are discussed.

Conclusions: The availability of information, however, does not evaluate whether information is effectively retrieved by consumers and whether it is easily accessible, which needs to be further evaluated.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1) To get familiar with the potentials of social listening and the way patients use this to retrieve information about neuromodulation. 2) To gain insight in what type of information is available online about neuromodulation for pain, i.e. the quality of information, which content and the availability in terms of modes and languages. 3) The know the influence of online information on healthcare settings.

Financial Disclosures: Maarten Moens has received speaker fees from Medtronic, Nevro and Saluda Medical. Philippe Rigoard reports grants and consultant fees from Medtronic, Abbott and Boston Scientific, outside the submitted work. Lisa Goudman is a postdoctoral research fellow funded by the Research Foundation Flanders (FWO), Belgium (project number 12ZF622N). STIMULUS received independent research grants from Medtronic. There are no other conflicts of interest to declare.

Disclosure: No significant relationships.

257

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

SUPRASPINAL HYPOTHESES ABOUT SPINAL CORD STIMULATION AND DORSAL ROOT GANGLION STIMULATION: A SYSTEMATIC REVIEW

Lisa Goudman, PhD[1], Ann De Smedt, MD[2], Bengt Linderoth, MD, PhD[3], Sam Eldabe, FRCA[4], Rui Duarte, PhD[5], Maarten Moens, MD[6]
[1]Laarbeeklaan 103, Stimulus Research Group, Jette, Belgium, [2]Universitair Ziekenhuis Brussel, Stimulus Research Group, Jette, Belgium, [3]Karolinska Institutet, Tomtebodavägen, Department Of Clinical Neuroscience, Stockholm, Sweden, [4]James Cook Hospital, Pain Department, Middlesbrough, United Kingdom, [5]university of liverpool, Institute Of Population Health, LIVERPOOL, United Kingdom, [6]Vrije Universiteit Brussel, Stimulus Research Group, Jette, Belgium

Introduction: Despite the established efficacy and effectiveness of Spinal Cord Stimulation (SCS) for the management of chronic pain, there is still no consensus on the supraspinal mechanisms of action of this therapy. The purpose of this study was to systematically review previously raised hypothesis concerning supraspinal mechanisms of action of SCS in human, animal and computational studies.

Materials / Methods: Searches were conducted using four electronic databases (PubMed, EMBASE, SCOPUS and Web of Science), backward reference searching and consultation with experts to identify observational and experimental studies investigating supraspinal mechanisms of SCS. The study protocol was registered prior to initiation of the review process (PROSPERO CRD42020161531).

Results: A total of 54 publications were included, 21 of which were animal studies and 33 human studies. The supraspinal hypothesis (n=69) identified from the included studies could be categorized into six groups concerning the proposed supraspinal hypothesis, namely 1) descending pathway (n=24); 2) ascending medial pathway (n=13); 3) ascending lateral pathway (n=10); 4) affective/motivational influence (n=8); 5) spinal-cerebral (thalamic)-loop (n=3); and 6) miscellaneous (n=11). Scientific support is provided for the hypotheses identified.

Discussion: Modulation of the descending nociceptive inhibitory pathways, followed by a modulation of the ascending medial and lateral pathways were the most frequently reported hypotheses about the supraspinal mechanism of action of SCS.

Conclusions: All hypotheses were supported by both human and animal studies, indicating that basic/fundamental and clinical research suggest similar hypotheses. Nevertheless, it remains unclear whether these working mechanisms reflect direct effects of electrical stimulation or indirect effects obtained by creating pain relief.

Supplemental Data:

References: Goudman L, De Groote S, Linderoth B, De Smedt A, Eldabe S, Duarte RV, Moens M. Exploration of the Supraspinal Hypotheses about Spinal Cord Stimulation and Dorsal Root Ganglion Stimulation: A Systematic Review. J Clin Med. 2021 Jun 23;10(13):2766. doi: 10.3390/jcm10132766.

Acknowledgements:

Learning Objectives: 1) To receive an overview of the published mechanisms of action of SCS and DRG stimulation. 2) To know the scientific evidence underlying mechanisms of action based on humans versus animal studies. 3) To know gaps in current evidence about mechanisms of action of SCS and DRG stimulation.

Financial Disclosures: Rui V. Duarte has received consultancy fees from Medtronic Ltd., Boston Scientific Corp, Mainstay Medical and Saluda Medical. Sam Eldabe has received consultancy fees from Medtronic Ltd., Mainstay Medical, Boston Scientific Corp and Abbott. He has received department research funding from the National Institute of Health Research, Medtronic Ltd. and Nevro Corp. Bengt Linderoth serves as a consultant to Elekta AB. Maarten Moens has received speaker fees from Medtronic and Nevro. STIMULUS received independent research grants from Medtronic.

Disclosure: No significant relationships.

258

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

GOALS, EXPECTATIONS, AND THE DEFINITION OF SUCCESS FOR NEUROMODULATION FOR PAIN ACCORDING TO HEALTHCARE PROVIDERS AND REPRESENTATIVES OF NEUROMODULATION DEVICE MANUFACTURERS

Maarten Moens, MD[1], Ann De Smedt, MD[2], Maxime Billot, PhD[3], Manuel Roulaud, MSc[3], Philippe Rigoard, MD[4], Lisa Goudman, PhD[5]
[1]Vrije Universiteit Brussel, Stimulus Research Group, Jette, Belgium, [2]Universitair Ziekenhuis Brussel, Stimulus Research Group, Jette, Belgium, [3]CHU de Poitiers, Neurosurgery Departement/prismatics Lab, Poitiers, France, [4]Poitiers University, Spinal Neurosurgery, Neuromodulation, Poitiers, France, [5]Laarbeeklaan 103, Stimulus Research Group, Jette, Belgium

Introduction: Neuromodulation for pain has been successfully applied for decades, in that the goals and expectations that patients aim to achieve are clearly described. Nevertheless, the point of view of health care providers and representatives of neuromodulation device manufacturers is less clear. Representatives of neuromodulation device manufacturers are expected to facilitate the relationship between patients and healthcare providers. Therefore, this study aimed to explore the goals, expectations, and definition of success for neuromodulation for pain according to health care providers and representatives.

Materials / Methods: An online survey was developed and spread at the 2nd Joint Congress of the International Neuromodulation Society (INS) European Chapters in September 2021 in Paris. Respondents were asked 1) to select the goals to treat patients with neuromodulation for pain, 2) to indicate factors that they expect to change according to neuromodulation for pain, and 3) to provide their definition of success of neuromodulation for pain.

Results: In total, 88 healthcare providers and 39 representatives at least partly completed the survey. Increasing mobility/functionality (26.7%), decreasing pain intensity (24.5%), and decreasing medication use (16.6%) were the most frequently reported goals of neuromodulation according to healthcare providers. To provide excellent service for patients (22.4%), to become a trusted partner for physicians (21.5%), and to provide excellent service for physicians (20.7%) were the highest ranked goals stated by representatives of device manufacturers.Healthcare providers expected that pain intensity will be influenced the most by neuromodulation (27.2%),followed by the expectation that mobility/functionality is changed (26%) and by pain medication use (18.7%).The most frequently reported factors that were expected to change by representatives were pain intensity (23.1%), patient satisfaction (19.7%), mobility/functioning (14.5%), and capacity to return to work (13.7%). For the definition of success, quality of life of patients outranked other definitions.

Discussion: Goals and expectations of healthcare providers are not completely in line with previously explored patient goals that are related to pain relief and improving walking abilities. Healthcare providers put a high emphasis on the quality of life when evaluating the success of neuromodulation. The goals of representatives of neuromodulation device manufacturers seem to focus on ensuring a good relationship with physicians on the one hand and providing good service towards patients on the other hand, whereby pain control, quality of life, and patient satisfaction seem to be important for company representatives.

Conclusions: These results could question the current reimbursement criteria, which are mainly focusing on obtaining pain relief, instead of emphasizing health-related quality of life.

Supplemental Data:

References: 1) Moens M, Alliet W, Billot M, De Smedt A, Flamée P, Vanhonacker D, Roulaud M, Rigoard P, Goudman L.Goals, Expectations, and the Definition of Success for Neuromodulation for

Pain According to Representativesof Neuromodulation Device Manufacturers. J Pers Med. 2022 Sep 6;12(9):1457.
2) Goudman L, De Smedt A, Billot M, Roulaud M, Rigoard P, Moens M. Opinions of Health Care Providers AboutNeuromodulation for Pain: Results of an Online Survey at the 2nd Joint Congress of the InternationalNeuromodulation Society European Chapters. Neuromodulation. 2022 May 9:S1094-7159(22)00643-2.

Acknowledgements:

Learning Objectives: 1) To gain insight in the importance of goalsetting for chronic pain management.
2) To learn about the goals, expectations and definition of success of neuromodulation, according to physicians and representatives of device manufacturers.
3) To evaluate differences and commonalities in goalsetting between chronic patients, healthcare providers and device manufacturers and the influence of these differences for clinical practice.

Financial Disclosures: Lisa Goudman is a postdoctoral research fellow funded by the Research Foundation Flanders (FWO), Belgium (project number 12ZF622N). Philippe Rigoard reports grants and personal fees from Medtronic, Abbott, and Boston Scientific outside the submitted work. Maarten Moens has received speaker fees from Medtronic and Nevro. STIMULUS received research grants from Medtronic. There are no other conflicts of interests to declare.

Disclosure: No significant relationships.

259

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

HOLISTIC COMPOSITE MEASURE FOR SPINAL CORD STIMULATION OUTCOMES - 10 YEARS REAL WORLD DATA FROM A RURAL IMPLANTING CENTRE IN THE SOUTH WEST OF ENGLAND.

Juan Graterol, MSc, Kate Fleming, RN, Jayne Thomas, RN, Neil Roberts, MSc
Royal Cornwall Hospitals NHS Trust, Pain Clinic, Truro, United Kingdom

Introduction: The Royal Cornwall Hospitals NHS Trust has been an implanted centre for more than 2 decades. For the last 10 years, we have prospectively collected patient reported outcome measures following recommendations from IMMPACT, ICHOM and the National Neuromodulation Registry of the Uinted Kingdom. We have further developed our data capture to include other items beyond minimum standards. Recent publications have urged a holistic view of outcomes (1) that encompass more than pain intensity scores. We would like to present our outcomes using such an approach.

Materials / Methods: Every patient considered suitable for spinal cord stimulation was consented to obtain prospective data using validated outcome measures like: Brief Pain Inventory, Oswestry Disability Index, Hospital Anxiet and Depression scores and EQ-5D. Data was captured at baseline (pre-trial), 3 months, 6 months, 12 months followed by yearly reviews post implant. These are stored in a databse in house and relevant points were retrieved anonymised to produce report below. This report will include all patients up to the latest review point. Some as long as 10 years, others more recently implanted.

Results: This will be presented as a graph modelled on paper published in Neuromodulation by Levy et all in July 2023 (2)

Discussion: Quantification of an experience is difficult. We use validated questionnaires to objectively analyse impact of this treatment modality. There are various issues with this type of data including biased recall, patient's perception and collection method. The global impression of change seems to be a more consistent meaure of patient satisfaction.

Conclusions: Prospectively gathered real world outcomes are a very valuable tools to assess impact of neuromodulation in various settings. This information, along side complication rates and ease of access, might be relevant to patients if they have a choice of providers. Even when no such choice exists - due to geographical constraints for example - this information may be use to improve and refine selection criteria.

Supplemental Data:

References: 1. Goudman L, Pilitsis JG, Russo M, et al. From pain intensity to a holistic composite measure for spinal cord stimulation outcomes. *Br J Anaesth*. 2023;131(2):e43-e48. doi:10.1016/j.bja.2023.05.016 2. Levy RM, Mekhail N, Abd-Elsayed A, et al. Holistic Treatment Response: An International Expert Panel Definition and Criteria for a New Paradigm in the Assessment of Clinical Outcomes of Spinal Cord Stimulation. *Neuromodulation*. 2023;26(5):1015-1022. doi:10.1016/j.neurom.2022.11.011

Acknowledgements: No external funding was provided for this project

Learning Objectives: 1. Application of a holistic treatment response paradigm as proposed by international expert panel 2. Observations derived from prospectively gathered data 3. Recommendations for future service developments

Financial Disclosures: None of the authers have commercial interests to declare

Disclosure: No significant relationships.

260

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

DEVELOPING A LOCALLY-LED SPINAL CORD STIMULATOR REPROGRAMMING SERVICE USING TELEMEDICINE AT A RURAL IMPLANTATION CENTRE IN THE SOUTH WEST OF ENGLAND

Neil Roberts, MSc, Jayne Thomas, RN, Kate Fleming, RN, Juan Graterol, MSc
Royal Cornwall Hospitals NHS Trust, Pain Clinic, Truro, United Kingdom

Introduction: Patients with implanted spinal cord stimulators need regular and accessible troubleshooting and optimisation through device interrogation and reprogramming. This has previously required direct attendance in clinic by company representatives. The 2020 pandemic left a legacy of increased use of telemedicine. In rural areas, this provides an opportunity to reduce environmental impact of unnecessary travel while increasing the number of patients that can be assessed in a timely fashion. The patients attend their local centre where experienced nurses are able to re-program their device with remote advice from company representatives as needed. We were the first UK hospital to implement this. We used implementation science methods to analyse this service development from the point of view of staff and patients.

Materials / Methods: An 18-question survey for specialist nurses assessed barriers and enablers towards the new telemedicine service using the Theoretical Domains Framework. Each domain had at least one free-text question. Responses were coded by domain then summarised into overarching belief statements. Results of this informed a patient questionnaire to assess their beliefs about the new service.

Results: 2/2 responses received from specialist nurses. The service was enabled by pre-existing experience, with device-specific training to give appropriate knowledge, skills and confidence, with decision-making facilitated by user guides. There is wider departmental and company support, and belief that the service enhances both nursing role and therapeutic nursing-patient relationship. There is perception of wider environmental benefit of reducing rep travel, and more timely troubleshooting appointments with less wait for patients. Staff intend to increase telemedicine clinics due to strong beliefs in multiple positive consequences outweighing negatives, optimism and a positive impact on job satisfaction. Barriers included a need for good hospital internet, sufficient charge on the telemedicine link dongle, and patients who were slightly more fatigued after longer appointments. 4/4 responses received from patients. All reported that a therapeutic relationship with the programmer was very important, with free text comments valuing continuity of care with nursing staff. Most reported that timely appointments were very important. All preferred to have a degree of face-to-face interaction within their appointment. Half reported that reducing environmental impact was important.

Discussion: Setting up a successful telemedicine-supported locally-led SCS re-programming service is possible within a well-supported and well-planned service, with small environmental barriers to negotiate. The main benefit perceived by both nurses and patients is an improved therapeutic relationship, vital to both parties.

Conclusions: Our findings could be used to guide others in implementing similar developments.

Supplemental Data:

References: None

Acknowledgements: The support of Boston Scientific for this project is gratefully acknowledged.

Learning Objectives: 1. To elicit organisational barriers and enablers towards a locally-led spinal cord stimulator reprogramming stimulus using telemedicine 2. To use replicable implementation

science methodology to analyse a neuromodulation service development 3. To analyse the patient voice in this service development and look for concordance or discordance with the perceived benefits/risks of the service development

Financial Disclosures: No significant relationships for any authors.

Disclosure: No significant relationships.

261

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

WAVEFORM UTILIZATION AND OUTCOMES OF SPINAL CORD STIMULATION IN CRPS PATIENTS: A MULTICENTER REAL-WORLD OBSERVATIONAL STUDY

Ashish Gulve, MD[1], Jennifer Robinson, RN[1], Irene Wilkinson, RN[1], Sarah Love Jones, MBBS BSc FRCA FFPMRCA EDPM[2], Philippe Rigoard, MD[3], Georgios Kyriakopoulos, MD[4], Jose Paz Solis, MD[5], Sylvie Raoul, MD[6], Jose Llopis-Calatayud, MD[7]
[1]James Cook University Hospital, Department Of Pain Medicine, MIDDLESBROUGH, United Kingdom, [2]Southmead Hospital, Pain Medicine, Bristol, United Kingdom, [3]Poitiers University, Spinal Neurosurgery, Neuromodulation, Poitiers, France, [4]St. Marien Hospital Hamm, Pain Unit, Hamm, Germany, [5]University Hospital La Paz, Neurosurgery, Madrid, Spain, [6]University Hospital Nantes, Neurosurgery, Nantes, France, [7]University Hospital La Ribera, Pain Unit, Valencia, Spain

Introduction: Spinal cord stimulation (SCS) is an established therapeutic option for patients with Complex Regional Pain Syndrome (CRPS) suffering from severe chronic pain. Recent SCS devices are versatile and offer multiple waveforms options with distinct mechanisms of action. One of them is a recently-developed fast-acting sub-perception therapy which acts on the surround inhibition mechanism[1] and could be a valuable option for CRPS patients[2,3]. Here we report real-world long-term outcomes from a subset of over 80 CRPS patients who have been implanted with versatile SCS systems since 2016 and analyze their outcomes and waveform preferences.

Materials / Methods: This is a consecutive, observational, multicenter case-series based an on-going, real-world evaluation of SCS outcomes for chronic pain (Clinicaltrials.gov: NCT01550575). All evaluated patients were implanted with an SCS device and documented data from their medical records were used to assess their condition at baseline and post-implant follow-up visits. Data collection includes diagnosis and medical history, pain scores, and preferred SCS settings. All data were collected by site personnel, as per standard practice and without sponsor involvement.

Results: To date, the review of over 80 CRPS cases implanted with SCS has been performed, including 90% de novo patients. Patients had a baseline pain score of 8.0, and the average follow-up after SCS implant is 3.2 years. Patients have all been implanted with SCS systems with versatile programming capabilities (standard rate, high rate, burst, combination therapy), and for half of them, recent devices could also offer a new fast-acting sub-perception therapy. Overall outcomes at last follow-up (3.2 years after implant) show a that the most preferred waveforms were fast-acting sub-perception therapy, followed by combination therapy and standard rate SCS. In patients preferring fast-acting sub-perception therapy, pain scores decreased by 4.7-point. Over 60% of them had a profound response and reported 76% reduction in overall pain NRS score, from 8.3 to 2.0 at last follow-up (-6.3 point, average follow-up 313 days).

Discussion: Spinal cord stimulation is diverse and offers the possibility to use waveforms with different mechanisms of action, which may help personalize SCS therapy to specific pain conditions.

Conclusions: Our results show a significant efficacy of various SCS waveforms in CRPS patients, with a profound pain relief in most patients using fast-acting sub-perception therapy. These outcomes suggest that this new modality may act on a specific mechanism (loss of surround inhibition) that plays a role in CRPS condition.

Supplemental Data:

References: 1. Gilbert JE, Titus N, Zhang T, Esteller R, Grill WM. Surround Inhibition Mediates Pain Relief by Low Amplitude Spinal Cord Stimulation: Modeling and Measurement. eNeuro. 2022 Oct 5;9(5):ENEURO.0058-22.2022. doi: 10.1523/ENEURO.0058-22.2022. PMID: 36150892; PMCID: PMC9536854. 2. Loss of Surround Inhibition and After Sensation as Diagnostic Parameters of

Complex Regional Pain Syndrome. Marie Wojcik Wolanin, Robert J. Schwartzman, Guillermo Alexander, John Grothusen. Neuroscience & Medicine, 2012, 3, 344-353 3. Deconstructing Complex Regional Pain Syndrome. Schwartzman R. Pract Pain Manag. 2010;10(2)

Acknowledgements:

Learning Objectives: 1. The use of surround inhibition SCS mechanism for the treatment of CRPS 2. Waveform preferences and outcomes of SCS for CRPS 3. Real-world evidence from a multicentre European review

Financial Disclosures: Ashish Gulve has received honoraria for consulting as well as advisory board meetings for Nevro Corp, Boston Scientific Corp, and Abbott Jennifer Robinson and Irene Wilkinson: no significant relationships Sarah Love-Jones has undertaken paid consultancy work for Abbott Medical, Boston Scientific, Medtronic, Nevro Corporation and Pfizer. She has research support from Boston Scientific, Medtronic, Abbott Medical, Nevro Corporation, Nalu Medical and Mainstay Medical Philippe Rigoard reports grants and paid consultancy work for Boston Scientific, Abbott Medical and Medtronic Georgios Kyriakopoulos: no significant relationships Jose Paz-Solis reports paid consultancy work for Boston Scientific Sylvie Raoul: no significant relationships Jose Llopis-Calatayud reports paid consultancy work for Boston Scientific

Disclosure: I am an employee of Boston Scientific Neuromodulation (sponsor of the Patient Retrospective Outcomes (PRO)study), and part of the Clinical Research Team.

262

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

A QUESTIONNAIRE-BASED STUDY OF THE USABILITY AND EFFICACY OF RECHARGEABLE IMPLANTABLE PULSE GENERATORS WITH ECAP-CONTROLLED CLOSED-LOOP SPINAL CORD STIMULATION

Mohammad Mehdi Hajiabadi, MD, Paliz Vicheva, MD, Martin Jakobs, MD, Sandro M. Krieg, MD, Rezvan Ahmadi, MD
Heidelberg University Hospital, Neurosurgery, Heidelberg, Germany

Introduction: Since 2004, rechargeable implantable generators (r-IPGs) for spinal cord stimulation (SCS) have promised extended lifetimes of up to 25 years. Novel closed-loop SCS (cl-SCS), based on evoked compound action potentials (ECAPs) as feedback, maintain consistent stimulation and mitigate potential over- or under-stimulation. However, long-term data on these devices, their recharging, interruption during recharging and effort are limited.

Materials / Methods: A standardized 48-item questionnaire was sent to all chronic pain patients using a cl-SCS device. The primary endpoint was the overall convenience of the recharging process, rated on an ordinal scale from "very easy" (0 points) to "very difficult" (100 points). Secondary endpoints were charge burden (time spent recharging per week), user confidence and complication rates. Endpoints were analysed for multiple subgroups.

Results: Data sets of 8 SCS patients (62% return rate) were returned and eligible for data analysis. The mean age was 50.1 ± 7.8 (± SD) years. The duration of therapy with the IPG was 16.0± 8.3 months (mean ± SD). All patients checked and handled the IPG themselves. The overall handling of recharging was rated as "very easy" with 12.6 ± 12.7 points (mean ± SD). The mean charge burden was 202 ± 222 min/week (mean ± SD); 87.5% of the patients felt confident recharging the neurostimulator. Failed recharges and interruption of stimulation were reported in one patient.

Discussion: No Discussion

Conclusions: Chronic pain patients using cl-SCS are confident in using the IPG. It is more comfortable, but requires more effort than conventional devices, but has fewer problems with recharging and interruptions. These first data on the comfort and maintenance of cl-SCS call for a broader comparison with conventional SCS in future studies.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. Chronic pain patients using cl-SCS are confident in using the IPG 2. Using the cl-SCS IPG is more comfortable but requires more effort than using conventional devices. 3. Using the cl-SCS IPG has fewer problems with recharging and interruptions than conventional devices.

Financial Disclosures: No significant relationships!

Disclosure: No significant relationships.

263

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

EVALUATING THE EFFICACY OF THE PILOTPAIN APP IN ENHANCING CLOSED-LOOP EPIDURAL SPINAL CORD STIMULATION OUTCOMES: A PROSPECTIVE PILOT STUDY

Mohammad Mehdi Hajiabadi, MD[1], Sena Soylik, MD[2], Leonie Ader, DPsych[2], Ulrich Reininghaus, MD[2], Sandro M. Krieg, MD[1], Rezvan Ahmadi, MD[1]
[1]Heidelberg University Hospital, Neurosurgery, Heidelberg, Germany, [2]Zentralinstitut für Seelische Gesundheit, Public Mental Health, Mannheim, Germany

Introduction: Epidural closed-loop spinal cord stimulation (cl-SCS) is an established intervention for chronic neuropathic pain. Complementing it with additional health-promoting modalities, such as mobile health applications grounded in positive psychology techniques, can provide supplementary and pragmatic health enhancement.

Materials / Methods: In this prospective, non-controlled pilot study, we assess the PilotPAIN App's feasibility, safety, acceptance, and initial impact on quality of life in patients undergoing cl-SCS. Evaluations were conducted before training (T0), post-training (T1), and 4 weeks after training (T2), utilizing questionnaires such as WEMWBS, EQ5D5L, PANAS, PSQI, VAS, HADS, ODI, etc (Figure 1).

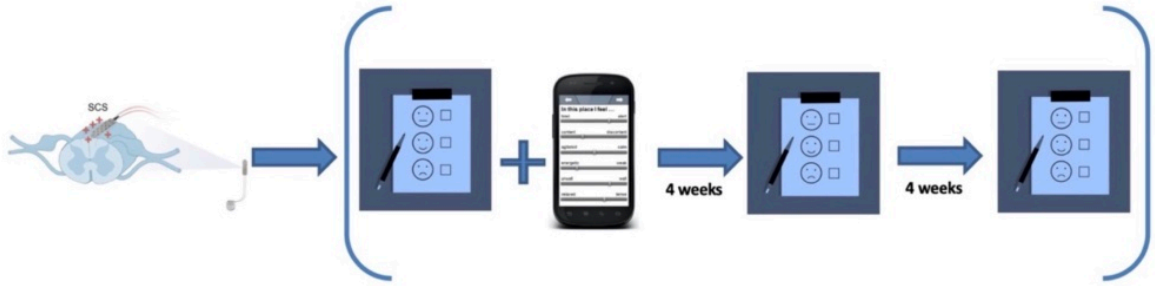


Figure 1 *Phase of the study in T0, T1 and T2*

Results: Thus far, the study comprises N=9 female patients, averaging 50 ± 14 years of age (mean ± SD). Among them, N=4 have completed the study, N=3 have transitioned from T1 to T2, and N=2 have concluded T0. The average duration of cl-SCS therapy was 9.6 ± 8.8 months (mean ± SD). This resulted in a notable decrease in pain intensity ($p<0.001$), with VAS scale measurements showing a decline from an initial 8.9 ± 0.9 (mean ± SD) to 2 ± 1.1 (mean ± SD). Over an average follow-up of 230 days, the VAS pain intensity stabilized at 2.5 ± 1.6 (mean ± SD). For the N=4 patients completing the study, the PilotPAIN app revealed no significant alterations in quality of life, functionality, or sleep

quality. Preliminary data can be referenced in the appended graphs (Figure 2).

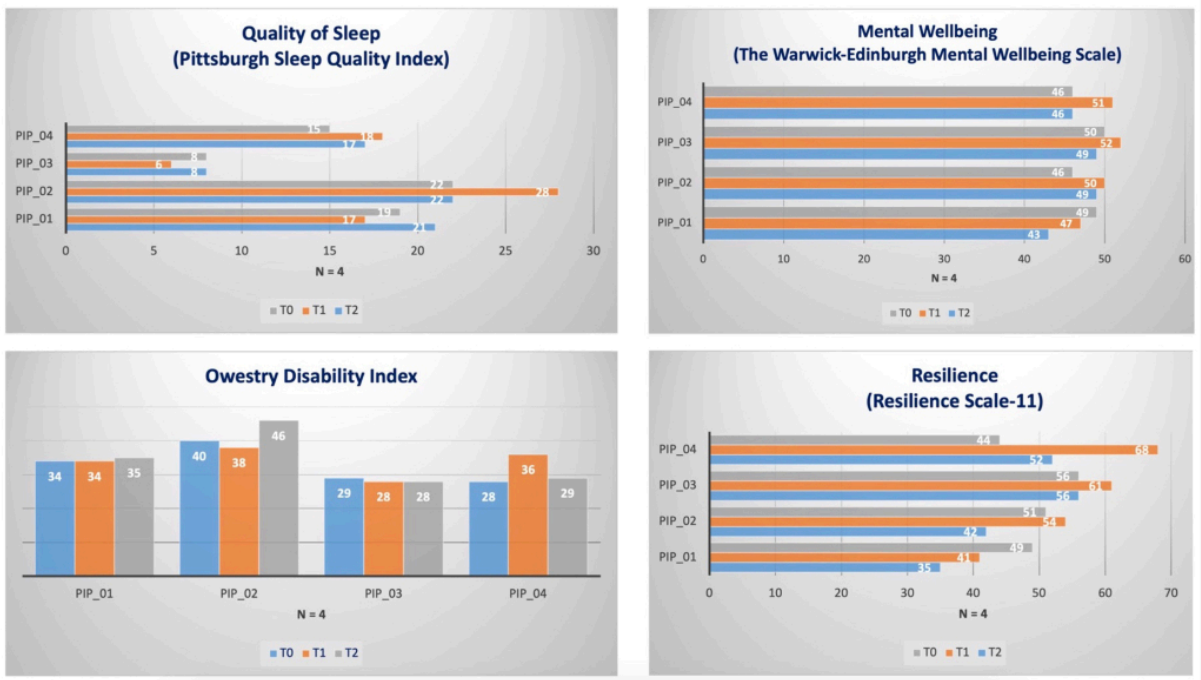


Figure 2 PSQI, Mental Wellbeing, ODI and Resilience of N=4 patients

Discussion: No Discussion

Conclusions: Current data suggests that patients benefiting from cl-SCS express confidence and interest in the mobile PilotPAIN application. However, questionnaire evaluations indicate varied outcomes, with no discernible trend in changes to quality of life, functionality, or sleep quality.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. Patients benefit significantly from cl-SCS. 2. Patients express confidence and interest in mobile PilotPAIN application. 3. The using of the PilotPAIN app indicates no discernible trend in the change of quality of life, functionality or quality of sleep.

Financial Disclosures: No significant relationships!

Disclosure: No significant relationships.

264

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

EFFICACY AND LONGEVITY OF FIRST GENERATION 10KHZ SPINAL CORD STIMULATORS : A SINGLE-CENTRE ANALYSIS AT 10 YEAR FOLLOW-UP

Stephany Harris, RN, Matthew Stubbs, MBBS, Samantha Weil, RN, Karen Sanderson, RN, Terrance Ramrattan, RN, Stefano Palmisani, MD, Adnan Al-Kaisy, MBBS, Thomas Smith, MBBS, David Pang, MBBS
Guy's and St Thomas' NHS Foundation Trust, Pain Management & Neuromodulation Center, London, United Kingdom

Introduction: Since its introduction in UK in 2010, the 10kHz SCS paradigm has been used to treat a number of pain conditions. However, limited long-term performance data are available. Our aim was to retrospectively assess reliability and efficacy of one such commercially available system over a 10 year period, at a tertiary referral neuromodulation centre in the UK.

Materials / Methods: Case notes were reviewed for all patients who underwent full-implantation of a 10KHz SCS device (Senza system, Nevro Corp., Redwood City, California, USA) between May 2010 and October 2013 at our centre (unless opted-out of data sharing). Patient demographics, indication for implant and device technical problems before 10 years were recorded. Efficacy data including pain intensity and patient global impression of change (PGIC – table 1) were recorded beyond 10 years (mean 11.4 years).

Patients Global Impression of Change

Since beginning this treatment, how would you describe the change (if any) in **ACTIVITY LIMITIATIONS, SYMPTOMS, EMOTIONS** and **OVERALL QUALITY OF LIFE** related to your painful condition? (Please tick ONE box)

0 - ☐ Worsening
1 - ☐ No change
2 - ☐ Almost the same, hardly any change at all
3 - ☐ A little better but not noticeable change
4 - ☐ Somewhat better, but the change has not made any real difference
5 - ☐ Moderately better, and a slight but noticeable change
6 - ☐ Better and a definite improvement that has made a real and worthwhile difference
7 - ☐ A great deal better and a considerable improvement that has made all the difference.
8 -

Table 1: PGIC scooring tool used to collect patient-reported satisfaction scores beyond 10 years

Results: 78 patients were identified (38 women, 40 men, mean age 50 years). Indications for implant were PSPS2 (52.5%), PSPS1 (25.5%), CRPS (9%), neuropathic pain (9%), craniofacial pain (3%), unknown (1%) At 10 years, 10 patients had been explanted, 9 were deceased, 9 were lost to follow-up, and one was incapacitated. Reasons for explant are shown in figure 1. 10-year explant rate was 13-17% (range using denominators excluding and including lost to follow-up/deceased patients, respectively). A further 9% had stopped using their device. Of the remaining 49 patients, 5 (10%) underwent a revision procedure within 10 years:
- 1 lead revision (for high impedances), during which the IPG was prophylactically replaced.
- 3 IPG changes for charging issues
- 1 IPG change for undocumented reason. 43 patients had a complete data-set for efficacy sub-analysis. 67% reported ≥50% pain relief at 10 years (average 58% reduction in pain). 67% reported that they felt 'moderately to a great deal better' (see figure
2).

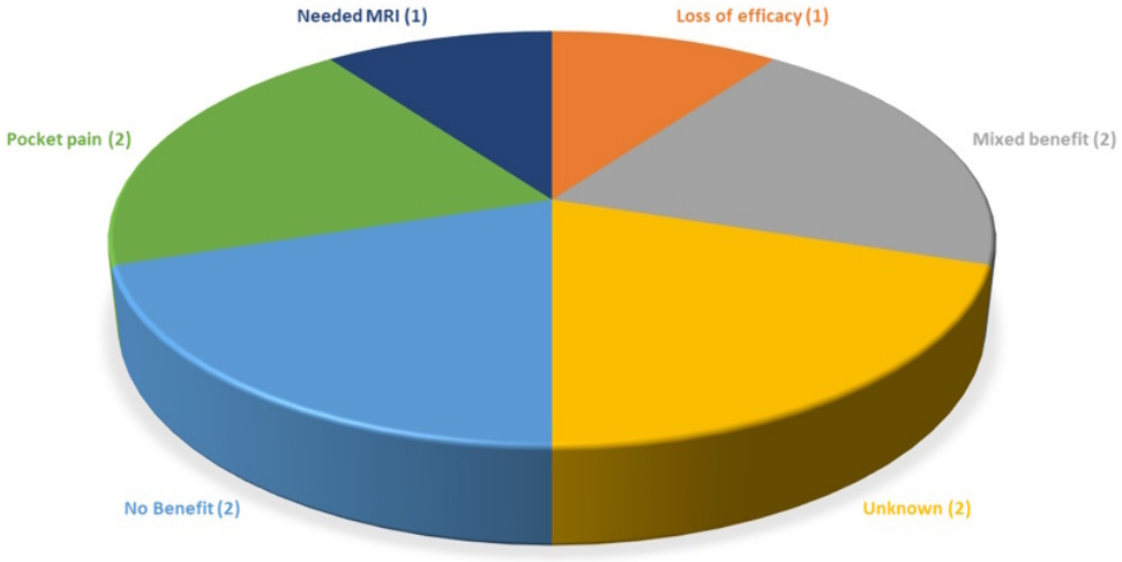


Figure 1: Reasons for explant of device before 10 years

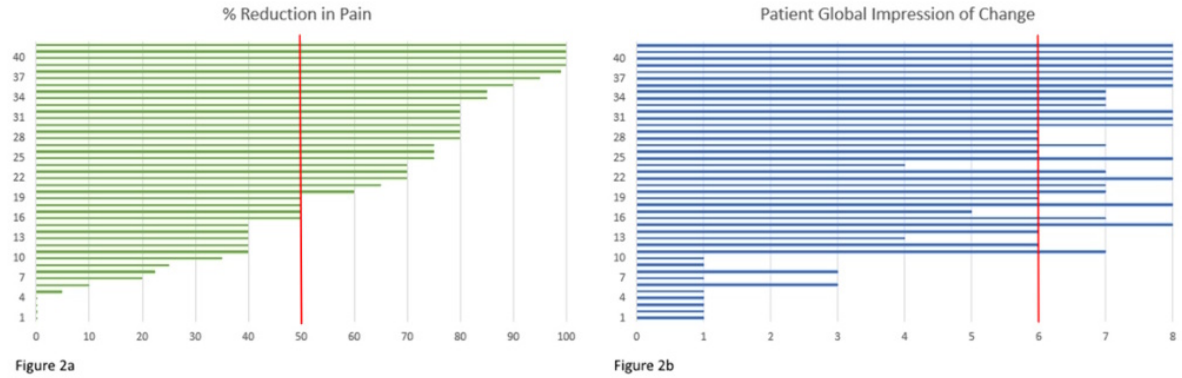


Figure 2a Figure 2b

Figure 1 : Patient reported efficacy data beyond 10 years. ***Figure 1 (a)*** shows a tornado graph of % reduction in pain. ***Figure 1 (b)*** shows PGIC scores, ranked by % reduction in pain for direct comparison (0= worsening; 8= a great deal better and considerable improvement that has made all the difference – see table 1). Red marks indicate values above which were considered a meaningful positive outcome (Pain reduction ≥50% ; PGIC ≥6),

Discussion: To our knowledge, this is the largest 10 year follow-up data-set of this SCS system. Approximately three-quarters of patients were still implanted and using their device at 10 years. QoL and pain were both improved, but the imperfect correlation between groups demonstrates the importance of multimodal assessment. A limitation of 10 year follow-up is inevitable organic changes in patients' pain states: some may develop new pain conditions, others may resolve. In general, however, outcomes were favourable in comparison to conservative, interventional and surgical treatment options. The device technical longevity has largely performed as predicted by the manufacturer.

Conclusions: At our centre, 1st generation 10kHz spinal cord stimulators demonstrated both technical longevity and maintained efficacy at 10 years.

Supplemental Data:

References:

Acknowledgements: No commercial support has been received in relation to this work.

Learning Objectives: 1. To demonstrate that, in our experience, the first generation 10kHz SCS system offers good efficacy to 10 years (as measured by pain reduction and quality of life). 2. to demonstrate that, in our experience, the device is technically reliable to 10 years. 3. To be aware that measures of pain intensity and quality of life may not be entirely correlated. We recommend both of these important outcome measures are considered in clinical practice.

Financial Disclosures: No significant relationships None of the authors have any financial conflict of interest to declare.

Disclosure: No significant relationships.

265

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

TWELVE-MONTH RESULTS OF DIFFERENTIAL TARGET MULTIPLEXED SPINAL CORD STIMULATION IN JAPANESE PATIENTS

Naoki Higashiyama, MD, Tamura Shinya, MD, Taku Sugawara, MD
Akita Cerebrospinal and Cardiovascular Center, Department Of Spinal Surgery, Akita, Japan

Introduction: Differential target multiplexed (DTM) spinal cord stimulation (SCS) is a new paresthesia-free stimulation programming where electrical signals are multiplexed spatially and temporally. DTM SCS has been reported to reduce pain significantly more than conventional SCS[1)]. In this study, we studied the efficacy of DTM SCS in Japanese patients.

Materials / Methods: This was a single-center retrospective study in FBSS patients who underwent permanent spinal cord stimulator implantation and were stimulated with DTM™ SCS programming between April 2021 and March 2022. Eligible patients were older than 18 years; diagnosed with FBSS; had low back pain or leg pain persisting for at least three months; and had a 100-mm visual analog scale (VAS) score of at least 50 mm for low back or leg pain. The VAS scores for low back pain and leg pain and ODI before and after 12 months of surgery, and the responder rate (percentage of patients whose pain decreased by ≥50%) were analyzed.

Results: Twenty patients (8 males, 12 females, mean age 75 years) underwent device implantation and were stimulated by DTM SCS programming. The VAS for low back pain and leg pain and the ODI were significantly reduced, and the responder rate was 80% for back pain and 85% for leg pain.

Discussion: DTM SCS was shown to improve low back and leg pain in Japanese patients, with a responder rate comparable to that reported in an RCT by Fishman et al [1)].

Conclusions: The present study shows the efficiency of DTM-SCS in Japanese patients.

Supplemental Data:

References: 1) Fishman M, Cordner H, Justiz R, et al. Twelve-month results from multicenter, open-label, randomized controlled clinical trial comparing differential target multiplexed spinal cord stimulation and traditional spinal cord stimulation in subjects with chronic intractable back pain and leg pain. Pain Pract. 2021;21:912-923.

Acknowledgements:

Learning Objectives: 1. Treatment outcomes of DTM SCS in Japanese patients. 2. Improved outcomes for patients with low back and leg pain due to FBSS. 3. Evaluate evidence from retrospective studies.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

266

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

TARGETING THE CONUS MEDULLARIS WITH DOSE-CONTROLLED CLOSED-LOOP SCS FOR THE TREATMENT OF CHRONIC PELVIC PAIN: A CASE-SERIES

Corey Hunter, MD[1,2], Jonathan Lee, DO[2]
[1]Ainsworth Institute of Pain Management, New York, United States of America, [2]Icahn School of Medicine, Department Of Rehabilitation & Human Performance, New York, United States of America

Introduction: Chronic pelvic pain (CPP) is defined as persistent, noncyclic pain located within the pelvic region lasting longer than 6 months[1,2] affecting 5%-26% of women and 2%-16% of males[1–3]. Etiology includes posttraumatic, postsurgical, somatic, or visceral pain syndromes. Several conditions predispose one to develop CPP, but the exact cause is unknown[4]. Treatment options include physical therapy, pharmacologic agents, and nerve blocks; however, efficacy is typically limited[5]. Neuromodulation is typically the next treAatment in the algorithm for patients' refractory to conventional medical management (CMM), but CPP possesses the highest explant rate of all diagnoses for which SCS has been used [6]. The reason for high explant rates might be due to the complexity of the pelvic region that is innervated by sympathetic and parasympathetic fibers, and somatic and splanchnic nerves from lumbar and sacral regions[7]. Efficacy of neuromodulation for CPP depends on adequate lead positioning, but there is no consensus on optimal lead placement due to complex pelvic innervation. Conus medullaris has been considered as an optimal target for stimulating the pelvic region due to the confluence of sacral fibers[8] and proximity to sympathetic innervation entering the cord at the L2 level. However, the mobility of the conus and large amount of adjacent CSF make it a suboptimal target for open-loop (OL) SCS given its inability to maintain consistent activation of the spinal cord (SC), let alone a mobile structure like the conus[9]. ECAP-controlled (evoked compound action potential) closed-loop (CL) SCS can consistently and accurately activate the SC[9] making it an ideal modality for stimulating the conus and thus reliably covering the pelvic region. We present a retrospective case series on CPP patients implanted with ECAP-controlled CL SCS targeting the conus – to our knowledge this is the first ever case series presented using closed loop stimulation for the treatment of pelvic pain, let alone successfully/consistently targeting the conus medullaris.

Materials / Methods: Preliminary data includes 3 patients with severe CPP refractory to CMM including OL-SCS. Three patients underwent successful trials before moving to permanent implantation; 1 was a revision of a failed SCS implant. All 3 patients were implanted with ECAP-controlled CL SCS (Evoke, Saluda Medical, Australia) using 2-leads positioned in a "train" configuration spanning T9-L1/2. Paresthesia mapping was performed to confirm activation of the painful dermatome. Objective neurophysiology was utilized to confirm neural activation prior to programming in CL.

Results: Baseline demographics and clinical characteristics are presented in Table 1. Pain scores were calculated using numeric rating scale (NRS) – values were recorded at baseline (pre-NRS) and post implant (post-NRS) at their most recent follow up. Mean time since implant is ~9.1 months. The average reduction in pain from baseline was 6.3 on NRS and 83.3% decrease.

Characteristics	
Gender, male/female (n)	0/3
Pain History	
CRPS Type II in Groin & Left Lower Limb	1
CRPS Type II in Groin/Sacral Region	2

Table 1. Baseline demographics and clinical characteristics

Pain Scores (NRS)	
Pre-NRS	7.7
Post-NRS	1.3
Pain Reduction	
Average Reduction	6.3
Percent Reduction	83.3%

Table 2. Mean pre- and post-Implant NRS and pain reduction

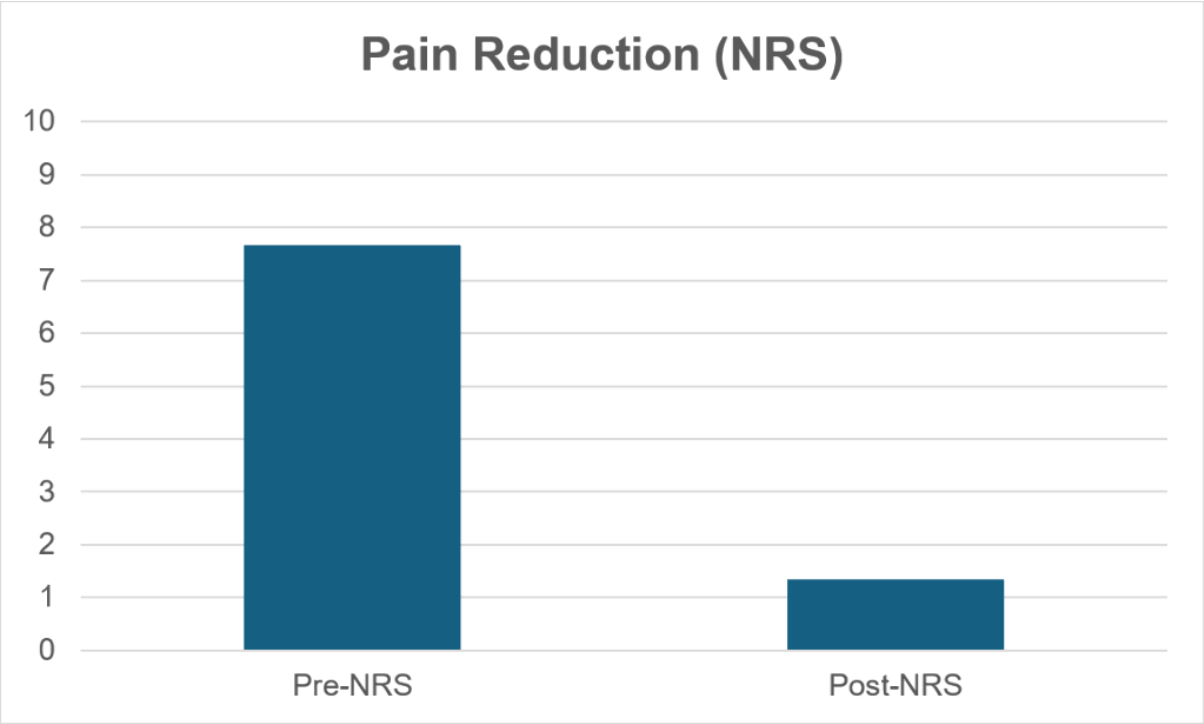


Table 3 – Graphic Illustration of Pre- and Post-Implant NRS Pain Scores

Discussion: The conus medullaris has long been thought to be an ideal target for the use of neurostimulation for the treatment of CPPS due to the fact that it contains the confluence of all the sacral fibers from the pelvic region. Unfortunately, the degree of movement of the conus as compared with the rest of the spinal cord, combined with the large amount of CSF surrounding it, made stimulation with conventional, open loop stimulation extremely difficult.
The conus can move over 1mm laterally and anterior/posteriorly – this means that a patient can go from receiving no stimulation one moment to being painfully overstimulated the next.
CLS was invented to account for the minor movements of the cord associated with positional changes in implanted patients (i.e. supine body orientation or coughing) that can lead to overstimulation and ultimately failure of the therapy. A CLS platform records ECAP's several contacts away from the point of stimulation to assess for over/understimulation associated with movement of the cord closer or away from the leads and adjusts the amplitude of stimulation on the very next impulse. Stimulation over the conus with CLS is a more extreme utilization of this particular technologic advancement that finally allows for neuromodulators to finally capture this particular segment of the cord successfully.

Conclusions: CPPS is a challenging condition to manage due the lack of consistently effective treatments (1, 2). While SCS has shown great efficacy in its ability to treat chronic pain, it has traditionally encountered difficulty with CPPS. While the conus has long been viewed as the "ideal" target for SCS with respect to CPPS, the technology lacked the ability to consistently stimulate it (3), largely due to the fact that it is highly mobile as compared to other portions of the spinal cord. This case series suggests a potential solution by using CLS over the conus to treat CPPS.

Supplemental Data:

References: 1. Stein, S. L. Chronic Pelvic Pain. *Gastroenterology Clinics* **42**, 785–800 (2013).
2. Smith, C. P. Male chronic pelvic pain: An update. *Indian J Urol* **32**, 34–39 (2016).
3. Valovska, A. T. *Pelvic Pain Management*. (Oxford University Press, 2016).
4. Hunter C, Dave N, Diwan S, Deer T. Neuromodulation of pelvic visceral pain: review of the literature and case series of potential novel targets for treatment. Pain Pract 2013;13:3-17.
5. Hunter, C. W., Stovall, B., Chen, G., Carlson, J. & Levy, R. Anatomy, Pathophysiology and Interventional Therapies for Chronic Pelvic Pain: A Review. *Pain Physician* **21**, 147–167 (2018).
6. Hayek SM, Veizi E, Hanes M. Treatment-Limiting Complications of Percutaneous Spinal Cord Stimulator Implants: A Review of Eight Years of Experience From an Academic Center Database. Neuromodulation 2015;18:603-8; discussion 8-9.
7. Levine, A. B., Parrent, A. G. & MacDougall, K. W. Stimulation of the Spinal Cord and Dorsal Nerve Roots for Chronic Groin, Pelvic, and Abdominal Pain. *Pain Physician* **19**, 405–412 (2016).
8. Buffenoir, K. *et al.* Spinal cord stimulation of the conus medullaris for refractory pudendal neuralgia: a prospective study of 27 consecutive cases. *Neurourol Urodyn* **34**, 177–182 (2015).
9. Mekhail, N. A. *et al.* ECAP-controlled closed-loop versus open-loop SCS for the treatment of chronic pain: 36-month results of the EVOKE blinded randomized clinical trial. *Reg Anesth Pain Med* (2023) doi:10.1136/rapm-2023-104751.
10. Rade M, et al. Normal multiplanar movement of the spinal cord during unilateral and bilateral straight leg raise: Quantification, mechanisms, and overview. J Orthop Res. 2017 Jun;35(6):1335-1342. doi: 10.1002/jor.23385. Epub 2017 May 3. PMID: 27504619.

Acknowledgements:

Learning Objectives: - Review the mechanisms of pelvic pain and why it is traditionally difficult to treat with conventional neurostimulation platforms
- Discuss the general concept of stimulating the conus medullaris and why it is so difficult with open loop systems
- Explain the concept of closed loop spinal cord stimulation

Financial Disclosures: Corey Hunter, Saluda Medical, Consultant/Advisory Board ($5,001 - $20,000 USD); Abbott - Consultant/ Advisory Board, Research ($20,001 - $100,000 USD); PainTEQ - Stock Options (> $100,000 USD); Vertos - Stock Options ($20,001 - $100,000 USD); Mainstay - Stock Options (> $100,000 USD); Nalu - Stock Options (> $100,000 USD); Vivex - Stock Options ($20,001 - $100,000 USD); Tissuegene - Research (> $100,000 USD); Spine Biopharma - Research ($5,001 - $20,000 USD); Avertitas - Research ($5,001 - $20,000 USD); FUSMobule - Research ($5,001 - $20,000 USD) Jonathan Lee has nothing relevant to disclose

Disclosure: No significant relationships.

267

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

MINIMIZING PATIENT BURDEN USING PRECISION DOSE CONTROL CLOSED-LOOP SPINAL CORD STIMULATION

Corey Hunter, MD[1], Sean Li, MD[2], Dawood Sayed, MD[3], Christopher Lam, MD[3], David Zub, MD[4], Peter Staats, MD[5]
[1]Ainsworth Institute of Pain Management, New York, United States of America, [2]Premier Pain Centers, Shrewsbury, United States of America, [3]The University of Kansas Medical Center, Kansas City, United States of America, [4]EmergeOrtho, Oxford, United States of America, [5]National Spine & Pain Centers, Shrewsbury, United States of America

Introduction: Fixed-output open-loop (OL) spinal cord stimulation (SCS) systems lack the ability to automatically account for large variations in neural activation induced by physiological activity and movement. This results in variable inhibition of pain processing pathways and suboptimal therapy[1,2] requiring the patient to adjust stimulation (> 30 daily button clicks)[1] or request for reprogramming (> 4-5 visits/year)[3]. Patient burden with OL SCS includes ~2 months/year of suboptimal therapy, and additional travel costs/days-off-work within the first 12-months post-implant[3]. Recent FDA guidance suggests accurate and consistent therapy delivered using physiologic closed-loop controlled (PCLC) devices can minimize human error and enhance medical care[4]. Evoked compound action potential (ECAP) controlled closed-loop (ECAP-CL) spinal cord stimulation (SCS) is PCLC-based technology that auto-adjusts 4+ million times/day to deliver precise and consistent neural activation of the target responsible for pain inhibition[5]. Here we evaluate the need for manual amplitude adjustments and unscheduled reprogramming visits in ECAP-CL SCS patients in the EVOKE randomized controlled trial (RCT) and real-world ECAP study.

Materials / Methods: EVOKE RCT [n=41; (NCT02924129)] and real-world ECAP [Interim results; n=156; (NCT04319887)] study patients utilizing ECAP-CL SCS were included in this analysis.

Results: ECAP-controlled CL SCS delivered consistent and accurate therapy (Tables 1 & 2). System (>80%) and therapy (stimulation above ECAP threshold >92% of time) utilization was also high in both EVOKE (Table 1) and ECAP study patients (Table 2) across all timepoints. Median unscheduled reprogramming visits/subject/month in the EVOKE RCT decreased from 0.5 (IQR:0-1.0) at 3-months to 0.0 (IQR:0-0.3) at 36-months (Figure 1A). Need for unscheduled reprogramming in the ECAP study (Figure 2A) was minimal at 3- [Median = 0 (IQR:0-0.5)], 6- [Median = 0 (IQR:0-0.3)], and 12-months [Median = 0 (IQR:0-0.1)]. Median daily button clicks to adjust stimulation amplitude in the EVOKE RCT decreased from 1.0 (IQR:0.3 -3.1) at 3-months to 0.1 (IQR:0-0.6) at 36-months (Figure 2B). Need for daily button clicks to adjust stimulation amplitude in the ECAP study (Figure 2B) was also minimal at 3- [Median = 0.7 (IQR:0.3-1.7)], 6- [Median = 0.6 (IQR:0.1-1.3)], and 12-months [Median = 0.4 (IQR:0-
1.0)].

Table 1. Objective physiologic measurements with ECAP-controlled CL-SCS in the EVOKE RCT through 36-months

	3-month	12-month	24-month	36-month
Dose Accuracy (in-clinic RMSE, μv)	3.1 [1.8-4.6]	3.9 [2.4-5.8]	3.2 [2.2-5.1]	3.7 [2.7-5.4]
System Utilization (% time on)	90.0 [76.9-97.8]	88.2 [65.6-95.9]	87.3 [48.4-96.5]	80.3 [6.6-96.0]
Percent Time Stimulating Above ECAP Threshold (%, out of time on)	98.5 [69.8-99.9]	99.6 [77.8-100.0]	95.7 [63.7-99.9]	97.2 [50.7-100.0]
ECAP Dose (normalized median ECAP amplitude, μv)	32.3 [16.9-69.8]	29.7 [11.7-67.6]	23.9 [9.7-50.2]	19.3 [1.9-33.3]
Dose Ratio (estimated current at median ECAP amplitude/current at ECAP threshold)	1.42 [1.23-1.58]	1.42 [1.31-1.53]	1.35 [1.24-1.52]	1.32 [1.17-1.42]

Table 2. Objective physiologic measurements with ECAP-controlled CL-SCS in the ECAP Study through 12-months

	3-month	6-month	12-month
Dose Accuracy (in-clinic RMSE, μv)	3.0 [2.1-4.6]	2.8 [2.0-4.5]	2.9 [2.0-4.2]
System Utilization (% time on)	89.0 [62.7-97.2]	88.3 [55.8-97.2]	87.0 [39.3-96.6]
Percent Time Stimulating Above ECAP Threshold (%, out of time on)	96.0 [63.9-99.8]	94.9 [59.0-99.8]	92.5 [58.0-99.9]
Therapy Dose (normalized median ECAP amplitude, μv)	22.5 [4.7-42.3]	17.5 [3.3-39.8]	16.8 [2.2-39.5]
Dose Ratio (estimated current at median ECAP amplitude/current at ECAP threshold)	1.3 [1.0-1.5]	1.3 [1.0-1.5]	1.2 [1.0-1.5]

Figure 1: Median (±IQR) Unscheduled Reprogramming Visits per subject per month (Figure 1A) and Median (±IQR) Daily Button Clicks to adjust stimulation amplitude (Figure 1B) in the EVOKE RCT (N=41) for Patients Using only ECAP-CL SCS through 36-months.

Figure 1A

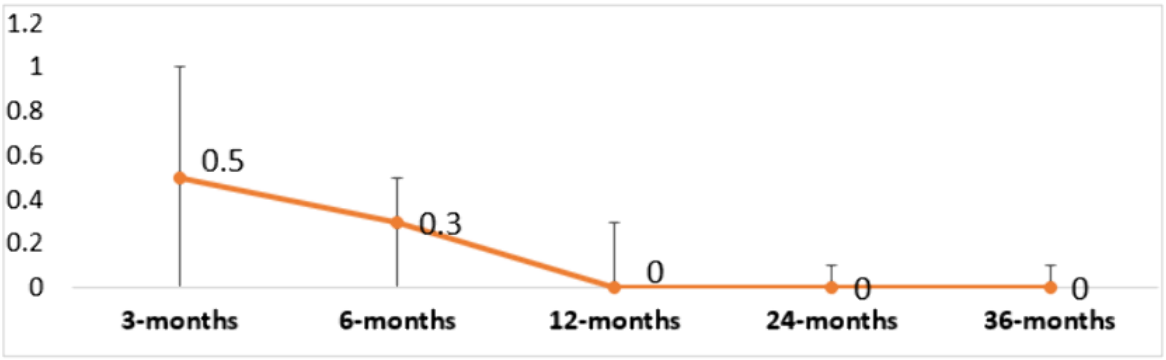


Figure 1B

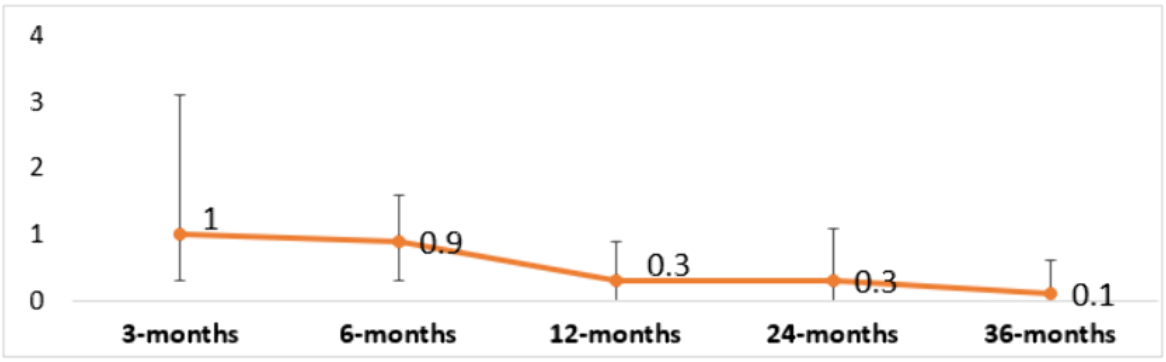


Figure 2: Median (±IQR) Unscheduled Reprogramming Visits per subject per month (Figure 2A) and Median (±IQR) Daily Button Clicks to adjust stimulation amplitude (Figure 2B) in the ECAP study through 12-months (Interim Results; N=156 at 12-months).

Figure 2A

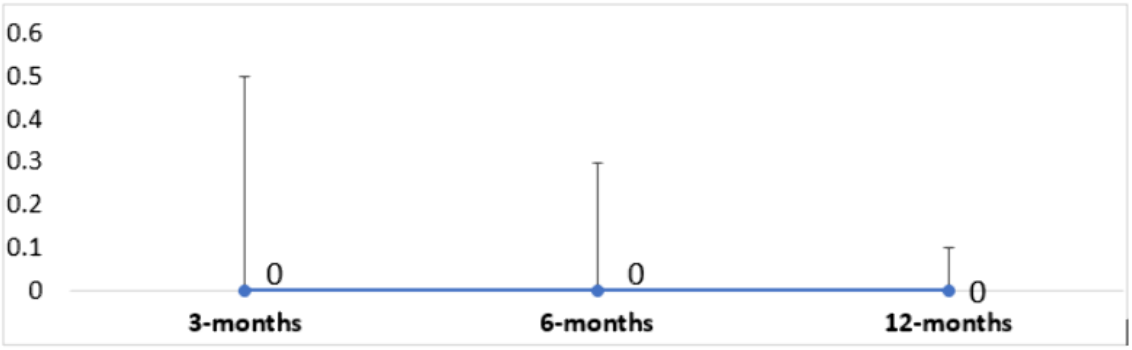
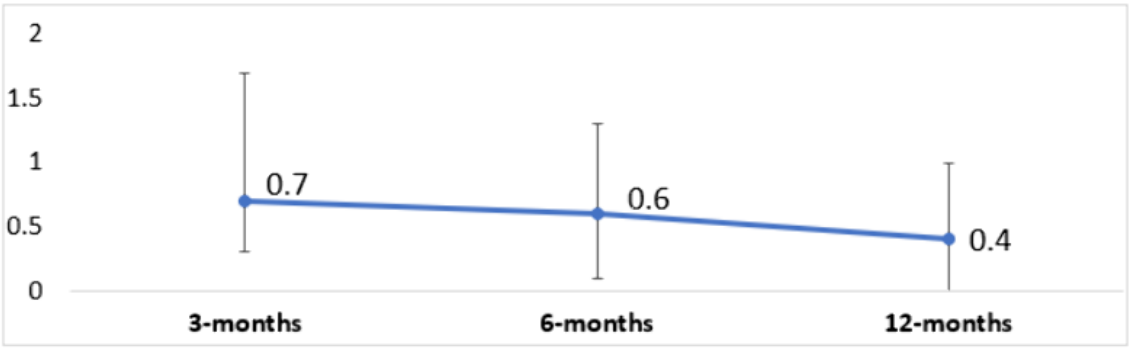


Figure 2B



Discussion: Precision dose control ECAP-CL SCS enabled by objective neurophysiology delivers consistent and accurate therapy that may reduce or eliminate the need for manual amplitude adjustments or unscheduled reprogramming visits.

Conclusions: This may lead to lower patient, physician, and practice burden involved in optimizing SCS therapy to maintain clinical benefit.

Supplemental Data:

References: 1. Schultz DM, Webster L, Kosek P, Dar U, Tan Y, Sun M. Sensor-driven position-adaptive spinal cord stimulation for chronic pain. Pain Physician. 2012 Jan-Feb;15(1):1-12. PMID: 22270733. 2. Ross E, Abejón D. Improving patient experience with spinal cord stimulation: implications of position-related changes in neurostimulation. Neuromodulation. 2014;17(S1):36-41. 3. Amirdelfan K, Antony A, Levy R, et al. Patient burdens associated with spinal cord stimulation: impact of wait times to address device-related issues in a real-world cohort with chronic back and leg pain. Poster presented at: World Institute of Pain World Congress; August 24, 2022; Budapest, Hungary. 4. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/technical-considerations-medical-devices-physiologic-closed-loop-control-technology 5. Mekhail NA, Levy RM, Deer TR, et al. ECAP-controlled closed-loop versus open-loop SCS for the treatment of chronic pain: 36-month results of the EVOKE blinded randomized clinical trial. Regional Anesthesia & Pain Medicine Published Online First: 27 August 2023. doi: 10.1136/rapm-2023-104751

Acknowledgements: Trial sponsored by Saluda Medical.

Learning Objectives: 1. ECAP-controlled closed-loop SCS is PCLC-based technology that enables precise and consistent neural activation of the target responsible for pain inhibition 2. ECAP-controlled closed-loop SCS may reduce/eliminate the need for manual amplitude adjustments or unscheduled reprogramming visits 3. ECAP-controlled closed-loop SCS has the potential to lower patient, physician, and practice burden involved in optimizing SCS therapy to maintain clinical benefit

Financial Disclosures: Corey Hunter, Saluda Medical, Consultant/Advisory Board ($5,001 - $20,000 USD); Abbott - Consultant/ Advisory Board, Research ($20,001 - $100,000 USD); PainTEQ - Stock Options (> $100,000 USD); Vertos - Stock Options ($20,001 - $100,000 USD); Mainstay - Stock Options (> $100,000 USD); Nalu - Stock Options (> $100,000 USD); Vivex - Stock Options ($20,001 - $100,000 USD); Tissuegene - Research (> $100,000 USD); Spine Biopharma - Research ($5,001 - $20,000 USD); Avertitas - Research ($5,001 - $20,000 USD); FUSMobule - Research ($5,001 - $20,000 USD) Sean Li, Consultant/Advisory Board, $20,001-$100,000 USD Dawood Sayed, Saluda Medical, Consultant/Advisory Board, $20,001-$100,000 USD Christopher Lam has no relevant conflicts of interest to disclose David Zub, Saluda Medical, Speaker, $500-$5000 USD Peter Staats, Saluda Medical, Consultant/Advisory Board, $5,001-$20,000 USD, Education/Research, $20,001-$100,000, Stock Options, $20,001-$100,000

Disclosure: Administrative support to authors funded by Saluda Medical.

268

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

UTILIZATION OF COMBINATION THERAPY-BASED SCS PROGRAMMING IN CHRONIC PAIN PATIENTS: A REAL-WORLD, OBSERVATIONAL EUROPEAN STUDY

Jan Willem Kallewaard, MD[1], Jose Paz Solis, MD[2], Philippe Rigoard, MD[3], Renaud Bougeard, MD[4], Hayat Belaid, MD[5], M. Angeles Canos-Verdecho, MD[6], Sylvie Raoul, MD[7], Jose Llopis-Calatayud, MD[8], Pasquale De Negri, MD[9], Isaac Peña, MD[10], Sarah Love Jones, MBBS BSc FRCA FFPMRCA EDPM[11], Simon Thomson, MBBS[12], Lilly Chen, MD[13], Edward Goldberg, MD[13]
[1]Amsterdam university centre, Anesthesiology And Pain Management, Arnhem, Netherlands, [2]University Hospital La Paz, Neurosurgery, Madrid, Spain, [3]Poitiers University, Spinal Neurosurgery, Neuromodulation, Poitiers, France, [4]Clinique de la Sauvegarde, Pain Management, Lyon, France, [5]Fondation Adolphe de Rothschild, Neurosurgery, Paris, France, [6]University and Polytechnic Hospital La Fe, Pain Management, Valencia, Spain, [7]University Hospital Nantes, Neurosurgery, Nantes, France, [8]University Hospital La Ribera, Pain Unit, Valencia, Spain, [9]AORN S. Anna & S. Sebastiano, Pain Management, Caserta, Italy, [10]Hospital Virgen Del Rocio, Pain Unit, Seville, Spain, [11]Southmead Hospital, Pain Medicine, Bristol, United Kingdom, [12]Mid & South Essex University Hospitals NHSFT, Pain And Neuromodulation Centre, Basildon, United Kingdom, [13]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: Spinal Cord Stimulation (SCS) programming customized to the individual needs of each patient is thought to be important for elucidation of the most effective clinical outcomes when using SCS for management of chronic pain. This is in part supported by the fact that experience of chronic pain itself is inherently dynamic and highly subjective in nature. Our previously published work has also shown that, when given the available option, a substantial proportion of patients using SCS for chronic pain prefer programming that combines neurostimulative modalities such as (but not limited to) utilization of supra- and sub-perception-based approaches.1 Here, we report the real-world outcomes of patient implanted with an SCS device, as part of a multi-center observational study, who preferred to use combination therapy to treat their chronic pain.

Materials / Methods: This is an observational case-series of patients permanently implanted with an SCS system (Spectra WaveWriter™ and Wave Writer Alpha™, Boston Scientific, Marlborough, MA USA) to treat chronic pain. All analyzed patients utilized combination therapy programming (i.e., sequential or simultaneously delivery) consisting of at least two distinct modes of applied neurostimulation (e.g., supraperception [standard rate, tonic]+ sub-perception [fast-acting sub-perception/high rate/burst/microburst/field targeting algorithm]). Demographic information, pain location, surgical history, medical history were collected for all patients. In addition, Numeric Rating Scale (NRS) scores, Percent Pain Relief (PPR) and other functional outcomes as available were collected as part of the chart review.

Results: To date, 156-patients have been assessed with a mean (SD) Baseline pain score (NRS) of 7.8 (1.5). Mean follow-up duration was 471 days. A mean 4.9 ± 2.4-point NRS score improvement ($p<0.0001$) in overall pain was consistently sustained from 3-months to 24-months follow-up (7.8 ⇒ 2.7). Disability assessment (Oswestry Disability Index, ODI) indicated improvement ($p<0.0001$) as assessed at last follow-up (ODI score = 36) versus Baseline (ODI score = 53). Additionally, evaluation of quality of life (EQ-5D-5L) in 65 patients (for whom data was available) indicated a substantial improvement from baseline measurement (36.4) out to last follow-up (69.7).

Discussion: Given the different mechanisms of action that are thought to govern the various modes of neurostimulation now increasingly accessible as part of commercially available devices, it is postulated that a substantial proportion of patients are likely to achieve highly effective outcomes using programming approaches that provide SCS as a combination therapy.

Conclusions: Data from this multicenter, real-world, observational, European-based case-series demonstrate significant improvement of chronic pain, disability, and quality-of-life in patients utilizing SCS-based combination therapy.

Supplemental Data:

References: 1. Kallewaard JW, Paz-Solis JF, De Negri Pet al. Real-World Outcomes Using a Spinal Cord Stimulation Device Capable of Combination Therapy for Chronic Pain: A European, Multicenter Experience. J Clin Med. 2021 Sep 10;10(18):4085.

Acknowledgements:

Learning Objectives: To evaluate the following in patients using combination therapy SCS out to 24-months follow-up:

1) real-world pain score improvement (NRS)

2) assess disability (ODI)

3) assess quality-of-life (EQ-5D-5L)

Financial Disclosures: This study sponsored by Boston Scientific. Dr. Kallewaard has a consulting agreement with Bsoton Scientific. a) Boston Scientific b) consultant c) 5-20k

Disclosure: This study is sponsored by Boston Scientific. Lilly Chen and Ed Goldberg are employees of Boston Scientific.

269

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

CERVICAL ECAP CONTROLLED CLOSED-LOOP SPINAL CORD STIMULATION THERAPY IN PATIENTS WITH CHRONIC NECK, UPPER LIMB AND MULTIFOCAL PAIN

Jan Willem Kallewaard, MD[1], Harold Nijhuis, MD[1], Caro Edelbroek, Nurse Practitioner[2], Wj Hofste, MD[1]
[1]rijnstate, Anesthesiology, arnhem, Netherlands, [2]rijnstate, Anesthesiology, Elst, Netherlands

Introduction: Cervical ECAP controlled closed-loop spinal cord stimulation therapy in patients with chronic neck, upper limb and multifocal pain Jan-Willem Kallewaard[1,2], Harold Nijhuis[3], Caro Edelbroek[1], Willem-Jan Hofsté[3] **Introduction:** Efficacy of spinal cord stimulation (SCS) is well established for treating chronic neuropathic pain of the trunk and limbs. But less evidence exists for its use in treating cervical axial spine and radicular pain (1) The cervical anatomy and its high mobility could result in suboptimal SCS therapy due to variable stimulation intensity. ECAP (evoked-compound-action-potential)-controlled closed-loop SCS (CL-SCS) automatically compensates for fluctuations in distance between the epidural leads and spinal cord in real time and ensures consistently neural activation and accurately adheres to the prescribed target (1). This case series will assess the effects and stimulation sensation of ECAP-controlled CL-SCS in patients with cervical lead placements.

Materials / Methods: Methods/Materials: This ongoing multi-centre case-series collected patient-reported-outcomes for pain relief (NRS), satisfaction, stimulation sensation awareness and quality. Neurophysiological and device data (stimulation parameters, patient usage) were collected during standard-of-care visits. All patients were diagnosed with chronic intractable pain of the upper limbs, some including additional pain in the lower limbs. All patients were implanted with one cervically placed lead and received ECAP-controlled CL-SCS therapy (Evoke® SmartSCS™, Saluda-Medical, Australia).

Results: Results: A total of 37 patients were included in this interim retrospective analysis. Most frequent pain aetiologies were PSPS-type-2 of the neck (n=9) and CRPS-type1/2 (n=13). Ten patient suffered from pain in the lower and upper extremities,). Overall, the NRS score decreased from 8.4 (n=37, SEM±0.16) at baseline to 3.8 (n=6, SEM±1.05) after 12-months (Fig 1A). All patients were “satisfied” or “very satisfied” with the therapy after 12 month (Fig 1B)). Most patients are aware of the stimulation (Fig 1C-D).

Discussion: Discussion: ECAP-controlled CL-SCS in patients with cervically placed leads resulted in a high degree of pain relief in patients suffering from chronic neck, upper limb and multifocal pain. At 12-months patients were satisfied with the therapy and most of the patients rated the stimulation as pleasant or were agnostic to it (neither pleasant nor unpleasant).

Conclusions: Conclusion: Preliminary real-world experience suggests that cervical ECAP-controlled CL-SCS therapy reduces pain in patients with neck, upper limb, and multifocal pain. The ability to maintain consistent and accurate neural activation using the real-time, closed-loop technology may especially be beneficial for patients requiring cervical lead placements as the region is highly mobile and is prone to suboptimal stimulation while using conventional open-loop SCS.

Supplemental Data:

References: References: Provenzano DA, Amirdelfan K, Kapural L, Sitzman BT. Evidence gaps in the use of spinal cord stimulation for treating chronic spine conditions. Spine. 2017;42(Suppl 14):S80–S92. Brooker C, Russo M, Cousins MJ, Taylor N, Holford L, Martin R, et al. ECAP-Controlled Closed-Loop Spinal Cord Stimulation Efficacy and Opioid Reduction Over 24-Months: Final Results of the Prospective, Multicenter, Open-Label Avalon Study. Pain Pract. 2021 May 2;papr.13008.

Acknowledgements:

Learning Objectives: Learning objectives: To demonstrate the effectiveness of ECAP controlled closed-loop SCS therapy with cervical lead placements To evaluate how patients feel stimulation (awareness and quality) To investigate if multiple pain areas can be stimulated with a cervical lead

Financial Disclosures: no significant relationships

Disclosure: No significant relationships.

270

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

NON-PAIN OUTCOMES AND THEIR RELATIONSHIP WITH PAIN RELIEF IN NONSURGICAL BACK PAIN PATIENTS TREATED WITH 10KHZ SPINAL CORD STIMULATION

Leonardo Kapural, MD[1], Jessica Jameson, MD[2], Naresh Patel, MD[3], Curtis Johnson, MD[4], Daniel Kloster, MD[5], Aaron Calodney, MD[6], Peter Kosek, MD[7], Julie Pilitsis, MD, PhD[8], Markus Bendel, MD[9], Erika Petersen, MD[10], Chengyuan Wu, MD, MSBmE[11], Taissa Cherry, MD[12], Nandan Lad, MD, PhD[13], Cong Yu, MD[14], Dawood Sayed, MD[15], Frances Rubenstein, PhD[16], Rose Azalde, MSBmE[16], David Caraway, MD[16]
[1]Carolinas Pain Institute, Winston-Salem, United States of America, [2]Axis Spine Center, Pain Management, Coeur d'Alene, United States of America, [3]Mayo Clinic, Neurosurgery, Phoenix, United States of America, [4]Midwest Pain Management Center, Overland Park, United States of America, [5]Crimson Pain Management, Overland Park, United States of America, [6]Precision Spine Care, Pain Management, Tyler, United States of America, [7]Oregon Neurosurgery Specialists, Springfield, United States of America, [8]Florida Atlantic University School of Medicine, Neurosurgery, Boca Raton, United States of America, [9]Mayo Clinic Rochester, Rochester, United States of America, [10]University of Arkansas for Medical Sciences, Department Of Neurosurgery, Little Rock, United States of America, [11]Thomas Jefferson University Hospitals, Philadelphia, United States of America, [12]Kaiser Permanente, Redwood City, United States of America, [13]Duke University, Pain Management, Durham, United States of America, [14]Swedish Pain and Heachache Center, Pain Management, Seattle, United States of America, [15]University of Kansas Medical Center, Pain Management, Kansas City, United States of America, [16]Nevro Corp., Clinical Research, Redwood City, United States of America

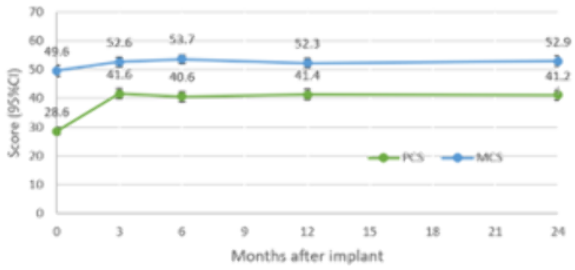
Introduction: Chronic refractory back pain has been shown to negatively impact quality-of-life and predict worse mental health.[1,2] The value of collecting non-pain outcomes, such as quality-of-life and mental health, to create a more holistic or multidimensional picture of patient response is being recognized in the spinal cord stimulation (SCS) field.[3,4,5] This analysis evaluates the durability of non-pain outcomes and their relationship with pain relief in patients with nonsurgical refractory back pain (NSRBP) from a randomized controlled trial evaluating treatment with 10kHz SCS (NSRBP-RCT).[6]

Materials / Methods: The NRSBP-RCT enrolled 159 patients who were randomized 1:1 to either conventional medical management (CMM) or high-frequency SCS (10kHz SCS) in addition to CMM. This analysis was done using the population of all patients who received a permanent implant (n = 125), with last observation carried forward (LOCF) imputation for missing values. Reported pain on the visual analog scale (VAS) and non-pain patient reported outcomes were collected at baseline, 3, 6, 12, and 24 months (M).[7] Multidimensional response to 10kHz SCS was quantified using minimum clinically important difference (MCID) for pain relief, Oswestry Disability Index (ODI), EQ5D5L, Pain Sleep Questionnaire (PSQ-3), patient health questionnaire 9-item [PHQ-9], and Patient Global Impression of Change (PGIC). Analysis of variance (ANOVA) was performed to examine the relationship between the number of MCID met for the five non-pain outcomes and pain relief.

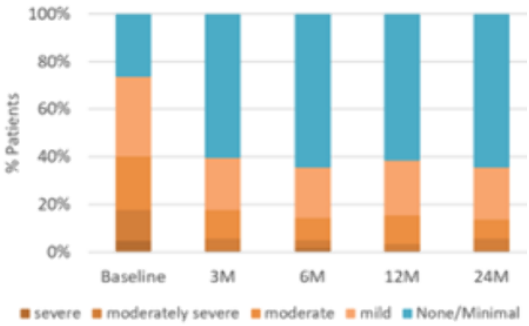
Results: Increases in quality of life and mental health were evident 3 months after implant and maintained through 24 months (mean increase, EQ5D5L: 0.19; SF-12 physical component score: 12.6; mean decrease, PHQ-9 score: 4.7, PSQ-3 score: 4.5, $p < 0.001$, Figure 1). Twenty-four months after implant, 93.6% of patients met MCID criteria for ≥1 of the five non-pain outcomes evaluated. The percent of patients achieving MCID for each individual measure was 74 to 79% (Figure 2). The 85.6% of patients meeting MCID for ≥2 non-pain outcomes had higher mean pain relief (ANOVA, Tukey comparison, $P < .001$, Figure 3).

Figure 1. Quality of life, mental health and Sleep outcomes through 24 months with 10 kHz SCS therapy.

A. SF-12



B. Depression based on PHQ9



C. Sleep Interference Due to Pain (PSQ-3)

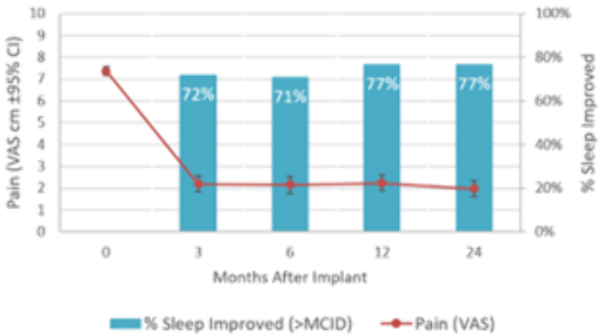


Figure 2. The percentage of patients in the PI group who met the MCID for each of the five non-pain assessments.

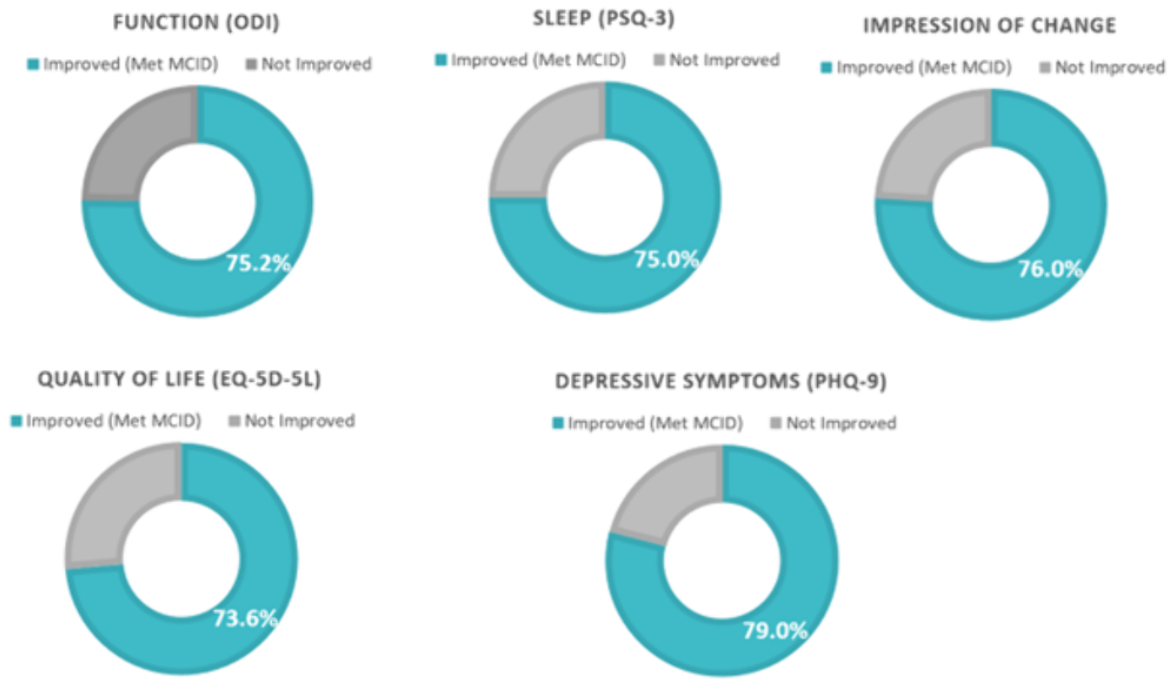
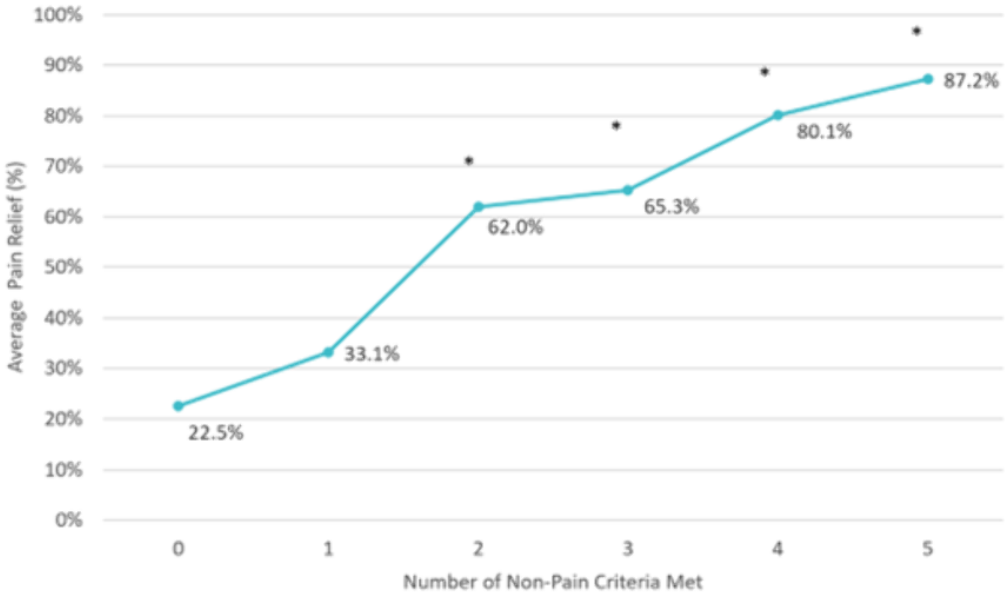


Figure 3. Pain relief at 24 months after 10 kHz Spinal cord stimulation implant in relationship to the number of non-pain outcomes meeting criteria for a minimal clinically important difference that the patient achieved (R^2 = 51%, p <0.001). * Indicates significantly higher pain relief compared to groups who met 0 or 1 non-pain criteria (one-way ANOVA, Tukey pairwise comparison, p <0.05).



Discussion: Pain relief correlates with the number of clinically important non-pain responses, but even patients with low pain relief met at least one non-pain criteria, supporting that outcome measures should not be limited to pain.

Conclusions: Among patient with NSRBP, non-pain benefits of 10 kHz SCS therapy are durable through 24 months. The multi-dimensional effect of 10 kHz SCS therapy is highlighted by the high percentage of patient who achieved MCIDs for function, mental health, sleep, quality of life and impression of change.

Supplemental Data:

References: 1) Tagliaferri SD, Miller CT, Owen PJ, et al. Domains of Chronic Low Back Pain and Assessing Treatment Effectiveness: A Clinical Perspective. *Pain Pract*. Feb 2020;20(2):211-225. 2) Loyland B, Miaskowski C, Paul SM, Dahl E, Rustoen T. The relationship between chronic pain and health-related quality of life in long-term social assistance recipients in Norway. *Qual Life Res*. Dec 2010;19(10):1457-65. doi:10.1007/s11136-010-9707-4 3) Kapural L, Mekhail NA, Costandi S, et al. Durable multimodal and holistic response for physiologic closed-loop spinal cord stimulation supported by objective evidence from the EVOKE double-blind randomized controlled trial. *Reg Anesth Pain Med*. Jul 25 2023 4) Levy RM, Mekhail N, Abd-Elsayed A, et al. Holistic Treatment Response: An International Expert Panel Definition and Criteria for a New Paradigm in the Assessment of Clinical Outcomes of Spinal Cord Stimulation. *Neuromodulation*. Jul 2023;26(5):1015-1022. 5) Goudman L, Pilitsis JG, Russo M, et al. From pain intensity to a holistic composite measure for spinal cord stimulation outcomes. *Br J Anaesth*. Aug 2023;131(2):e43-e48. 6) Kapural L, Jameson J, Johnson C, et al. Treatment of nonsurgical refractory back pain with high-frequency spinal cord stimulation at 10 kHz: 12-month results of a pragmatic, multicenter, randomized controlled trial. *J Neurosurg Spine*. Feb 11 2022:1-12. 7) Patel N, Calodney A, Kapural L, et al. High-Frequency Spinal Cord Stimulation at 10 kHz for the Treatment of Nonsurgical Refractory Back Pain: Design of a Pragmatic, Multicenter, Randomized Controlled Trial. *Pain Pract*. Feb 2021;21(2):171-183

Acknowledgements: We are grateful to the investigating sites and research staff for your work in acquiring this study data.

Learning Objectives: 1) How is nonsurgical refractory back pain defined? 2) What is the durability of the pain and non-pain outcomes for patients with nonsurgical refractory back pain treated with 10kHz SCS? 3) Does the number of non-pain outcomes where minimum clinically important difference was achieved correlate with reported pain relief?

Financial Disclosures: This study was funded by Nevro Corp. Dr. Kapural reported being on the advisory board for Avanos, Gimer, Neuralace, Neuros, Nevro, Painteq, and Presidio; research support from Avanos and Saluda; and speakers bureau for Avanos, Nevro, Saluda, and Nalu outside the submitted work. Dr. Jameson reported being a consultant for Nevro, Abbott, and Boston Scientific; and research support from Nevro, Abbott, Boston Scientific, and SPR outside the submitted work. Dr. Calodney reported personal fees from Medtronic, Nevro, Stryker, PainTeq, Saluda, and Boston Scientific outside the submitted work. Dr. Pilitsis reported fellowship grants from Medtronic, Boston Scientific, and Abbott; and grants from NIH (grant nos. 2R01CA166379, R01EB030324, and U44NS115111) and NIH Blueprint (grant no. 3U54EB015408) outside the submitted work; and medical advisor for and stock equity in Aim Medical Robotics. Dr. Petersen reported personal fees from Nevro, Saluda Medical, Presidio Medical, Biotronik, and Medtronic; grants from Nevro and Saluda Medical, and board of directors for and stock options in SynerFuse during the conduct of the study; personal fees from Nalu and grants from Mainstay Medical, Nalu, Neuros Medical, and SPR outside the submitted work; research support from Mainstay, Medtronic, Nalu, Neuros Medical, Nevro Corp, ReNeuron, SPR, and Saluda, personal fees from Abbott Neuromodulation, Biotronik, Medtronic Neuromodulation, Nalu, Neuros Medical, Nevro, Presidio Medical, Saluda, and Vertos; and stock options in neuro42. Dr. Wu reported personal fees from Nevro, Boston Scientific, Abbott, NeuroOne, NeuroPace, and Medtronic outside the submitted work. Dr. Lad reported grants from Nevro during the conduct of the study. Dr. Yu reported grants from Nevro during the conduct of the study and being a consultant for Nevro outside the submitted work. Dr. Sayed reported funded research from Nevro during the conduct of the study; personal fees from Saluda and Abbott; and stock options in Mainstay and PainTeq outside the submitted work. Ms. Azalde reported being an employee of Nevro Corp. during the conduct of the study. Dr. Caraway reported being an employee of Nevro during the conduct of the study.Dr. Patel reported grants from Mayo Clinic during the conduct of the study.

Disclosure: Rose Azalde is an employee of Nevro Corp.

271

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

OBJECTIVE NEUROPHYSIOLOGY USING A PRECISION, DOSE-CONTROL CLOSED-LOOP SCS ENABLES TRANSLATION OF CLINICAL EFFECTS FROM TRIAL TO PERMANENT IMPLANT

Leonardo Kapural, MD[1], Robert Levy, PhD[2], Jason Pope, MD[3], Shrif Costandi, MD[4], Peter Staats, MD[5], Sam Eldabe, FRCA[6]
[1]Carolinas Pain Institute and Wake Forest University School of Medicine, Winston-Salem, United States of America, [2]Anesthesia Pain Care Consultants, Tamarac, United States of America, [3]Evolve Restorative Center, Santa Rosa, United States of America, [4]Cleveland Clinic, Cleveland, United States of America, [5]National Spine & Pain Centers, Shrewsbury, United States of America, [6]James Cook University Hospital, Middlesbrough, United Kingdom

Introduction: Neural dose optimization has been an elusive concept in spinal cord stimulation (SCS) due to the inability to measure spinal cord activation. A novel physiologic closed-loop (CL) SCS system measures spinal cord activation via evoked-compound action potentials (ECAPs) and delivers CL therapy to maintain accurate and consistent neural activation with every stimulus. It is, therefore, now possible to use physiologic data from the spinal cord to optimize SCS therapy. This study evaluates the clinical utility of neurophysiologic data during the SCS trial phase to inform reproducibility of clinical effect following SCS implant.

Materials / Methods: Participants in the EVOKE RCT randomized to CL-SCS were included (n=54).[1] The percent reduction in pain intensity (VAS) obtained with CL-SCS during the trial phase and post-implant (maximum percent pain reduction visit within the first 3-months) were measured alongside the neurophysiologic data that produced that effect. The neural panel metrics that produced the clinical effect were analyzed.

Results: There were no differences between the percent pain reduction observed at trial phase (82% [SD=12]) and at implant visit (82%, [SD=17] p=0.611). CL-SCS therapy accuracy was optimized at 2.1μV (IQR=1.5-3.0) during trial and 2.4μV (1.8-4.6) at post-implant visit (p=0.334). Patients used the system ≥81% of the time (trial=81% [IQR=63-93], post-implant=92% [IQR=73-98], p=0.005). There were no differences in time the stimulation was above ECAP threshold (trial=100% [IQR=97-100], post-implant=100% [IQR=96-100], p=0.314), ECAP dose (trial=35.1μV [IQR=21.0-71.2], post-implant=40.4μV [IQR=18.8-83.4], p=0.889) and dose-ratio; trial=1.4 [IQR=1.3-1.6], post-implant=1.5 [IQR=1.3-1.6],

p=0.572).

EVOKE CL Study: Trial vs. Implant MAE & Objective Measurements	EVOKE **Trial phase**	EVOKE **MAE Implant Visit**	p-value (difference between trial and implant) (n=54)
Percent change from baseline in VAS back and/or leg pain intensity (mean (SD))	82.2% (11.8)	82.4% (17.4)	P=0.611
Frequency (of use)			
System Utilization – percent time (median [IQR])	81% [63-93%]	92% [73-98%]	P=0.005
Physiologic Dose Metrics			
Percent Time Above ECAP Threshold (out of total stimulating time) (median [IQR])	100% [97-100%]	100% [96-100%]	P=0.314
ECAP Dose (normalized median ECAP amplitude, µV) (median [IQR])	35.1 [21.0-71.2]	40.4 [18.8-83.4]	P=0.889
Dose Ratio (estimated current at median ECAP/ECAP threshold current) (median [IQR])	1.4 [1.3-1.6]	1.5 [1.3-1.6]	P=0.572
Loop Performance			
Dose Accuracy (in-clinic deviation from ECAP target, RMSE (µV))	2.1 [1.5-3.0]	2.4 [1.8-4.6]	P=0.334

Discussion: The clinical utility of SCS trial phase has been questioned,[2,3] but the advent of technology that confirms intended target and measures therapy delivery may improve its diagnostic value of long-term response. Reproducibility of profound clinical benefit observed in the trial phase was reproduced in the implant phase when the same neural activation was utilized. Additionally, we observed that of the subjects that completed the 36-month follow-up, 84% continued to be ≥50% pain reduction responders.

Conclusions: ECAP-controlled CL-SCS provides a biomarker of therapy delivery and adherence. The reproducible results of the trial phase observed post-implant suggest the potential to maximize the utility of the trial phase with objective measurements, develop neural dosing guidelines to optimize clinical benefit, and monitor adherence for long-term durability.

Supplemental Data:

References: 1. Mekhail N, et al. Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial. Lancet Neurol 2020; 19: 123-134. 2. Eldabe S, et al. Does a screening trial for spinal cord stimulation in patients with chronic pain of neuropathic origin have clinical utility and cost-effectiveness (TRIAL-STIM)? A randomised controlled trial. Pain 2020; 161: 2820-2829. 3. Eldabe S, et al. Does a screening trial for spinal cord stimulation in patients with chronic pain of neuropathic origin have clinical utility (TRIAL-STIM)? 36-month results from a randomized controlled trial. Neurosurgery 2023; 92: 75-82.

Acknowledgements: Submitted on behalf of the EVOKE investigators. Trial sponsored by Saluda Medical.

Learning Objectives: 1. Clinical benefits and neural activation observed during the trial phase are reproducible following SCS implant 2. ECAP-controlled closed-loop SCS enables evaluation of spinal cord physiologic data and development of neural dosing guidelines to optimize SCS therapy 3.

Objective neural panel data consisting of physiologic metrics has the potential to maximize clinical benefit for patients and better inform SCS programming and prescribing guidelines using objective physiologic measurements

Financial Disclosures: Leonardo Kapural, Saluda Medical, Consultant/Advisory Board, $500-$5000 USD; Education/Research, $500-$5000 Robert Levy, Saluda Medical, Stock Options Jason Pope, Saluda Medical, Consultant/Advisory Board, >$100,000 USD Shrif Costandi's institute, Cleveland Clinic, has received research funding from Saluda Medical Peter Staats, Saluda Medical, Consultant/Advisory Board, $5,001-$20,000 USD, Education/Research, $20,001-$100,000, Stock Options, $20,001-$100,000 Sam Eldabe has no relevant conflicts of interest to disclose

Disclosure: Administrative support to authors funded by Saluda Medical.

272

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

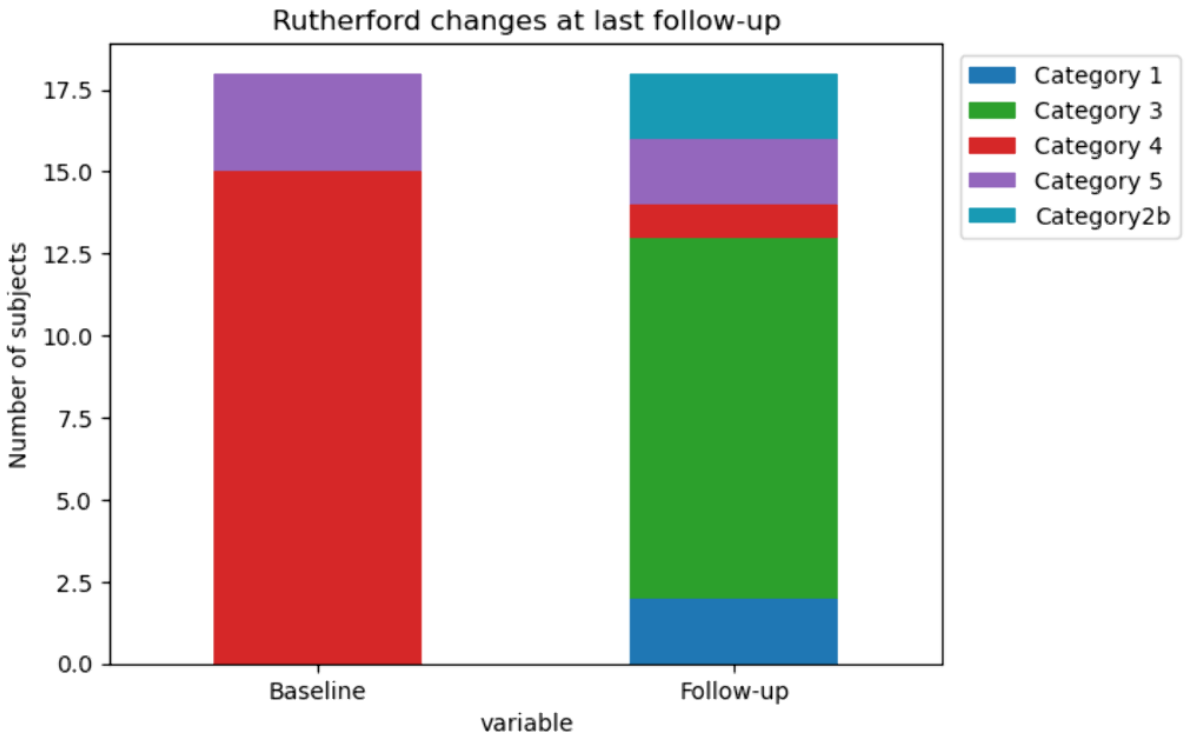
PAIN RELIEF AND CHANGES IN DISEASE STATE FOLLOWING SPINAL CORD STIMULATION FOR TREATMENT OF CHRONIC LIMB THREATENING ISCHEMIA

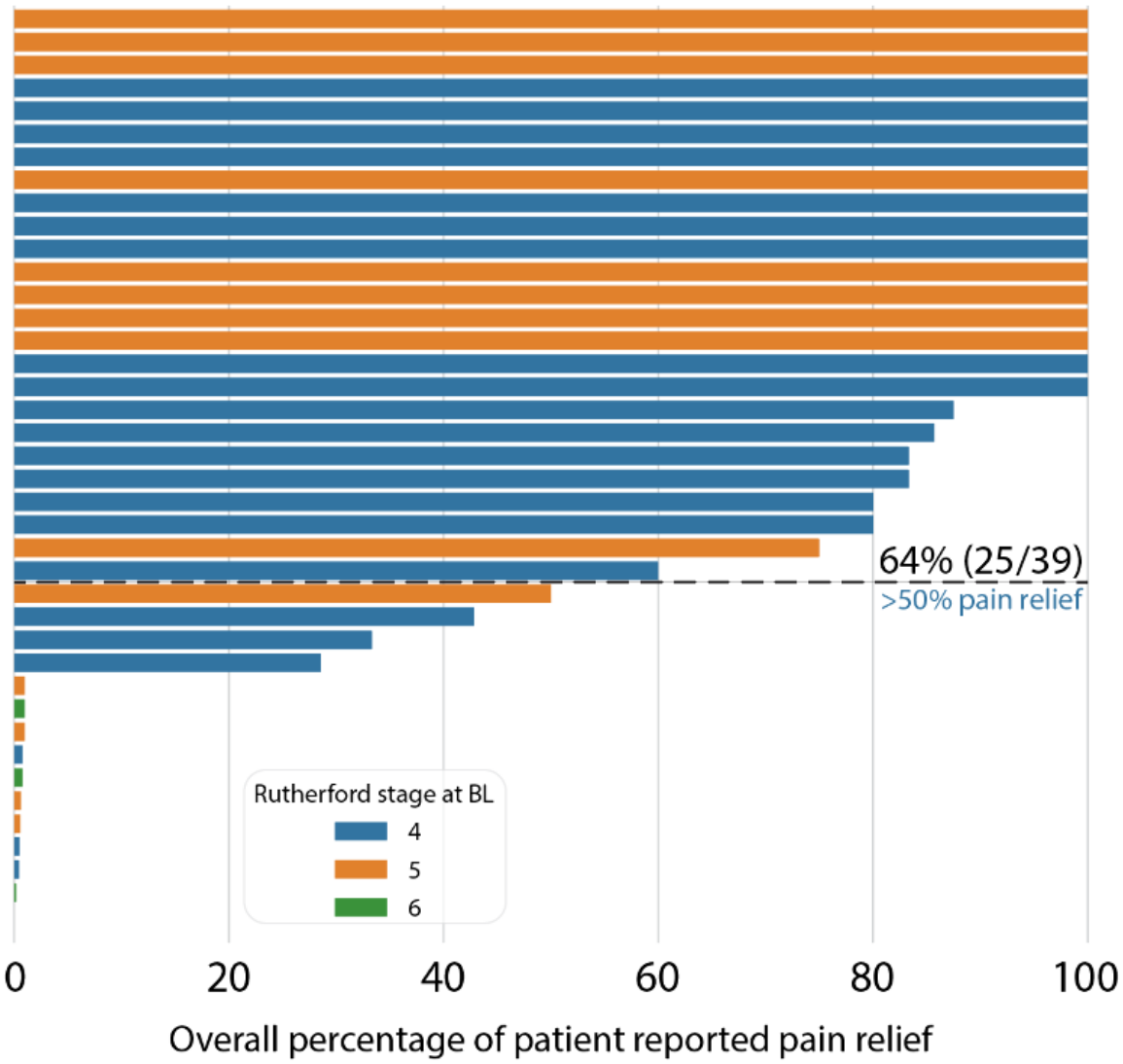
Michael Kretzschmar, PhD[1], Matthias Tenholt, MD[2], Udoka Okaro, PhD[3], Ameya Nanivadekar, PhD[4]
[1]SRH Wald-Klinikum Gera, Pain Service And Palliative Care, Gera, Germany, [2]Vascular Centre at Theresien Hospital, Mannheim, Germany, [3]St Jude Medical, Neuromodulation, Austin, United States of America, [4]6901 Preston Rd, Plano, United States of America

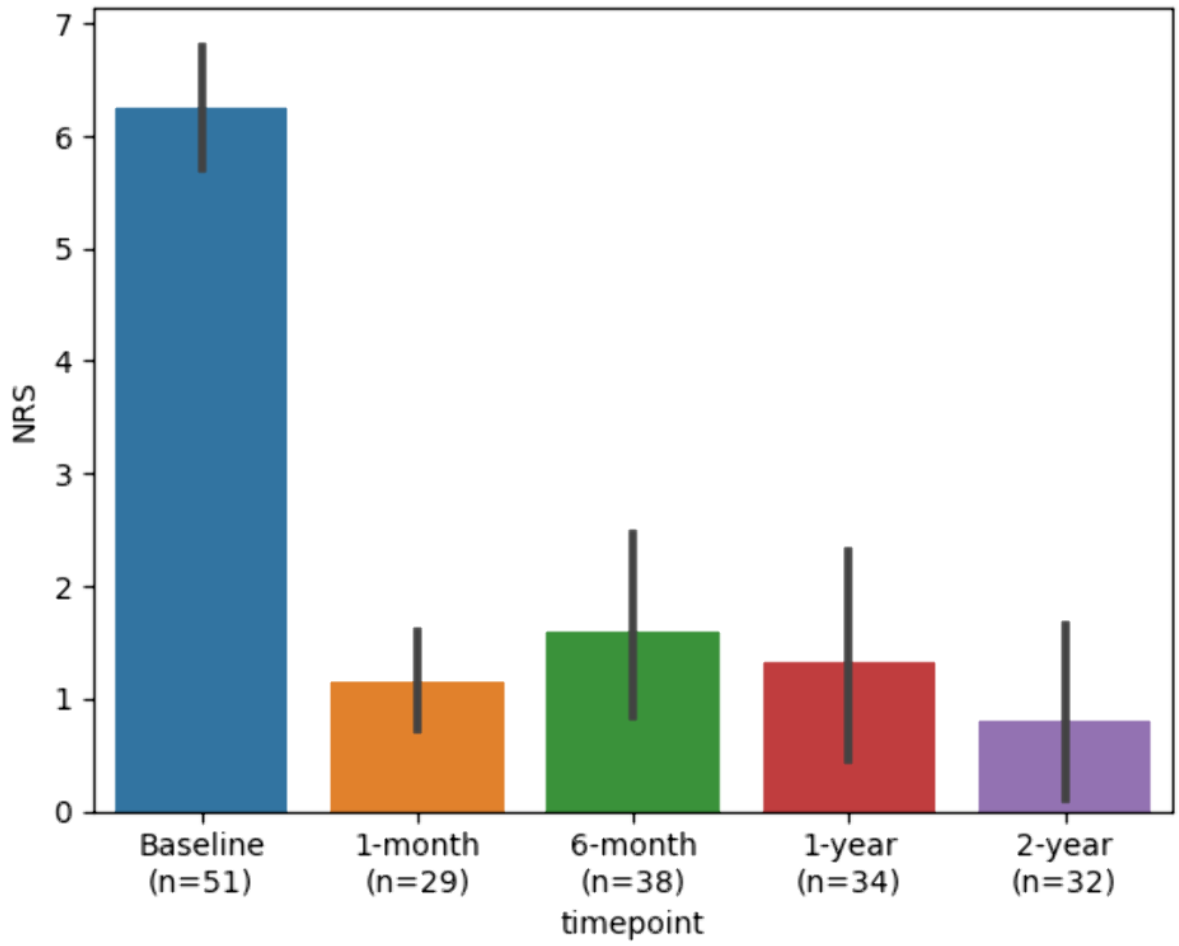
Introduction: Introduction: Spinal cord stimulation (SCS) is a neuromodulation therapy representing an alternative treatment for patients with chronic limb threatening ischemia (CLTI) who are unsuitable for vascular reconstruction procedures. Several studies have shown that SCS is both safe and effective in this patient population. However, long-term evidence of effectiveness is lacking. The objective of this retrospective audit was to examine the long-term outcomes (up to two years) of 51 patients who received spinal cord stimulation for CLTI.

Materials / Methods: Methods: We performed a retrospective audit of 51 patients across 3 clinical sites in Germany. Patients that received SCS for treatment of CLTI and were categorized as stage 4 to 6 on the Rutherford scale were included in this analysis. For patients where disease state was recorded at follow-up visits, the proportion of patients in each Rutherford category was compared between baseline and the last follow-up visit. Additionally, the proportion of patients that reported a clinically significant decrease in their NRS score following SCS was calculated. The responder rate for SCS was defined as the number of patients that reported a >50% change in their NRS scores.

Results: Results: For 18 patients, the Rutherford category was recorded at the last follow-up visit. 15 patients were Rutherford category 4 at baseline. At the last follow-up 11 of these patients were recorded as Rutherford category 3. The proportion of patients within each category is shown in Figure 1. Across all patients, the baseline NRS score was 6.25 ± 1.9 and the NRS score at 1-year follow up was 1.32 ± 2.5. 39 patients reported a reduction in their pain at the last follow-up visit and 71% of these patients showed a minimum clinical important difference of 30% in their reported pain intensity from baseline. 17 patients reported a 100% pain relief at the last follow-up. The responder rate for SCS was 64% across these patients (Figure 2). The mean NRS scores recorded at 1-month, 6-month, 1-year and 2-year post SCS implant are shown in Figure
3.


Rutherford changes at last follow-up
Number of subjects
17.5
15.0
12.5
10.0
7.5
5.0
2.5
0.0
Baseline
Follow-up
variable
Category 1
Category 3
Category 4
Category 5
Category2b


64% (25/39)
>50% pain relief
Rutherford stage at BL
4
5
6
0
20
40
60
80
100
Overall percentage of patient reported pain relief



Discussion: CLTI is associated with significantly increased cardiovascular morbidity and comorbidities such as diabetes which reduce limb salvage and survival rates. In this retrospective analysis we report significant improvements in NRS pain scores as well as disease state up to 2 years after SCS is introduced in a majority of patients who are not candidates for revascularization.

Conclusions: We demonstrate that SCS offers an alternative effective treatment option for CLTI patients considered not candidates for revascularization

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: Safety and efficacy of SCS for treatment of CLTI

Financial Disclosures: Michael Kretzschmar was involved in studies organized by Abbott Neuromodulation Udoka Okaro and Ameya Nanivadekar are employees of Abbott Neuromodulation Matthias Tennholt was involved in studies supported by Abbott Neuromodulation

Disclosure: No significant relationships.

273

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

FEASIBILITY OF IMPLANTATION OF EPIDURAL THIN-FILM PADDLE LEADS – AN IN VIVO ANIMAL AND EX VIVO HUMAN CADAVERIC STUDY

Aura Kullmann, PhD[1], Maria Porto Cruz, PhD[1], Marcus Szamlewski, BSc (Hons)[2], Bill Norman, BSc (Hons)[2], Ryan Opansky, BSc (Hons)[2], Masoud Samet, PhD[2], Alec Kelly, BSc (Hons)[2], Fernando Di Caprio, MSc[2], Samuel Ong, BSc (Hons)[1], Mary McNeil, MSc[1], Alfonso Chavez, BSc (Hons)[1], Camilo Diaz-Botia, PhD[1], Maria Vomero, PhD[1]
[1]NEUROONE, Eden Prairie, United States of America, [2]QX Medical, Roseville, United States of America

Introduction: Silicone based epidural paddle and percutaneous leads for spinal cord stimulation (SCS) have been used for decades for pain relief in patients suffering from chronic lower back pain. Traditional silicone leads are thick (>1.5 mm) and bulky, and consequently they occupy a large portion of the epidural space, pressing against the spinal cord. Recent advances in thin-film technology have shown that these leads are suitable for spinal cord stimulation, but the main challenge remains the difficulty of implantation. With the current techniques, thin-film leads cannot be implanted percutaneously nor pushed through a laminectomy to the target location like their silicone-based counterparts because they buckle and fail to advance in the epidural space. This study evaluated the feasibility of implanting thin-film paddle leads in the epidural space of sheep and human cadaver, using custom made implantation tools and techniques.

Materials / Methods: Different sizes and shapes of thin-film paddle leads (4-9 mm wide, 40-60 mm long, 50 µm thick) were tested. In the sheep, leads were inserted using customized tools through a small laminectomy, with the animal under anesthesia. In the human cadaver, leads were implanted percutaneously using a traditional 14G needle and custom-made tools. Correct positioning was verified using radiopaque markers under fluoroscopy. User feedback was obtained using a questionnaire.

Results: In the sheep, all devices were easily implanted and advanced to the target location. The leads fit comfortably in the epidural space. In the human cadaver, 4 mm leads were successfully placed percutaneously through a 14G needle. The 9 mm paddles were inserted percutaneously using an introducer sheath and advanced to the targeted position. The paddles unfolded well during deployment. User feedback indicated that the tools and techniques were feasible and would not introduce significant time delays in the procedure.

Discussion: Although optimization is still required, these first trials indicate that the methods under development are promising alternatives to the current ones. Given that the existing paddle leads are currently implanted only using a laminectomy, the development of new methods that allow percutaneous implantation of wide (4-9mm) paddle leads represents a significant advancement in the field. This could greatly benefit the patients by eliminating the need for an invasive surgical procedure while still offering large spinal cord coverage for custom stimulation.

Conclusions: These data support the conclusion that novel thin-film paddle leads can be successfully implanted either though a laminectomy or percutaneously into the epidural space.

Supplemental Data:

References:

Acknowledgements: The authors thank Drs. Anthony Berg, MD, Dan Kloster, MD and David Darrow, MD for their participation in the cadaver study.

Learning Objectives: Thin-film paddle leads are appropriate for spinal cord stimulation. New methods, tools and techniques are being developed to allow percutaneous implantation of thin-film paddle in the epidural space. Thin-film leads have a very small footprint in the epidural space.

Financial Disclosures: This study was funded by NeuroOne Medical Technologies Corporation. The authors: Maria Francisca Porto Cruz, Mary McNeil, Samuel Ong, Alfonso Chavez, Aura Kullmann, Camilo Diaz-Botia, Maria Vomero are employees of NeuroOne Medical Technologies Corporation. The level of compensation is $20,001 - $100,000 USD The authors Marcus Szamlewski, Bill Norman, Ryan Opansky, Masoud Samet, Alec Kelly, Fernando Di Caprio are employees of QX Medical, a company collaboration with NeuroOne Medical Technologies Corporation. The level of compensation is $20,001 - $100,000 USD

Disclosure: No significant relationships.

274

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

INTERLAMINAR ENDOSCOPIC UNIPORTAL APPROACH FOR PADDLE LEAD OVER 10MM IMPLANTATION FOR SPINAL CORD STIMULATION

Gustavo Lages, MD[1], José Oswaldo Oliveira Júnior, PhD[2], Ramon Barbosa, MD[1], Natally Santiago, MD[3], Thiago Afonso, MD[4], Leandro Batista, MD[4], Maria Fernanda Toledo, BChir[5], Camille Silva, BChir[5]
[1]Medular Clinic, Montes Claros, Brazil, [2]IAMSPE, São Paulo, Brazil, [3]Beneficiência Portuguesa Hospital, São Paulo, Brazil, [4]Santa Casa, Montes Claros, Brazil, [5]Unifipmoc-AFYA, Montes Claros, Brazil

Introduction: A new work endoscopic cannula was developed for the passage ofto pass a paddle lead width between 10 and 13mm. The distal portion of the cannula was designed with a larger opening, providing better visibility of the anterior portion of the adjacent structures, thus allowing a panoramic view of the electrode passage. An electrode was implanted in an 11mm.

Materials / Methods: After searching the PubMed, Cochrane and Lillacs virtual portals, no mention was made of the implantation of, and Lillacs virtual portals, I found no mention of implanting an electrode in a paddle with a width greater than 10 mm.

Results: It is observed that it is possible to pass electrodes safely and effectively with a paddle width between 10 and 13mm via spinal endoscopy via uniportal interlaminar access. However, it is necessary to expand studies to elucidate this technique of endoscopic implantation of electrodes for neurostimulation.

Discussion: The endoscopic technique for plate electrode implantation in the spinal cord transforms the classic method by microlaminectomy into a less invasive one, which provides minimal tissue damage, insignificant bleeding, lower rate of infection and other complications. In addition, there is less pain, and thus, the use of pain medication is reduced in the postoperative period. The eletrocde Penta has 11mm plate width, 60 cm length, 20 poles, 9mm matrix width, and 25mm plate length. Thus, its passage through the endoscopic work portal is impossible. Thus, a method of passing the electrode in a plate greater than 10mm via endoscopic approach was made possible by creating a single working portal, with direct visualization of the free dural sac and adjacent structures. This allows the placement of the electrode without any spinal cord compression, safe access through the interlaminar window, and without electrode fracture. Thus, we describe, for the first time, the step-by-step insertion of the electrode in an 11mm by endoscopy, safely and effectively.

Conclusions: It is essential to know that you can safely and effectively pass electrodes with a plate width greater than 10 mm by endoscopy. In this report, we show that creating a working cannula with a larger internal diameter can be achieved via an uniportal interlaminar. However, it is necessary to expand studies to elucidate whether this technique is superior to traditional techniques.

References: 1. SHAMJI, Mohammed F.; DE VOS, Cecile; SHARAN, Ashwini. The advancing role of neuromodulation for the management of chronic treatment-refractory pain. Neurosurgery, v. 80, n. 3S, p. S108-S113, 2017.
2. Wolter T, Kieselbach K. Cervical spinal cord stimulation: an analysis of 23 patients with long-term follow-up. Pain Physician. 2012 May-Jun;15(3):203-12.
3. Jeon, Younghoon, and Billy K. Huh. "Spinal cord stimulation for chronic pain." Annals Academy of Medicine Singapore 38.11 (2009): 998.
4. Simpson K., and Rphael J. Spinal cord stimulation for the management of pain: recommendations for best clinical practice. The British Pain Society, 2009.
5. Kim, D. H., Choi, G., Lee, S. H., & Fessler, R. G. Endoscopic Spine Surgery. (2nd edition). São Paulo. Thieme Revinter Brazil, 2019

6. Benyamin, KY Dr. "Spinal cord stimulation for patients with failed back surgery syndrome: a systematic review." Pain physician 12 (2009): 379-397.
7. Martins, Marielza R. Ismael, et al. Spinal epidural electric stimulation in the treatment of poorresponse pain patients and improvement in quality of life. Brazilian Journal of Neurosurgery 21.4 (2010): 225- 229.

Acknowledgements:

Learning Objectives: Present a new working cannula for electrode implantation
Present surgical technique for electrodes greater than 10mm
Assess the risks and benefits of the technique

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

275

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

IS THERE A BETTER PLATE ELECTRODE FOR IMPLANTATION BY ENDOSCOPY?

Gustavo Lages, MD[1], Ramon Barbosa, MD[1], José Oswaldo Oliveira Júnior, PhD[2], Maria Toledo, BChir[3], Leandro Batista, MD[4]
[1]Medular Clinic, Montes Claros, Brazil, [2]IAMSPE, São Paulo, Brazil, [3]Unifipmoc-AFYA, Montes Claros, Brazil, [4]Santa Casa, Montes Claros, Brazil

Introduction: Endoscopy has been used for various spine problems, such as lumbar, thoracic, and cervical disc herniations, as well as lumbar stenosis. Since it has many advantages over open surgery, endoscopy has been taking space for more invasive techniques, making it, in many cases, the golden standard method.Up to now, five cases of plate electrodes placed by endoscopy have been performed with different companies and types of electrodes. In all procedures, we had a direct view of the free dural sac and clear access through the interlaminar window. The electrode placement was inserted nicely and smoothly as well. Therefore, we describe the step-by-step insertion of paddle electrodes by full monoportal endoscopy.

Materials / Methods: This is a retrospective and comparative analysis of two cases with electrode Specify Medtronic, one case with electrode Specify 5x6x5 Medtronic, one Abbot Tripole, and one Abbot penta. The objective of the study was to elucidate the positive and negative points of each electrode.

Results: There were observed that the Specify Medtronic electrode has favorable dimensions, malleability, shape, and volume for endoscopic implantation. Abbot's penta electrode was challenging to insert, even with developing a working cannula suitable for its dimensions, implying that its format seems unfavorable to the method. The Medtronic Specify 5x6x5 electrode, despite its favorable shape, its characteristics of thickness, malleability, and width, made it difficult to progress through the endoscopic working cannula and position it in the epidural space.

Discussion: The endoscopic technique for implanting plate electrodes is less invasive one, which provides minimal tissue damage, negligible bleeding, lower infection rate, and other complications. However, there aren't, yet, plate electrodes developed for this technique, as well as compatible instruments explicitly. In this study, no electrodes were implanted of other companies. Therefore, it is impossible to determine whether there is one more suitable to implant.

Conclusions: The best characteristics that will assist the implantation of the electrodes by endoscopy are the shape, thickness, and malleability. Its characteristics deserve a more in-depth analysis of the development of a specific electrode for endoscopic implantation. However, new Comparative studies must be carried out to determine which electrode is best for the technique and, mainly, new products must be produce for this purpose.

References: 1. Muthu S, Ramakrishnan E, Chellamuthu G. Is Endoscopic Discectomy the Next Gold Standard in the Management of Lumbar Disc Disease? Systematic Review and Superiority Analysis. Global Spine Journal. 2021;11(7):1104-1120.
2. North, Richard B. MD*; Kidd, David H. MA*; Olin, John PA*; Sieracki, Jeffrey M. MS*; Farrokhi, Farrokh MD*; Petrucci, Loredana MS*; Cutchis, Protagoras N. MD†. Spinal Cord Stimulation for Axial Low Back Pain: A Prospective, Controlled Trial Comparing Dual With Single Percutaneous Electrodes. Spine: June 15, 2005 - Volume 30 - Issue 12 - p 1412-1418.
3.Thissen J, Bara GA. Placement of Surgical Spinal Cord Stimulation Leads Using Spinal Process Splitting Laminotomy: Technical Note. World Neurosurg. 2021; 155:109-114.
4.. Shamji MF, Paul D, Mednikov A. Minimally Invasive Placement of Spinal Cord Stimulator Paddle Electrodes Is Associated With Improved Perioperative and Long-Term Experience Among Neuropathic Pain Patients. Spine (Phila Pa 1976). 2018;43(5):324-330.

5. Kim, D. H., Choi, G., Lee, S. H., & Fessler, R. G. Endoscopic Spine Surgery. (2nd edition). Saõ Paulo. Thieme Revinter Brazil, 2019.

Learning Objectives: Compare the types of electrodes for implantation via endoscopy Discuss the advantages and disadvantages of spinal cord stimulation electrodes Evaluate the benefitis and risks of electrode implantation by endosocpy

Financial Disclosures: No significant relatioships

Disclosure: No significant relationships.

276

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

FAST-ACTING SUB-PERCEPTION THERAPY FOR THE TREATMENT OF CHRONIC PAIN: PRELIMINARY STUDY

Catarina Lins, MD[1], Laura Barros, MD[2], Andre Marcondes, MD[3], Pedro Martins, MEDICAL STUDENT[4]
[1]Pain Center, University of São Paulo School of Medicine, São Paulo – SP, SAO PAULO, Brazil, [2]Department of Pain, Hospital São Luiz de Osaco- SP, OSASCO, Brazil, [3]Department of Coluna, Sirio Libanês Hospital, SAO PAULO, Brazil, [4]Federal University of Juiz de Fora School of Medicine, JUIZ DE FORA, Brazil

Introduction: FAST is a new sub-perception-based SCS method developed that exploits the feeling of paresthesia as a marker for precise targeting of sub-perception stimulation with surround inhibition(2). This study aims to evaluate pain relief and quality of life among subjects with chronic pain symptoms who were implanted a SCS with the FAST-SCS approach.

Materials / Methods: Patients included in this prospective analysis were programmed using 90 Hz and 210 ± 50 µs. Two leads were placed in T8-T10 parallel . All patients used their external controller to adjust intensity values within a range of 30–70% of their perception threshold. The BPI, VAS and SF 12 scales were used.

Results: The average age of those assessed in this study was 48 years and 65% (13/20) were female, and 75%of patients were classified with Failed Back Surgery Syndrome.

Table 1. Visual Analogue Scale Decrease		
Moments	Decrease (95% CI)	P Value
Baseline - 10 minutes after	5.75 (5.41 - 6.09)	<0.001
Baseline - 3 months	7.55 (7.06 - 8.04)	<0.001
Baseline - 6 months	8.05 (7.49 - 8.61)	<0.001
10 minutes after - 3 months	1.80 (1.44 - 2.16)	<0.001
10 minutes after - 6 months	2.30 (1.82 - 2.78)	<0.001
3 months - 6 months	0.50 (0.14 - 0.86)	0.008

Table 2. BPI Decrease		
Variable	Decrease (95% CI)	P Value
BPI Severity	7.01 (6.36 - 7.67)	<0.001
BPI Interference	7.36 (6.67 - 8.05)	<0.001

Table 3. SF-12 Improvement		
Variable	Improvement (95% CI)	P Value
SF12 - PCS	19.47 (16.55 - 22.38)	<0.001
SF12 - MCS	29.49 (25.06 - 33.91)	<0.001

Discussion: The selectively stimulation of dorsal columns from the surround may overcome the excitatory effects of activating dorsal columns originating from the center—inhibition that would not be possible by stimulation of the center alone(6). A study in Germany showed an average pain score reduction of 6.9 points, and notable improvements in ODI and EQ-5D-5L were also observed at the 6-month follow-up(4). In our case series, after 3 months with FAST stimulation, there was an approximately 80% reduction in the VAS. We observed that our patients also showed a decrease in the values referred to in BPI scale after 6 months of stimulation.The SF12 scale showed a significant improvement in the quality of life of all patients.

Conclusions: The FAST therapy is a treatment that has proven to be effective in reducing pain, and it has shown promise in improving quality of life and reducing disability.

Supplemental Data:

References: 1. Melzack R, Wall PD. Pain mechanisms: A new theory. Pain Clin. 1994;7(1):57–72. 2. Paz-Solís J, Thomson S, Jain R, Chen L, Huertas I, Doan Q. Exploration of High- and Low-Frequency Options for Subperception Spinal Cord Stimulation Using Neural Dosing Parameter Relationships: The HALO Study. Neuromodulation. 2022;25(1):94–102. 3. North RB, Ewend MG, Lawton MT, Piantadosi S. Spinal cord stimulation for chronic, intractable pain: Superiority of “multi-channel” devices. Pain. 1991;44(2):119–30. 4. Matis G, Jain R, Wang J, Doan Q. Clinical Utilization of Fast-Acting Sub-Perception Therapy (FAST) in SCS-Implanted Patients for Treatment of Mixed Nociceptive and Neuropathic Pain. Neuromodulation Technol Neural Interface [Internet]. 2022;25(6):S5. Available from: https://doi.org/10.1016/j.inpm.2022.100165 5. Al-Kaisy A, Van Buyten JP, Smet I, Palmisani S, Pang D, Smith T. Sustained Effectiveness of 10kHz High-Frequency Spinal Cord Stimulation for Patients with Chronic, Low Back Pain: 24-Month Results of a Prospective Multicenter Study. Pain Med (United States). 2014;15(3):347–54. 6. Gilbert JE, Titus N, Zhang T, Esteller R, Grill WM. Surround Inhibition Mediates Pain Relief by Low Amplitude Spinal Cord Stimulation: Modeling and Measurement. eNeuro. 2022;9(5). 7. Metzger CS, Hammond MB, Paz-Solis JF, Newton WJ, Thomson SJ, Pei Y, et al. A novel fast-acting sub-perception spinal cord stimulation therapy enables rapid onset of analgesia in patients with chronic pain. Expert Rev Med Devices [Internet]. 2021;18(3):299–306. Available from: https://doi.org/10.1080/17434440.2021.1890580 8. Zhang TC, Janik JJ, Grill WM. Modeling effects of spinal cord stimulation on wide-dynamic range dorsal horn neurons: Influence of stimulation frequency and GABAergic inhibition. J Neurophysiol. 2014;112(3):552–67.

Acknowledgements:

Learning Objectives: DISCUSS ABOUT A NEW WAVEFORM INCREASE KNOWLEDGE ABOUT NEUROMODULATION IN PAIN THE USE OF SCS IN PAIN

Financial Disclosures: NO SIGNIFICANT RELATIONSHIPS

Disclosure: No significant relationships.

277

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

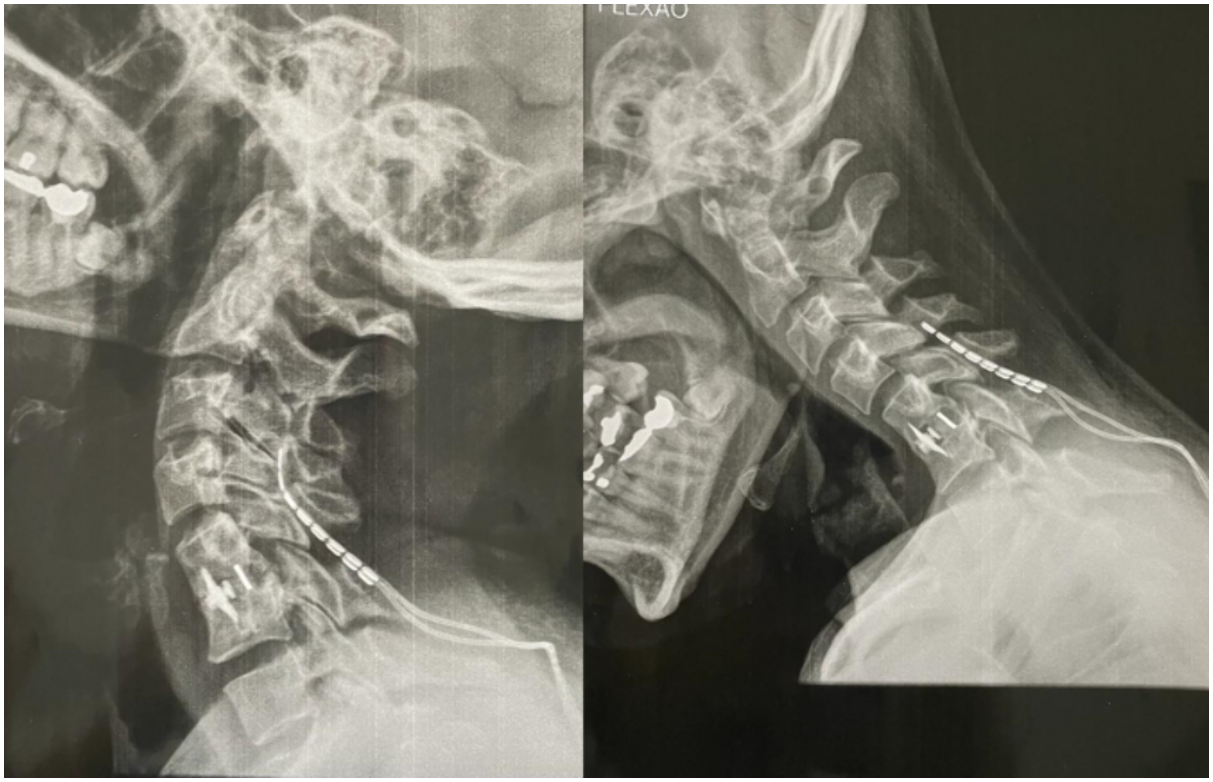
NEW TECHNIQUE FOR ANCHORING IN OPEN PLACEMENT OF PADDLE-TYPE SPINAL CORD STIMULATOR ELECTRODE AND CASE REPORT

Catarina Lins, MD[1], Laura Barros, MD[2]
[1]Pain Center, University of São Paulo School of Medicine, São Paulo – SP, SAO PAULO, Brazil, [2]Department of Pain, Hospital São Luiz de Osaco- SP, OSASCO, Brazil

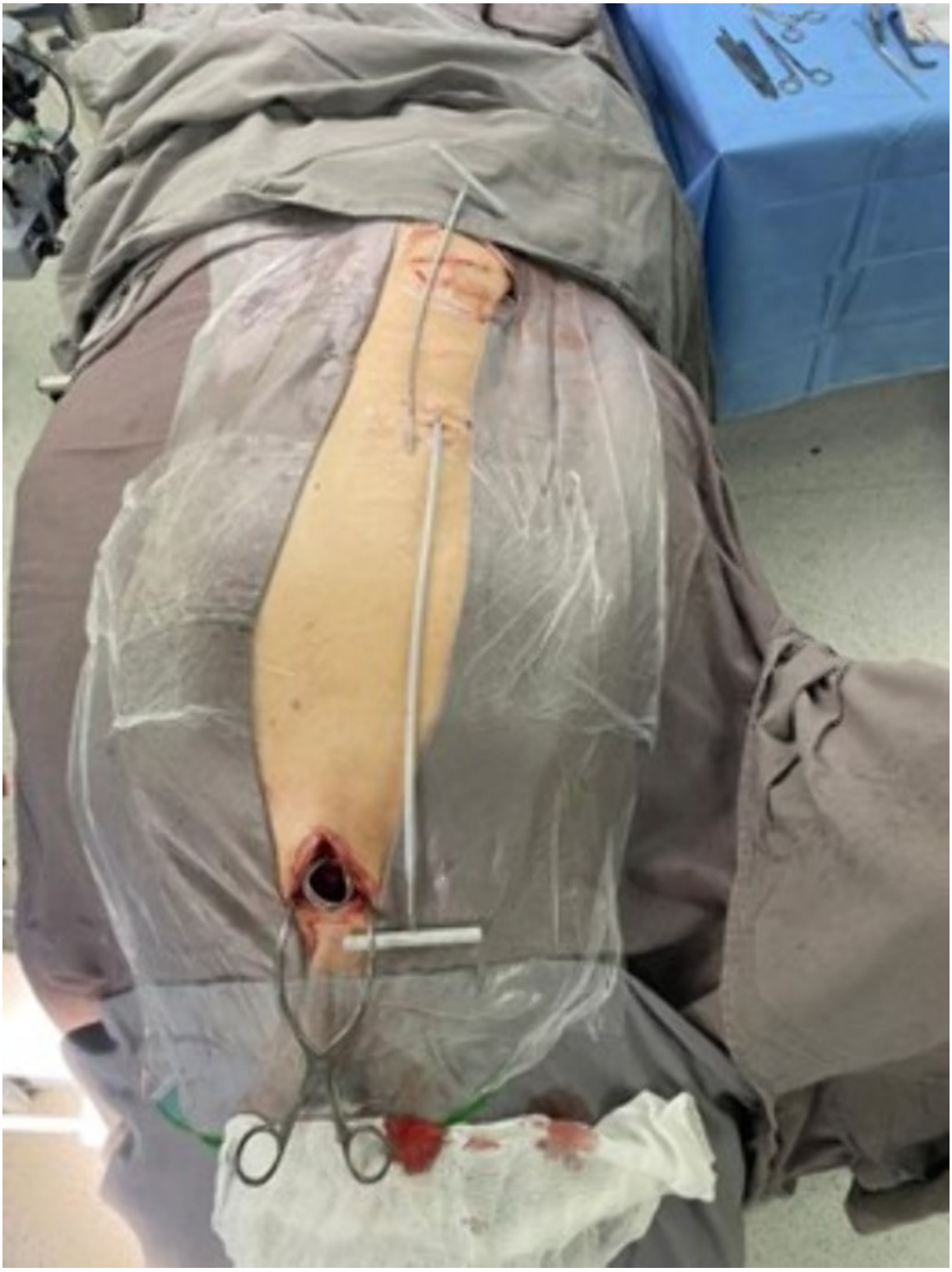
Introduction: Although not very common, the migration of the plate electrode is a serious complication of spinal cord stimulation (1). It is anticipated in cervical implants where the generator is placed in the lumbar region, leaving the electrode wire under significant tension and at risk of electrode displacement.

Materials / Methods: We performed a new technique of "Anchoring with skull closure plate" for the open paddle-type surgery and describe case report.

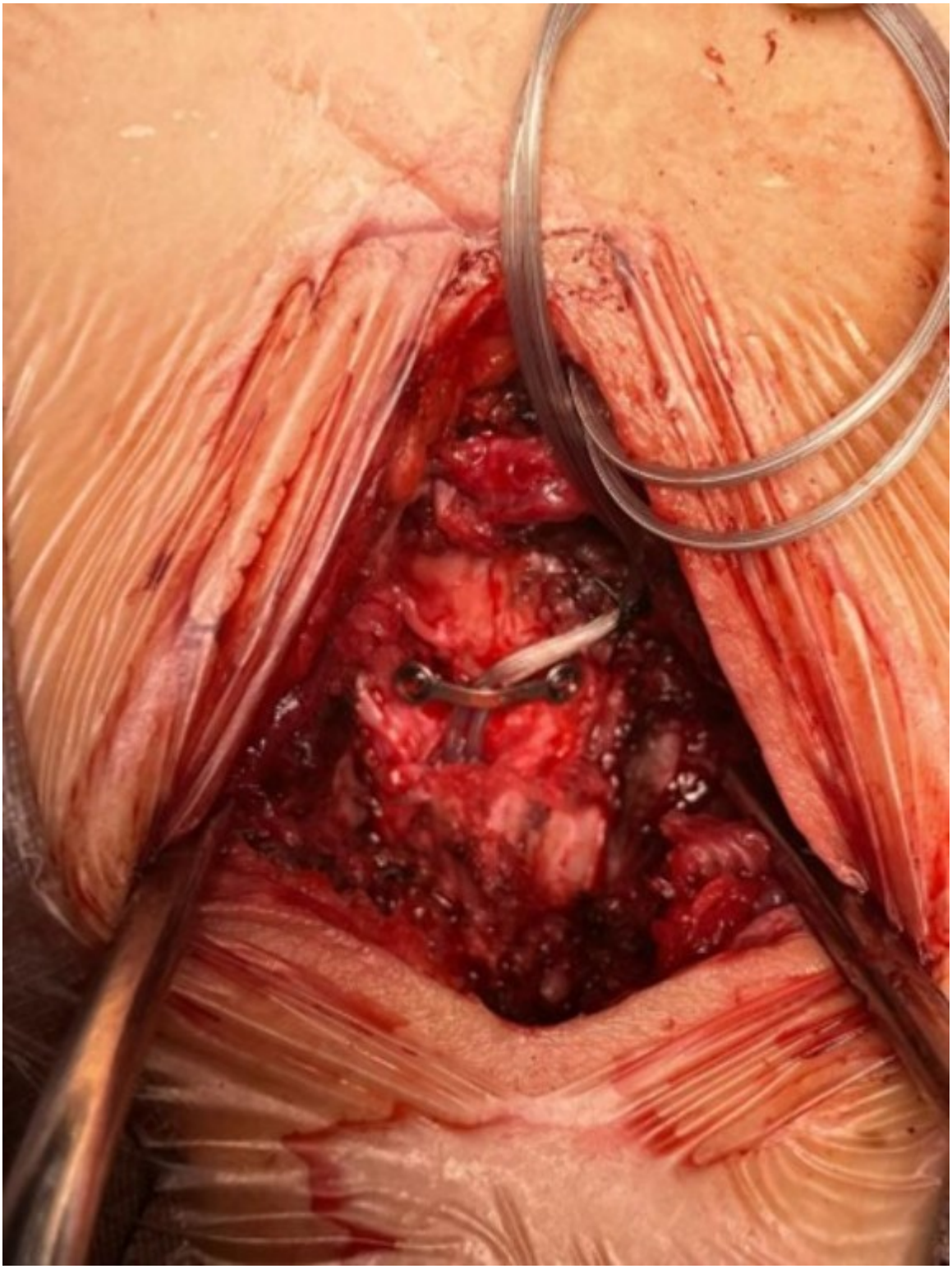
Results: A 32-year-old woman presented with a four-year history of intractable pain in the left upper extremity and thoracic region, previously controlled by SCS. Imaging revealed plate displacement of the cervical electrode (Figure 1). The generator, previously implanted in the lumbar region, was retained during the reapproach at the patient's request to avoid additional scarring in other areas (Figure 2). The electrode revision was performed using the skull closure plate anchoring technique (Figure 3). **Figure 1**



Figure



2 FIGURA



3

Discussion: The literature reports a range of migration rates, spanning from 13% up to 69% (2). In an analysis conducted by Turner and colleagues, they determined the typical migration rate to be close to 24% (3). The expense of altering or substituting the lead falls between $2700 and $5450 (4), resulting in an escalation in the procedure's overall cost by an estimated 15-20%.

Conclusions: The "Anchoring with skull closure plate" technique produces electrode stability, reducing the incidence of its migration.

Supplemental Data:

References: 1. Mironer YE, Brown C, Satterthwaite JR, Cohen M, Tonder LM, Grumman S. A New Technique of “Midline Anchoring” in Spinal Cord Stimulation Dramatically Reduces Lead Migration. Neuromodulation. 2004 Jan;7(1):32–7. 2. Funct S, Spincemaille GH, Klomp HM, Steyerberg EW, Van Urk H, Habbema JDF. Original Paper Technical Data and Complications of Spinal Cord Stimulation: Data from a Randomized Trial on Critical Limb Ischemia [Internet]. Vol. 74, Neurosurg. 2000. Available from: www.karger.comwww.karger.com/journals/sfn 3. Turner JA;, Loeser JD;, Bell KG. Spinal Cord Stimulation for Chronic Low Back Pain: A Systematic Literature Synthesis Clinical Study. Vol. 37, Neurosurgery. 1992. 4. Bell GK, Kidd D, North RB. Cost-Effectiveness Analysis Stimulation in Treatment Surgery Syndrome. Vol. 13, Journal of Pain and Symptom Management. 1997.

Acknowledgements:

Learning Objectives: DISCUSS ABOUT NEW TECHNIQUE IN OPEN PLACEMENT OF PADDLE-TYPE SPINAL CORD STIMULATOR ELECTRODE INCREASE KNOWLEDGE ABOUT INVASIVE NEUROMODULATION IN PAIN DISCUSS ABOUT SURGICAL ADVERSITIES

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

278

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

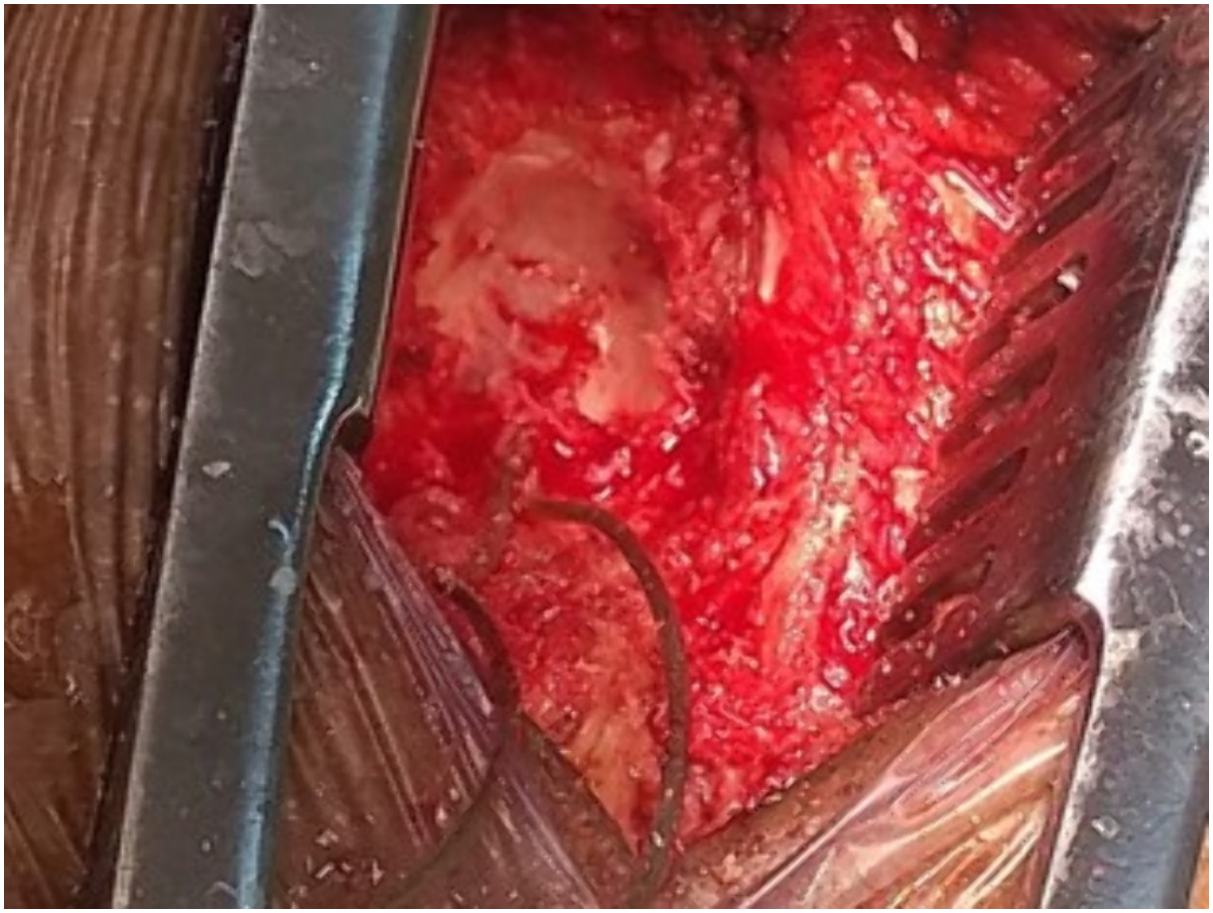
NEW TECHNIQUE FOR LAMINOPLASTY IN OPEN PLACEMENT OF PADDLE-TYPE SPINAL CORD STIMULATOR ELECTRODE IN THE PRESENCE OF EPIDURAL SCAR TISSUE

Catarina Lins, MD[1], Laura Barros, MD[2]
[1]Pain Center, University of São Paulo School of Medicine, São Paulo – SP, SAO PAULO, Brazil, [2]Department of Pain, Hospital São Luiz de Osaco- SP, OSASCO, Brazil

Introduction: The implantation of the paddle-type electrode is a relatively safe procedure. However, in the case of reoperation, the removal of the plate becomes challenging due to the presence of scar tissue (1). Another challenge is the fixation of this new plate in situations that require laminectomy for the removal of the previous plate.

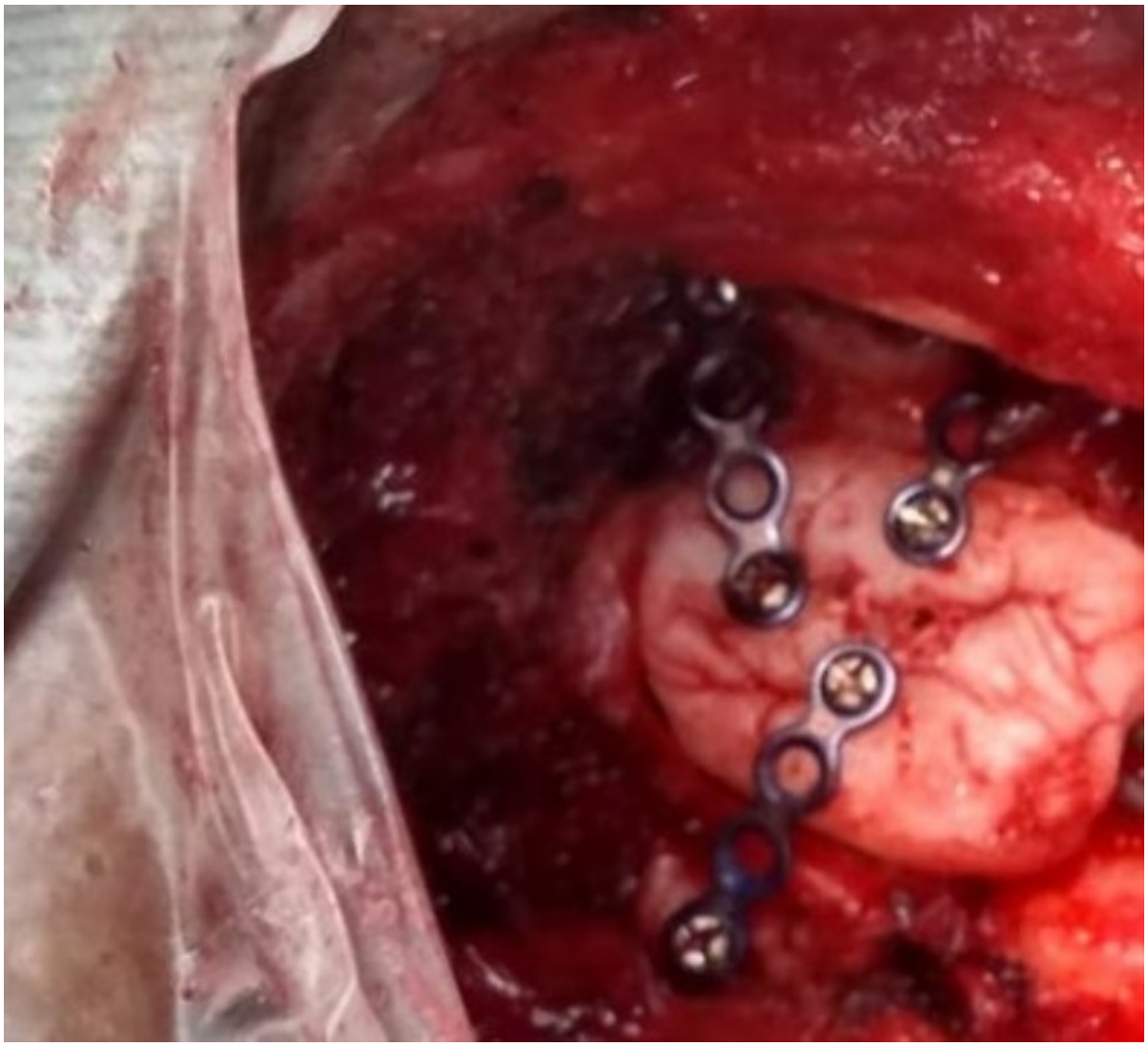
Materials / Methods: This technique involves the creation of a laminectomy for the removal of the previously implanted electrode and meticulous dissection of the scar tissue, combined with a laminoplasty, which serves to maintain better contact of the electrode with the posterior horn of the spinal cord.

Results: We perform drilling using a 5mm cutting drill until we reach the plate, which will be adhered to the dura mater through fibrosis (Figure 1). Dissection and removal of the plate are then carried out. Following this, the new plate is placed and anchored through laminoplasty and secured with skull closure plates (Figure 2). Figure
1



Figura

2



Discussion: To achieve optimal stimulation and coverage, electrode placement is crucial. A central position of the electrode, cephalad to the spinal segment corresponding to the most rostral and bilaterally painful area, is considered ideal (2). Thus, we advocate for the performance of laminoplasty after the removal of the previous electrode by laminectomy. Laminoplasty allows the active contacts of the electrode to be closer to the dorsal columns, an important factor in determining the effectiveness of stimulation, as advocated by Holsheimer(3).

Conclusions: Using our "Laminectomy with Laminoplasty" technique, the issue of removing the previously implanted plate and securing the new plate, while maintaining contact with the posterior horn of the spinal cord, can be safely navigated without increasing the size of the dorsal CSF layer.

Supplemental Data:

References: MacDonald JD, Fisher KJ. Technique for steering spinal cord stimulator electrode. Neurosurgery. 2011 Sep;69(SUPPL. 1). Pabaney AH, Robin AM, Schwalb JM. New technique for open placement of paddle-type spinal cord stimulator electrode in presence of epidural scar tissue. Neuromodulation. 2014 Dec 1;17(8):759–62. Holsheimer J, Barolat2 G, Struijk JJ, He J. Significance of the Spinal Cord Position in Spinal Cord Stimulation. Vol. 64, Acta Neurochir. 1995.

Acknowledgements:

Learning Objectives: DISCUSS ABOUT NEW TECHNIQUE IN OPEN PLACEMENT OF PADDLE-TYPE SPINAL CORD STIMULATOR ELECTRODE INCREASE KNOWLEDGE ABOUT INVASIVE NEUROMODULATION IN PAIN DISCUSS ABOUT SURGICAL ADVERSITIES

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

279

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

DORSAL COLUMN STIMUATION OR SPINAL NERVE ROOT STIMULATION FOR POST HERPETIC NERUALGIA : 2 SUCCESSFUL CASE REPORTS

Ken-Yi Lui, MD[1], Pranab Kumar, MD[1], Anuj Bhatia, MD[1], Victoria Bains, RN[1], Danielle Alvares, PhD[2]
[1]Toronto Western Hospital, Department Of Anesthesia And Pain Management, Toronto, Canada, [2]University Health Network, Department Of Anesthesia, Toronto Western Hospital, Toronto, Canada

Introduction: Neuropathic pain resolves within several months after herpetic rash but 9-14% progress to post herpetic neuralgia (PHN). The pain most commonly affects one or few adjacent dermatomes in cervical, thoracic or ophthalmic regions. Treatment options of PHN are suboptimal and consist of conservative management, topical analgesics, pharmaceutical managements including opioids and nerve blocks. Peripheral nerve stimulation and spinal cord stimulation (SCS) are best reserved as a last resort. Success of SCS depends on activation of anatomically intact spinal pathway correlating to the level of deafferentation. Spinal nerve root stimulation (SNRS) is an infrequent modality that can target pain within specific dermatomal distribution.

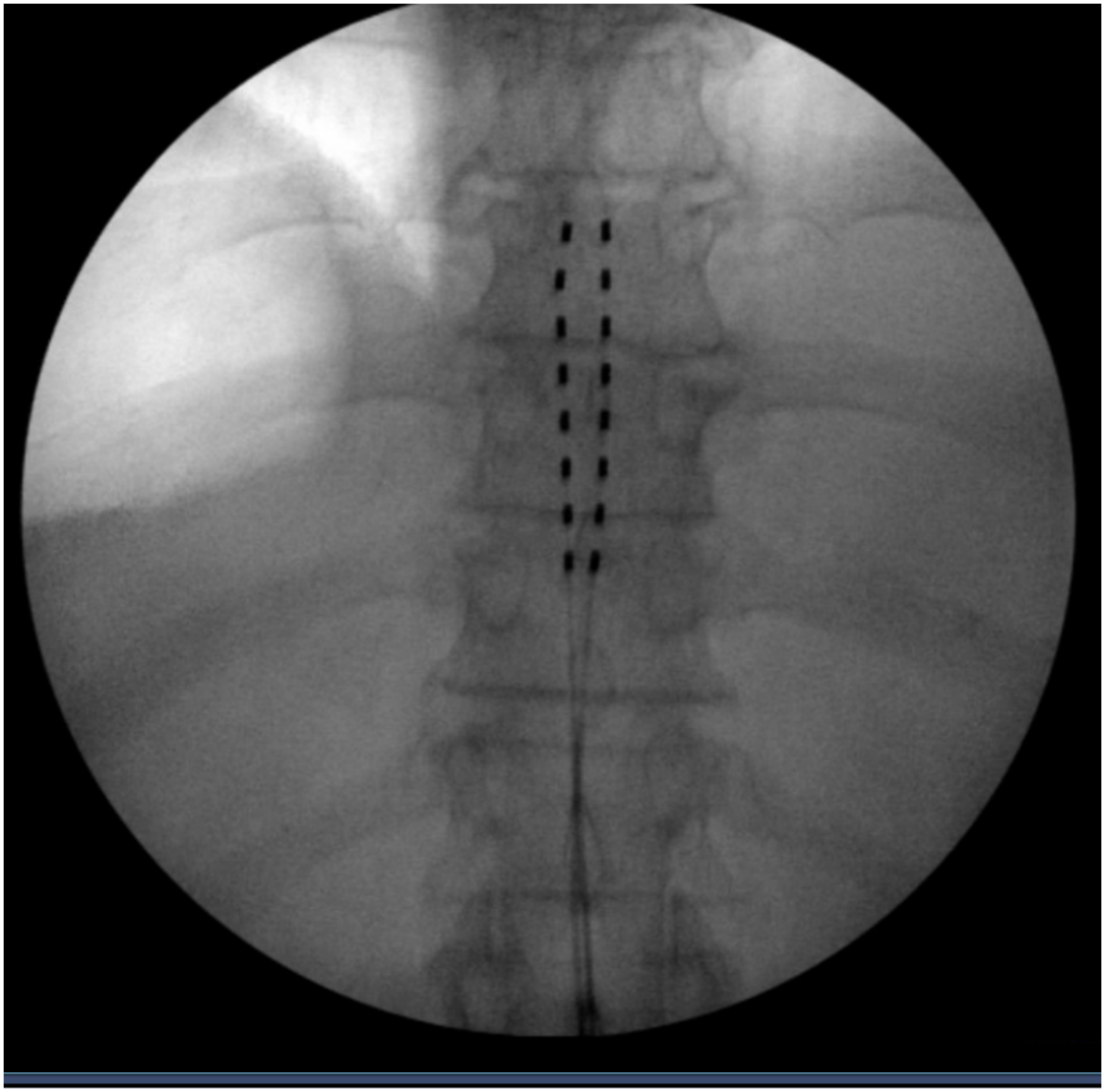
Materials / Methods: Retrospective chart review of 3 patients (patient A, B, C) that underwent SCS therapy for PHN at a single tertiary academic center PUBMED, EBMR, Google scholar was searched for all case reports that has the following keywords : post herpetic neuralgia, spinal cord stimulation Primary outcome was reduction in pain severity (visual analogue scale, VAS, measured at baseline, 1 month, 3 months, and 6 months post implant)

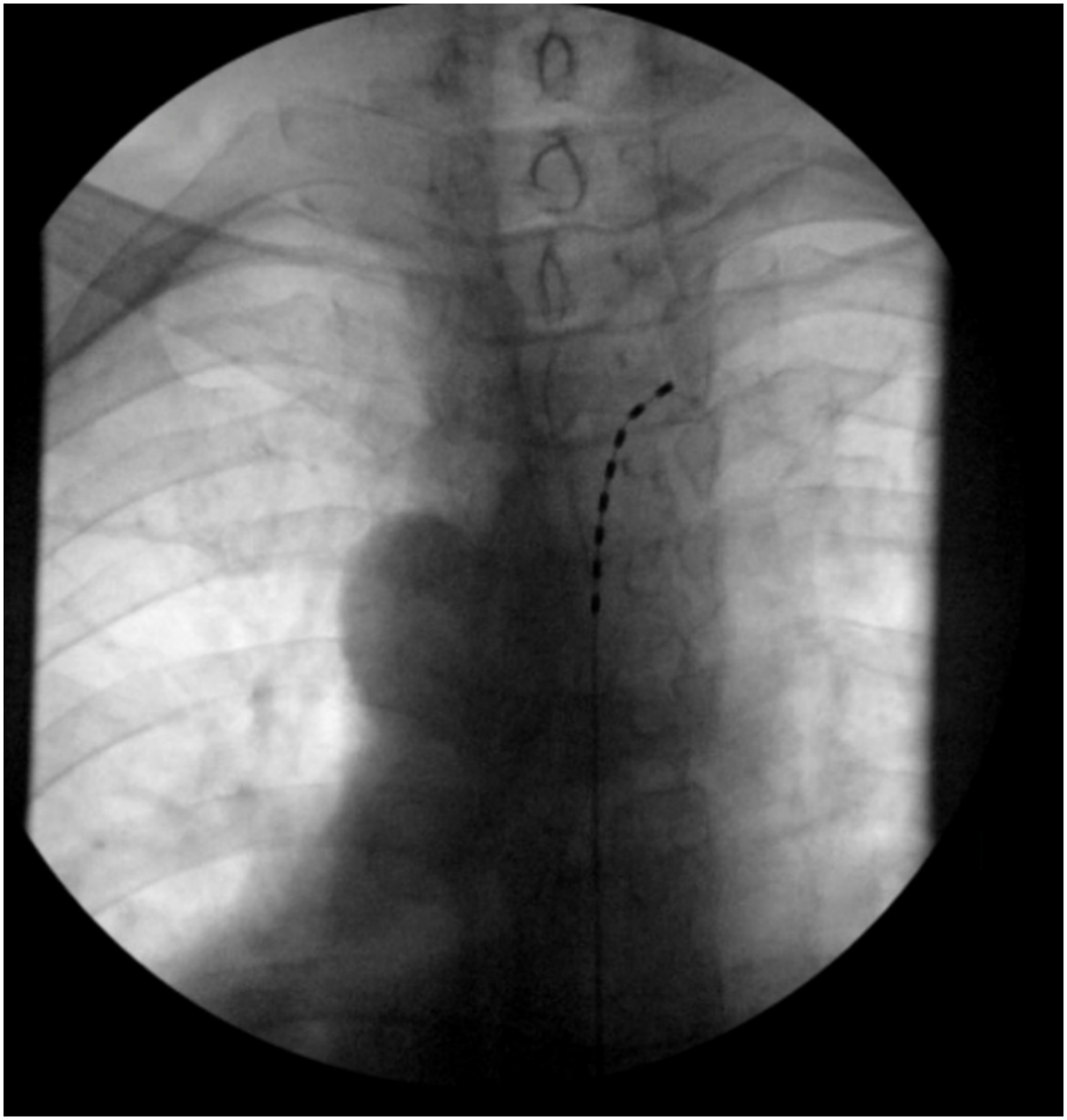
Results: We are reporting 3 cases of PHN of which failed conservative therapy and proceeded for advanced SCS therapy. Two patients who had successful trials who then proceeded further with SCS implantation.

Discussion: Literature review has shown that response of PHN to SCS is less predictable, with a success rate of 27%. Deafferentation and degeneration of dorsal column fibers are the dominant mechanisms that dictate the outcome of pain relief with SCS therapy.

Conclusions: We present results of outcomes of our patients with PHN presenting with intractable dermatomal neuropathic deafferentation pain treated with spinal nerve root stimulation (SNRS) and conventional dorsal column stimulation (DCS). We demonstrated its effectiveness in providing pain reduction which was comparable in both modalities of spinal cord neuromodulation without producing uncomfortable paresthesia.

Supplemental
Data:





	Baseline VAS	Mode of SCS therapy	SCS trial Average VAS	1 month	3 months	6 months
Patient A	9	DCS	7	Did not proceed for implantation		
Patient B	10	SNRS	5	3	4	4
Patient C	9	DCS	3	4	3	3

VAS : visual analogue scale, (10 means the worst pain the patient can imagine, 0 means the least pain the patient can imagine)

References: Gan EY, Tian EA, Tey HL. Management of herpes zoster and post herpetic neuralgia. Am J Dermatol 2013; 14: 77-85 Isagulyan E, Tkachenko V, Semenov D, Asriyants S, Dorokhov E, Makashova E, Aslakhanova K, Tomskiy A. The Effectiveness of Various Types of Electrical Stimulation of the Spinal Cord for Chronic Pain in Patients with Postherpetic Neuralgia: A Literature Review. Pain Res Manag. 2023 Mar 24;2023:6015680. doi: 10.1155/2023/6015680. PMID:

37007861; PMCID: PMC10065853. Harke H, Gretenkort P, Ladleif HU, Koester P, Rahman S. Spinal cord stimulation in postherpetic neuralgia and in acute herpes zoster pain. Anesth Analg. 2002 Mar;94(3):694-700; table of contents. doi: 10.1097/00000539-200203000-00040. PMID: 11867400. Gruver C, Guthmiller KB. Postherpetic Neuralgia. [Updated 2023 Apr 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493198/# Kellner CP, Kellner MA, Winfree CJ. Spinal nerve root stimulation. Prog Neurol Surg. 2011;24:180-188. doi: 10.1159/000323050. Epub 2011 Mar 21. PMID: 21422788.

Acknowledgements:

Learning Objectives: 1. Stimulation of dorsal spinal column or spinal nerve root stimulation can target pain within specific dermatomal distribution 2. Spinal cord stimuation could be an alternative to management of intractable post herpetic neuralgia

Financial Disclosures: No significant relationships declared from all authors

Disclosure: No significant relationships.

280

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

SPINAL CORD STIMULATION THERAPY CAPABLE OF RUNNING IN JAPAN

Hiroyuki Maeda, MD, PhD
Maeda hospital, Orthopedics, Tokyo, Japan

Introduction: In Japan, spinal cord stimulation therapy is covered by insurance and indicated for chronic intractable pain.
At Tokyo Spinal Cord Stimulation Center, the spinal cord stimulation therapy trial is not a post-surgical FBSS, but an active surgical procedure.
In fact, only about 20% of patients undergo implantation after the trial.
We evaluated the feasibility of running the spinal cord stimulation therapy trial in combination with rehabilitation. In addition, walking time and pain were also evaluated.

Materials / Methods: A spinal cord stimulation therapy trial was performed on a patient with chronic intractable pain seen by an orthopedic surgeon.
25 patients (10 men, 15 women), ages 57 to 93 years at Maeda Hospital(Tokyo Spinal Cord Stimulation Center)in Japan.During the one-week hospitalization, the patient was actively engaged in a spinal cord stimulation therapy trial and rehabilitation, as well as instructed in exercises that could be done back at home. During the spinal cord stimulation therapy trial, the patient did not take any oral pain medication.They were evaluated on their ability to run, improvement in walking time, and improvement in pain.

Results: Eleven people were allowed to run.
The Numerical Rating Scale (NRS) showed improvement from 10 before surgery to 2.72 after surgery.Eleven people were allowed to run.
The Numerical Rating Scale (NRS) showed improvement from 10 before surgery to 2.72 after surgery.
Walking speed improved by an average of 3.48 seconds.

Discussion: Spinal cord stimulation therapy may improve pain when performed prior to spinal surgery. Trial alone may also improve in patients who are unable to undergo surgery. Muscle strength improves when rehabilitation is also used. Once the patient is able to do one thing, he/she may feel more positive and may be able to run.A 94-year-old man was able to run after spinal cord stimulation therapy at the Tokyo Spinal Cord Stimulation Center.In the future, we would like to provide spinal cord stimulation therapy to improve quality of life in combination with rehabilitation.

Conclusions: Combined spinal cord stimulation therapy and rehabilitation may allow running regardless of age.

Supplemental Data:

References: None

Acknowledgements: I would like to acknowledge the staff of Tokyo Spinal Cord Stimulation Center, Maeda Hospital in JAPAN.

Learning Objectives: patient make happy

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

281

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

CASE REPORT: 10 KHZ STIMULATION FOR LUMBAR PAIN IN PATIENT WITH MUTATIONS IN THE PSTPIP1 GEN

Beatriz Mansilla, MD, María Román De Aragón, MD, Jose Paz Solis, MD
University Hospital La Paz, Neurosurgery, Madrid, Spain

Introduction: This abstract presents a case of a patient with lumbar pain radiating to MMII, diagnosed with Axonal Motor PNP, a motor polyneuropathy that decrease their ability to move, in addition to PAPA syndrome caused by a mutation of the PSTPIP1 gene. This mutation changes the function of the protein that encodes the gen and this protein plays an important role in the regulation of the inflammatory response. Patient implanted with a first SCS tonic system with a reduction of the 50% of his VAS and then implanted with a 10Khz stimulation system with an 80% reduction of the VAS.

Materials / Methods: Women of 40 years old, with discal herniations since the age of 9 years old, referred to our department after refusing L4-L5-S1 arthrodesis to the trauma service of another hospital. She is referred to me for implanting a neurostimulator VAS of 10/10, with Durogesic treatment (3/4 every 48 hours) and Adolonta (1-2 pills every 6 hours) First implant of the medullar neurostimulator with tonic stimulation was in 2012, with a pain relief of 50%. Subsequently, due to problems caused by immunosuppressive drugs we consider that is necessary the removal of the neurostimulator due to an infection. Patient with Axonal Motor PNP, causing cramps and weakness of MMII, in addition to diagnosis of PFAPA Syndrome. SCS is implanted at 10KHz compatible with whole body RMI, reducing his VAS to 3/10, with programming according to protocol in T9 - T10 disc

Results: Improvement is shown on day 15 after implantation: The patient reports more than 50% of paint relief, especially in pain intensity and duration of crises. The one with the most relief is program 1, with a T9-T10 disc bipole and an intensity of 2.5mA

Discussion: It is possible to use SCS 10Khz in patients with low back pain radiating to MMII, diagnosed with Axonal Motor PNP.

Conclusions: During the last few years, there have been new modalities that have proven to be more effecteive than the classical tonic stimulation. In this Case Report, we present a complicated patient due her associated pathologies, with herniated discs from a very early age, where high frequency stimulation (10,000Hz) has a greater reduction of pain than tonic or sub-threshold stimulation systems, in addition to better control of crises. This system also has other added advantages, such as the compatibility of RMI, the absence of paresthesia and the consequent postural advantages, in addition to other improvements in the patient's quality life.

Supplemental Data:

References: 1.Kapural L, Sayed D, Kim B, Harstroem C, Deering J. Retrospective Assessment of Salvage to 10 kHz Spinal Cord Stimulation (SCS) in Patients Who Failed Traditional SCS Therapy: RESCUE Study. J Pain Res. 2020;13:2861-2867. Published 2020 Nov 10. doi:10.2147/JPR.S281749 2.Cordero Tous, N, Sánchez Corral, C, Ortiz García, IM, Jover Vidal, A, Gálvez Mateos, R, Olivares Granados, G. High-frequency spinal cord stimulation as rescue therapy for chronic pain patients with failure of conventional spinal cord stimulation. Eur J Pain. 2021; 25: 1603– 1611. https://doi.org/10.1002/ejp.1776 3. Sayed D, Kallewaard JW, Rotte A, Jameson J, Caraway D. Pain relief and improvement in quality of life with 10 kHz SCS therapy: summary of clinical evidence. CNS neuroscience & therapeutics 2020;26(4):403-415.

Acknowledgements:

Learning Objectives: - IS posibble the SCS in weird gene? - Is there any superior SCS modality? - High Frecuency SCS is effective long - term with mutations genes

Financial Disclosures: No significant relationships'.

Disclosure: No significant relationships.

282

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

USING SPINAL CORD STIMULATION (SCS) IN PATIENTS WITH CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHIC (CIPN) PAIN

Vahid Mohabbati, MD, Mohammadkazem Papan, PhD
Sydney Pain Management Centre, Sydney, Australia

Introduction: Chemotherapy can enhance survival but may lead to acute neuropathy and chronic chemotherapy-induced peripheral neuropathy(CIPN) in some patients. CIPN is a frequent side effect of chemotherapy, severely impacting daily functions and quality of life.[1] It affects over 60% of patients with cancer and is expected to become more prevalent due to the aging global population and the rising rates of cancer and chemotherapy.[2] CIPN is characterized by symptoms such as pain, numbness, tingling, and loss of sensation in the extremities.[3,4] Generally, the severity of neuropathic complications is determined by a number of factors, including chemotherapy (e.g., platinum compounds), chemotherapy duration, cumulative dose, underlying comorbidities, and other treatment variables.[5] The management of CIPN is challenging[6], and Pharmacological treatments for CIPN using conventional medications for neuropathic pain have been largely ineffective, with a wide variety of analgesics including opioids, anti-epileptic drugs, and tricyclic antidepressants used, but often without satisfactory relief of pain.[7,8] Spinal Cord Stimulation (SCS) is an alternative treatment for patients resistant to traditional medications, using electrical stimulation in the spinal cord to relieve chronic pain, including neuropathy, and enhance quality of life.[9] This study aims to investigate the potential benefits of SCS for patients with chronic CIPN.

Materials / Methods: In this single-centre, prospective, open-label study, participants were enrolled. According to the protocol, patients were scheduled for follow-up visits 1, 3, 6, and 12 months post-procedure to monitor outcomes. To monitor outcomes, patients were scheduled for follow-up visits 1, 3, 6, and 12 months post-procedure. Participants were selected based on a clinical diagnosis of chemotherapy-induced peripheral neuropathy (CIPN) persisting for a minimum of 6 months post-adjuvant chemotherapy, including Taxol, Folfox, or Docetaxel. Eligible participants reported pain intensities ≥6/10 on the VAS, maintained stable neurological status, and adhered to a consistent analgesic regimen.

Results: Chemotherapy-induced peripheral neuropathy (CIPN) often results from six primary chemotherapy drugs, with certain risk factors like age and diabetes amplifying its onset. While some medications can be adjusted or ceased to combat neuropathy, many patients don't find relief even with optimal treatments.

Discussion: This research proposes Spinal cord stimulation (SCS) as an effective surgical intervention, especially for those with neuropathic pain unresponsive to other treatments. Successful SCS outcomes in CIPN cases have been documented.

Conclusions: This research highlights the long-term efficacy of SCS in treating CIPN, primarily targeting neuropathic pain. The present study indicates that SCS may be a viable solution to neuropathy that does not respond to traditional medical treatments.

Supplemental Data:

References: 1. Ma J, Kavelaars A, Dougherty PM, Heijnen CJ. Beyond symptomatic relief for chemotherapy-induced peripheral neuropathy: Targeting the source. *Cancer*. 2018;124(11):2289-2298. doi:10.1002/cncr.31248 2. Colloca L, Ludman T, Bouhassira D, et al. Neuropathic pain. *Nat Rev Dis Primers*. 2017;3(1):17002. doi:10.1038/nrdp.2017.2 3. Kerckhove N, Collin A, Condé S, Chaleteix C, Pezet D, Balayssac D. Long-Term Effects, Pathophysiological Mechanisms, and Risk Factors of Chemotherapy-Induced Peripheral Neuropathies: A Comprehensive Literature

Review. *Front Pharmacol*. 2017;8. doi:10.3389/fphar.2017.00086 4. Fukuda Y, Li Y, Segal RA. A Mechanistic Understanding of Axon Degeneration in Chemotherapy-Induced Peripheral Neuropathy. *Front Neurosci*. 2017;11. doi:10.3389/fnins.2017.00481 5. Windebank AJ, Grisold W. Chemotherapy-induced neuropathy. *Journal of the Peripheral Nervous System*. 2008;13(1):27-46. doi:10.1111/j.1529-8027.2008.00156.x 6. Lopes A, Duarte K, Lins C, et al. Spinal Cord Stimulation as a Treatment Option for Refractory Chemotherapy-Induced Peripheral Neuropathy: Case Report. *Arquivos Brasileiros de Neurocirurgia: Brazilian Neurosurgery*. 2020;39(03):228-231. doi:10.1055/s-0040-1709985 7. Smith EML, Pang H, Cirrincione C, et al. Effect of Duloxetine on Pain, Function, and Quality of Life Among Patients With Chemotherapy-Induced Painful Peripheral Neuropathy. *JAMA*. 2013;309(13):1359. doi:10.1001/jama.2013.2813 8. Cata JP, Cordella J V, Burton AW, Hassenbusch SJ, Weng HR, Dougherty PM. Spinal cord stimulation relieves chemotherapy-induced pain: a clinical case report. *J Pain Symptom Manage*. 2004;27(1):72-78. doi:10.1016/j.jpainsymman.2003.05.007 9. Deer TR, Mekhail N, Provenzano D, et al. The Appropriate Use of Neurostimulation of the Spinal Cord and Peripheral Nervous System for the Treatment of Chronic Pain and Ischemic Diseases: The Neuromodulation Appropriateness Consensus Committee. *Neuromodulation: Technology at the Neural Interface*. 2014;17(6):515-550. doi:10.1111/ner.12208

Acknowledgements: We extend our heartfelt gratitude to Mohammadkazem Papan for his invaluable contributions and unwavering dedication to the execution of this research.

Learning Objectives: Objective 1: Understanding the Mechanism and Implications of CIPN Desired Result: By the end of this session, participants should be able to describe the pathophysiology of chemotherapy-induced peripheral neuropathy (CIPN), identify the common chemotherapeutic agents responsible, and understand its implications on a patient's quality of life. **Objective 2: Comprehensive Overview of Spinal Cord Stimulation (SCS) as a Treatment Option Desired Result**: Participants will gain a comprehensive understanding of how SCS works, its potential benefits for CIPN patients, and its efficacy in comparison to conventional treatments. They will be able to determine when to consider SCS as a treatment option and its potential side effects or contraindications. **Objective 3: Integration of Knowledge into Clinical Practice Desired Result**: Armed with the knowledge from the research, participants should be equipped to assess CIPN patients more effectively and incorporate spinal cord stimulation into their treatment plans when deemed appropriate. They will also be more prepared to discuss this treatment option with patients, covering potential risks and benefits, and set realistic expectations about outcomes.

Financial Disclosures: Dr. Vahid Mohabbati discloses that he serves as a consultant and advisor for several medical technology companies. Specifically, he has professional affiliations with Medtronic, Nevro, and Abbott. These affiliations may involve financial relationships or other potential conflicts of interest. The views and opinions expressed in any related presentations or publications are those of Dr. Mohabbati and do not necessarily reflect the official positions or policies of these companies. Any discussions related to the products or technologies of these companies are based on Dr. Mohabbati's expert opinion and not influenced by his affiliations.

Disclosure: No significant relationships.

283

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

PROSPECTIVE, LONG-TERM, REAL-WORLD, PRACTICE AUDIT ON OMNIA SPINAL CORD STIMULATION THERAPY IN A COHORT OF CHRONIC PAIN PATIENTS

Vahid Mohabbati, MD, Mohammadkazem Papan, PhD
Sydney Pain Management Centre, Sydney, Australia

Introduction: Spinal cord stimulation (SCS) is a therapeutic approach used to manage chronic pain in various etiologies.[1] One specific type of SCS is high-frequency spinal cord stimulation (HF-SCS) at 10 kHz, which has shown efficacy in treating chronic back and leg pain.[2] HF-SCS has been found to provide paresthesia-free pain relief for a wide range of pain indications.[3] It has also been shown to reduce pain, disability, and opioid consumption in non-surgical refractory back pain subjects.[4] The use of SCS has been explored in the treatment of painful diabetic neuropathy (PDN).[5] Among patients treated with HF-SCS , a high percentage (85%) experienced treatment response (≥50% pain relief) at six months, and this response persisted over 12 months.[6] Furthermore, case reports have highlighted the successful use of HF-SCS in managing conditions such as thoracic postherpetic neuralgia[7], neuropathic pelvic pain[8], and lower limb pain with foot drop.[9] In this study by utilizing a SCS device that offering a wide range of frequencies and waveform capabilities. It allows precise targeting of pain pathways through customizable stimulation settings, including HF10, Tonic-SCS, Burst, Burst10k™, and Frequency pairing. This flexibility in therapy options contributes to higher rates of durable response and mitigates the risk of device explantation. This study aims to evaluate the clinical performance of this SCS in individuals with chronic, intractable pain as part of the centres' routine practice (on-label use of TGA approved).

Materials / Methods: Study subjects undergo a 14-day Trial Phase for SCS therapy. Success is a 50% pain reduction. Successful subjects received a permanent OMNIA IPG (Implantable Pulse Generator). All subjects will initially be provided with HF10 (+/- duty cycling). If additional therapeutic support is required, the subjects will be provided with additional waveforms/frequency. The final visit evaluated pain, function, sleep, medication, satisfaction, and adverse events.

Results: A study involving 20 chronic pain patients undergoing spinal cord stimulation (SCS) treatment showed promising results. Thirteen patients completed the trial, receiving implants, while seven either failed or withdrew. Over 12 months, pain scores decreased significantly from an average baseline of 7.13 to 4.36, with disability levels improving notably from 52.15% to 33.17%. Patients with low back and leg pain experienced the most substantial improvements.

Discussion: A study tracked pain evaluations and treatment outcomes over 12 months for spinal cord stimulation (SCS) recipients, noting significant improvements in pain and disability metrics, surpassing established minimal clinically important difference (MCID) thresholds, with a high implantation success rate indicating intervention efficacy.

Conclusions: While many patients experienced notable pain relief, some trials were unsuccessful, highlighting the need for continuous evaluation and personalized treatment strategies in pain management with OMNIA SCS therapy.

Supplemental Data:

References: 1. Baranidharan G, Edgar D, Bretherton B, et al. Efficacy and Safety of 10 kHz Spinal Cord Stimulation for the Treatment of Chronic Pain: A Systematic Review and Narrative Synthesis of Real-World Retrospective Studies. *Biomedicines*. 2021;9(2):180. doi:10.3390/biomedicines9020180 2. Stauss T, El Majdoub F, Sayed D, et al. A multicenter real-world review of 10 <scp>kH</scp> z <scp>SCS</scp> outcomes for treatment of chronic trunk and/or limb pain. *Ann Clin Transl Neurol*. 2019;6(3):496-507. doi:10.1002/acn3.720 3. Sayed D, Kallewaard JW, Rotte A, Jameson J, Caraway

D. Pain relief and improvement in quality of life with 10 kHz SCS therapy: Summary of clinical evidence. *CNS Neurosci Ther*. 2020;26(4):403-415. doi:10.1111/cns.13285 4. Al-Kaisy A, Van Buyten JP, Kapural L, et al. 10 kHz spinal cord stimulation for the treatment of non-surgical refractory back pain: subanalysis of pooled data from two prospective studies. *Anaesthesia*. 2020;75(6):775-784. doi:10.1111/anae.15036 5. Mekhail NA, Argoff CE, Taylor RS, et al. High-frequency spinal cord stimulation at 10 kHz for the treatment of painful diabetic neuropathy: design of a multicenter, randomized controlled trial (SENZA-PDN). *Trials*. 2020;21(1):87. doi:10.1186/s13063-019-4007-y 6. Callaghan BC. Author Response: Oral and Topical Treatment of Painful Diabetic Polyneuropathy: Practice Guideline Update Summary: Report of the AAN Guideline Subcommittee. *Neurology*. 2022;99(21):967-967. doi:10.1212/WNL.0000000000201550 7. Alla SP. A Case Report of Successful High-Frequency 10-kHz Spinal Cord Stimulator Trial in a Patient with Refractory Thoracic Postherpetic Neuralgia. *Pain Management Case Reports*. Published online March 1, 2021:55-58. doi:10.36076/pmcr.2021/5/55 8. Simopoulos T, Yong RJ, Gill JS. Treatment of Chronic Refractory Neuropathic Pelvic Pain with High-Frequency 10-kilohertz Spinal Cord Stimulation. *Pain Practice*. 2018;18(6):805-809. doi:10.1111/papr.12656 9. Feng H, Doherty P, Rotte A, Bovinet C. Amelioration of lower limb pain and foot drop with 10 kHz spinal cord stimulation: A case series. *Journal of International Medical Research.*

Acknowledgements: We would like to sincerely thank Dawn Augimeri and Dominic Bailey for their invaluable contributions and relentless efforts in the Omnia clinical research project. Their dedication and expertise have been instrumental in the project's success.

Learning Objectives: Understand the therapeutic use of Spinal Cord Stimulation (SCS) in chronic pain management. Differentiate between general SCS and high-frequency SCS. Recognize the paresthesia-free pain relief and reduced opioid consumption benefits of 10 kHz SCS. Learn about the application of 10 kHz SCS in various pain conditions, including diabetic neuropathy and postherpetic neuralgia. Comprehend the safety profile of 10 kHz SCS. Grasp the methodology and key results of the study. Recognize the importance of personalized treatment in pain management.

Financial Disclosures: This study was partially funded by a research grant from Nevro Corporation. The authors wish to disclose this financial relationship to ensure transparency. It is important to note that while Nevro Corporation provided funding, they did not influence the study's design, data collection, analysis, or results. The research findings and conclusions drawn are the independent work of the study's authors.

Disclosure: This study was partially funded by a research grant from Nevro Corporation. The authors wish to disclose this financial relationship to ensure transparency. It is important to note that while Nevro Corporation provided funding, they did not influence the

284

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

PSYCOLOGICAL EVALUATION IN NEUROMODULATION IMPLANTS

Sonia Sosa, DPsych, Cristina Abad, MD, Eva Monzón, MD, David Abejón, MD
Hospital Universitario Quironsalud Madrid, Pain Unit, Madrid, Spain

Introduction: Due to pain being biopsychosocial in nature, a prior assessment of the psychological aspects of the individual is crucial to identify risk factors that may compromise the effectiveness of the implant.

Materials / Methods: The evaluation consists of two phases: **Cuantitative evaluation:** A battery of 6 tests is administered: Lattinen: measuring 5 dimensions of pain (intensity, disability, frequency, analgesic consumption, and sleep), BDI de Beck: measures depression STAI: measures trait and state anxiety ECD catastrophizing: measures catastrophizing CAD-R: measures coping strategies related to pain Duke-UNC: measures perceived social support **Qualitative Evaluation** An interview is conducted to delve into different aspects involved in pain processing: Pain's issues: origin, chronology, pain dimensions. Cognitive sphere: beliefs about pain and disability, hopelessness, catastrophizing, and concerns emotional sphere: anxiety, depression, irritability, fear behavioral sphere: activity level, coping strategies social sphere: family and friend support other psychological conditions: somatic symptom disorders, substance abuse, psychotic states, suicide attempts secondary gains: attention due to illness, desire for financial compensation or disability benefits dimensions related to the SCS : fears regarding the intervention, commitment to treatment recommendations **After the evaluation**, two paths can be followed: The patient is deemed suitable, the implantation would proceed If the patient has risk factors, psychological treatment is recommended to improve them before the procedure.

Results: The data analyzed include from March 15 2019 to 12 October 2023. Suitable patients: 77 Patients that require previous phycological treatment: 18 did not receive treatment, and therefore were not implnated 28 received treatment: 10 underwent implantation 4 pending implantation 6 are currently in treatment 8 were not implanted for various reasons: 2 have psychiatric disorders 3 improve with the treatment 3 did not complete the treatment

Discussion: The data show a significant number of cases in which the implant procedure is not performed due to patients' refusal to receive psychological treatment, as they do not consider pain from a biopsychosocial perspective.Furthermore, three cases are observed in which, following psychological therapy, the neuromodulator is ultimately not required.

Conclusions: Generalization of assesment and psychoeducation to patients about pain is considered essential in neuromodulation.

Supplemental Data:

References: North RB, Kidd DH, Wimberly RL, Edwin D. Prognostic value of psychological testing in patients undergoing spinal cord stimulation: A prospective study. Neurosurgery 1996;39(2):301-11. Monsalve V, de Andrés JA, Valia JC. Application of a psychological decision algorithm for the selection of patients susceptible to implantacion of neuromodulation systems for the treatment of chronic pain. Neuromodulation 2000;3(4):191-200. Gallach-Solano E., Canós-Verdecho M. A., Morales Suárez-Varela M.. Protocolo psicológico para la evaluación de candidatos a implante de neuroestimulador. Rev. Soc. Esp. Dolor [Internet]. 2016 Dic [citado 2023 Oct 17] ; 23(6): 307-315. Available in: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S1134-80462016000600007&lng=es.

Acknowledgements: To Dr Abejón´s team

Learning Objectives: 1- Psychological evaluation of candidates for neuromodulation. 2- Alternatives to consider after the psychological evaluation. 3- Outcomes after receiving psychological therapy before the implant.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

285

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

COMPARING EFFICACY AND SAFETY OF DEXAMETHASONE, METHYLPREDNISOLONE AND BETAMETHASONE IN LUMBAR TRANSFORAMINAL EPIDURAL STEROID INJECTIONS

Alexandra Moreira, MD
University of Miami/JMH, Miami, United States of America

Introduction: Particulate steroids are thought to last longer at the injection site however carry higher risks when used in epidural steroid injections. Catastrophic spinal cord complications including sudden-onset paraplegia have been reported due to intravascular particulate steroid aggregation causing a spinal infarct. Clinicians, therefore, recommend non-particulate steroids to mitigate these adverse events. To our knowledge, this is the first retrospective study that addresses the efficacy and safety of using methylprednisolone, dexamethasone, and betamethasone in transforaminal epidural steroid injections (TFESI) for the treatment of lumbar radiculopathy.

Materials / Methods: This was a single center, IRB approved, retrospective review capturing data (n=1717) over a four-year period. The primary outcomes for this study were: (1) proportion of particulate vs non-particulate cohort that required zero and one or more repeat injections within 12 months of their initial injection, Secondary outcome measure was the proportion of patients ultimately requiring surgery.

Results: The non-particulate steroid cohort demonstrated a significantly greater proportion of zero repeat injections (87.5% vs 71.4%, $p < 0.001$). The particulate steroid cohort demonstrated a significantly greater proportion of repeat injections within 12 months from their initial injections (12.5% vs 29.6% $p < 0.001$). There were no significant differences among patients requiring surgery in both steroid cohorts. Other outcome measures included identification of risk factors significantly associated with repeat injections. There was a statistically significant weak positive correlation between age and repeat injections (Pearson corr= 0.102; $p < 0.001$), weak negative correlation between ethnicity/race and repeat injections (point-biserial corr = -0.093; $p < 0.001$). No adverse events were reported.

Discussion: Our study demonstrates superior clinical outcomes using non-particulate steroids in TFESI for the treatment of lumbar radiculopathy compared to particulate steroids.

Conclusions: This evidence from our study supports the use of non-particulate steroids in TFESI for lumbar radiculopathy treatment to mitigate unnecessary associated risks.

Supplemental Data:

References: Freburger JK, Holmes GM, Agans RP, Jackman AM, Darter JD, Wallace AS, Castel LD, Kalsbeek WD, Carey TS. The rising prevalence of chronic low back pain. Arch Intern Med. 2009 Feb 09;169(3):251-8 Manchikanti L, Singh V, Falco FJ, Benyamin RM, Hirsch JA. Epidemiology of low back pain in adults. Neuromodulation. 2014 Oct;17 Suppl 2:3-10. doi: 10.1111/ner.12018. PMID: 25395111. Longo UG, Loppini M, Denaro L, Maffulli N, Denaro V. Rating scales for low back pain. Br Med Bull. 2010;94:81-144. doi: 10.1093/bmb/ldp052. Epub 2010 Jan 10. PMID: 20064820. Berry JA, Elia C, Saini HS, Miulli DE. A Review of Lumbar Radiculopathy, Diagnosis, and Treatment. Cureus. 2019 Oct 17;11(10):e5934. doi: 10.7759/cureus.5934. PMID: 31788391; PMCID: PMC6858271. N. K. Arden and others, on behalf of the WEST Study Group, A multicentre randomized controlled trial of epidural corticosteroid injections for sciatica: the WEST study, *Rheumatology*, Volume 44, Issue 11, November 2005, Pages 1399–1406, https://doi.org/10.1093/rheumatology/kei028 Helm Ii S, Harmon PC, Noe C, Calodney AK, Abd-Elsayed A, Knezevic NN, Racz GB. Transforaminal Epidural Steroid Injections: A Systematic Review and Meta-Analysis of Efficacy and Safety. Pain Physician. 2021 Jan;24(S1):S209-S232. PMID: 33492919. Lee JH, Shin KH, Park SJ, et al. Comparison of clinical efficacy between transforaminal and interlaminar epidural injections in lumbosacral disc herniation: A

systematic review and meta-analysis. Pain Physician 2018; 21:433-448. Smith CC, McCormick ZL, Mattie R, et al. The effectiveness of lumbar transforaminal injection of steroid for the treatment of radicular pain: A comprehensive review of the published data. Pain Med 2020; 21:472-487. Chang A, Ng AT. Complications Associated with Lumbar Transforaminal Epidural Steroid Injections. Curr Pain Headache Rep. 2020 Sep 29;24(11):67. doi: 10.1007/s11916-020-00900-9. PMID: 32990823. Chatterjee N, Roy C, Das S, Al Ajmi W, Al Sharji NS, Al Mandhari A. Comparative Efficacy of Methylprednisolone Acetate and Dexamethasone Disodium Phosphate in Lumbosacral Transforaminal Epidural Steroid Injections. Turk J Anaesthesiol Reanim. 2019 Oct;47(5):414-419. doi: 10.5152/TJAR.2019.69741. Epub 2019 May 20. PMID: 31572994; PMCID: PMC6756306. Derby R, Lee SH, Date ES, Lee JH, Lee CH. Size and aggregation of corticosteroids used for epidural injections. Pain Med. 2008 Mar;9(2):227-34. doi: 10.1111/j.1526-4637.2007.00341.x. PMID: 18298706. Lyders EM, Morris PP. A case of spinal cord infarction following lumbar transforaminal epidural steroid injection: MR imaging and angiographic findings. AJNR Am J Neuroradiol. 2009;30(9):1691–3. Kennedy DJ, Dreyfuss P, Aprill CN, Bogduk N. Paraplegia following image-guided transforaminal lumbar spine epidural steroid injection: two case reports. Pain Med. 2009 Nov;10(8):1389-94. doi: 10.1111/j.1526-4637.2009.00728.x. Epub 2009 Oct 26. PMID: 19863744. Discussion sources Isabelle Denis, MD, FRCPC, BSc and others, Randomized Double-Blind Controlled Trial Comparing the Effectiveness of Lumbar Transforaminal Epidural Injections of Particulate and Nonparticulate Corticosteroids for Lumbosacral Radicular Pain, *Pain Medicine*, Volume 16, Issue 9, September 2015, Pages 1697–1708, https://doi.org/10.1111/pme.12846 Makkar JK, Singh PM, Jain D, Goudra B. Particulate vs Non-Particulate Steroids for Transforaminal Epidural Steroid Injections: Systematic Review and Meta-analysis of the Current Literature. Pain Physician. 2016 Jul;19(6):327-40. PMID: 27454262. Bensler, Susanne, et al. "Is there a difference in treatment outcomes between epidural injections with particulate versus non-particulate steroids?." European radiology 27 (2017): 1505-1511. Güven, Ayşegül, Ümit Akkemik, and Güngör Enver Özgencil. "Comparison of efficacy of particulate and non-particulate steroids in patients with lumbosacral pain, non-operated patients with chronic radicular symptoms." Agri: Agri (Algoloji) Dernegi'nin Yayin Organidir= The Journal of the Turkish Society of Algology 35.2 (2023): 68-75. Dydyk AM, Khan MZ, Singh P. Radicular Back Pain. [Updated 2022 Oct 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK546593/

Acknowledgements:

Learning Objectives: The primary outcomes for this study were: (1) proportion of patients in each cohort (particulate vs non-particulate) that required zero and one or more repeat injections within 12 months of their initial injection. Secondary outcome measure was the proportion of patients ultimately requiring surgery within four years. Our third outcome measure was to identify risk factors significantly associated with repeat injections.

Financial Disclosures: no significant relationships

Disclosure: No significant relationships.

286

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

TREATMENT OF SJÖGREN'S SMALL FIBER NEUROPATHY WITH DORSAL ROOT GANGLION STIMULATION

Alexandra Moreira, MD
University of Miami/JMH, Miami, United States of America

Introduction: Small fiber neuropathy is a chronic neuropathic pain disorder of the peripheral nerves described by symptoms of burning, sharp-shooting pain, allodynia, and hyperesthesia. There are a variety of diseases that may result in a small fiber neuropathy, including Sjogren's, diabetes, thyroid dysfunction, sarcoidosis and others. Primary Sjögren Syndrome is a systemic chronic autoimmune disease characterized by glandular and systemic extra-glandular organ involvement, including skin, lung, kidney, vascular, peripheral and central nervous system. Typically, it has been treated with anti-convulsant and anti-depressants however, some studies have shown success with neuromodulation via spinal cord stimulation. To our knowledge, this is the first case in the current literature demonstrating successful treatment of small fiber neuropathy using dorsal root ganglion (DRG) stimulation in a patient with Sjogren's syndrome.

Materials / Methods: A 49 year old female with history of chronic low back pain, hepatitis and Sjogren's syndrome with evidence of small fiber neuropathy presenting with CRPS II causalgia. Her initial symptoms began in 2014 with her pain described as pulsating, throbbing and burning in quality. It was localized to the plantar aspect of her right heel and anterior right anterior thigh. Her pain was a 6/10 on initial evaluation. She denied any inciting event or trauma causing her pain. Aggravating factors included prolonged sitting and standing. Alleviating factors included frequent repositioning, lower extremity stretching and nsaids. She failed conservative management with physical therapy, prior lumbar TFESI and SIJ injections.

Results: She had a successful DRG stimulator trial performed at an outside facility, providing 80% pain relief for several days. Patient underwent successful implantation of two DRG leads a few months later. A thoracic 4-contact electrode was placed to target the right lumbar T12 DRG (figure 1D). A second DRG electrode lead was placed to target the right lumbar S1 dorsal root ganglion (figure 1A and figure 1C). Implantable pulse generator (IPG) was implanted in a superficial skin pouch adjacent to the spine. Both leads were connected to the same IPG as shown in figure 1B. The DRG system was programmed and managed by Abbott representatives. At the patient's post-operative office visit, she reported > 50% improvement of her pain and overall function.

Discussion: This case report serves to increase awareness within the medical community that DRG stimulation can be a viable treatment option for patients suffering Sjogren's small fiber neuropathy.

Conclusions: Dorsal root ganglion stimulation can be a viable treatment option for patients with small fiber neuropathy.

Supplemental Data: Figure 1A: Sacral lead placement, AP view. 1B:IPG with leads attached, AP view. 1C: Sacral lead placed on right S1 DRG, lateral view. 1D: Thoracic lead placed on the right T12 dorsal root ganglion, AP view.

References: Sène D, Cacoub P, Authier FJ, et al. Sjögren Syndrome-Associated Small Fiber Neuropathy: Characterization From a Prospective Series of 40 Cases. *Medicine (Baltimore)*. 2013;92(5):e10-e18. doi:10.1097/MD.0000000000000005

Acknowledgements:

Learning Objectives: 1. Identify treatment options for patients with sjrogren's small fiber neuropathy. 2. Increase awareness to pain clinicians regarding treatments for small fiber neuropathy. 3. Increase awareness for patients with sjrogren's that DRG stimulation is a successful treatment option for some patients.

Financial Disclosures: no significant relationships

Disclosure: No significant relationships.

287

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

TREATMENT OF THALAMIC STROKE WITH SPINAL CORD STIMULATION

Alexandra Moreira, MD
University of Miami/JMH, Miami, United States of America

Introduction: Thalamic pain syndrome, a type of central post stroke pain (CPSP), occurs in patients who have sustained cerebrovascular lesions of the thalamic and lateral medullary areas and occurs in up 10% of patients. Pain is characterized as neuropathic with hyperalgesia and allodynia. CPSP syndrome often correlates with emotional changes, fatigue, cognitive impairment, sleep disorders, and algophobia [1]. Onset of symptoms emerge months or even years after initial injury. Over 40% of patients with CPSP syndrome have symptoms between one and 12 months after the stroke, and sometimes years post-stroke [2]. Treatment options include anti- convulsants, anti-depressants, deep brain stimulation, repetitive transcranial magnetic stimulation, electrical motor cortex stimulation and SCS [2]. SCS therapy for CPSP, has been studied in only a few cohort studies showing long-term pain relief with over 50% pain reduction [2].

Materials / Methods: A 52 y/o male with history of hemorrhagic thalamic stroke ~10 years ago presenting with right hemi body pain. He recovered well from his initial hemiparesis and numbness with rehabilitation. About 2-3 weeks after his stroke, he began noticing intense pain in his right lower leg, with dysesthesias in his right arm and right thorax, impairment to his cognitive ability, mentation, and mood changes. These symptoms have been constant since onset. He reports his pain is worst in the right lower extremity localized from approximately the right knee down to the right foot. He endorsed sharp shooting electric pain, paresthesias, numbness, cramping. and cognitive impairments with mood changes. He failed treatment options including neuropathic pain medications, NSAIDs, Tylenol, and was considered for opioids but declined.

Results: During the SCS trial, the patient endorsed 100% relief of his symptoms in his upper extremity and decreased severity of his right lower extremity discomfort by >50%. He also expressed significant improvement in his mood and cognition. Patient reported >80% overall improvement in pain and function after 3 months s/p permanent implantation consistent with SCS trial results.

Discussion: There is a paucity of information regarding outcomes after SCS therapy for patients with CPSP after a thalamic stroke. This case is unique in that it highlights SCS stimulation for treatment of thalamic hemi body thalamic pain syndrome and treatment for associated cognitive deficits and mood changes.

Conclusions: This case report serves to increase awareness within the medical community that spinal cord stimulation can be a viable treatment option for patients suffering CPSP syndrome with hemi-body pain and cognitive dysfunction.

Supplemental Data: Figure 1: (A,left) Thoracic lead placed. **(B,right)** Cervical lead placed.

References: [1] Henry, J.L.; Lalloo, C.; Yashpal, K. Central Poststroke Pain: An Abstruse Outcome. *Pain Res. Manag.* **2008**, *13*, 41–49. [2] Ri, S. The Management of Poststroke Thalamic Pain: Update in Clinical Practice. *Diagnostics* **2022**, *12*, 1439. https://doi.org/10.3390/ diagnostics12061439 [3] Klit, H., Finnerup, N. B., & Jensen, T. S. (2009). Central post-stroke pain: Clinical characteristics, pathophysiology, and management. *The Lancet Neurology*, *8*(9), 857–868. https://doi.org/10.1016/s1474-4422(09)70176-0 [4] Singer, J., Conigliaro, A., Spina, E., Law, S. W., et. al (2017). Central poststroke pain: A systematic review. International Journal of Stroke, 12(4), 343-355. https://doi.org/10.1177/1747493017701149 [4] Wan, L., Li, Z., Liu, T., et. al (2020). Epoxyeicosatrienoic acids: Emerging therapeutic agents for Central post-stroke pain. Pharmacological Research, 159, 104923. https://doi.org/10.1016/j.phrs.2020.104923 [5] Liampas, A.,

Velidakis, N., Georgiou, T., Vadalouca, A., Varrassi, G., Hadjigeorgiou, G. M., Tsivgoulis, G., & Zis, P. (2020). Prevalence and management challenges in central post-stroke neuropathic pain: A systematic review and meta-analysis. *Advances in Therapy*, *37*(7), 3278–3291. https://doi.org/10.1007/s12325-020-01388-w [6] Xu, W., Zhang, C., Sun, B., & Li, D. (2020). Sustainable effects of 8-year intermittent spinal cord stimulation in a patient with thalamic post-stroke pain. *World Neurosurgery*, *143*, 223–227. https://doi.org/10.1016/j.wneu.2020.07.195 [7] Noori, S., & Mehta, N. (2018). Management of medically refractory central poststroke pain using high-frequency spinal cord stimulation at 10 KHz. *Neuromodulation: Technology at the Neural Interface*, *21*(8), 823–825. https://doi.org/10.1111/ner.12718 [8] Aly, M. M., Saitoh, Y., Hosomi, K., Oshino, S., Kishima, H., & Yoshimine, T. (2010). Spinal cord stimulation for central poststroke pain. *Operative Neurosurgery*, *67*(3). https://doi.org/10.1227/01.neu.0000382965.95819.73 [9] Lopez, J. A., Torres, L. M., Gala, F., & Iglesias, I. (2009). Spinal cord stimulation and thalamic pain: Long-term results of eight cases. *Neuromodulation: Technology at the Neural Interface*, *12*(3), 240–243. https://doi.org/10.1111/j.1525-1403.2009.00221.x [10] Feierabend D, Frank S, Kalff R, Reichart R. Hochzervikale Rückenmarkstimulation bei Thalamusschmerz : Fallbericht und Übersicht zur aktuellen Literatur [Spinal cord stimulation for thalamic pain: Case report and review of the current literature]. Schmerz. 2016 Apr;30(2):152-7. German. doi: 10.1007/s00482-015-0073-6. PMID: 26491023. [11] Tanei, T., Kajita, Y., Takebayashi, S., Aoki, K., Nakahara, N., & Wakabayashi, T. (2019). Predictive factors associated with pain relief of spinal cord stimulation for Central Post-stroke pain. *Neurologia Medico-Chirurgica*, *59*(6), 213–221. https://doi.org/10.2176/nmc.oa.2018-0292 [12] Liampas, A.; Velidakis, N.; Georgiou, T.; Vadalouca, A.; Varrassi, G.; Hadjigeorgiou, G.M.; Tsivgoulis, G.; Zis, P. Prevalence and Man-agement Challenges in Central Post-Stroke Neuropathic Pain: A Systematic

Acknowledgements: none

Learning Objectives: 1. Increase awareness of thalamic pain syndrome for pain medicine doctors and interventionalists. 2. Increase awareness of successful treatment options with SCS for treatment of cognitive/mood symptoms as well as typically reported stroke pain symptoms for clinicians and patients. 3. To add upon the literature and reported cases of successful therapy with neuromodulation for patients with stroke pain.

Financial Disclosures: no significant relationships

Disclosure: No significant relationships.

288

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

THE MUSCLESCS TECHNIQUE – LONGTERM RESULTS: CLINICAL TRIAL WITH MUSCLESCS STIMULATION AND BURST SCS AS DEFINED BY DE RIDDER IN THE TREATMENT OF BACK PAIN

Matthias Morgalla, MD, Philipp Wetzel, MB ChB
University of Tuebingen, Neurosurgery, Tuebingen, Germany

Introduction: MuscleSCS is a new technique that makes it possible to stimulate the back muscles using an SCS electrode and this provides a pain-relieving massage. Our two clinical trials showed that the combined use of MuscleSCS and Burst SCS stimulation, as defined by De Ridder, resulted in a significant improvement in the treatment of lower back pain. We wanted to examine long-term outcomes now over a period of up to 4 years using this new method.

Materials / Methods: Patients with chronic lower back pain had previously received an SCS system (Octrode or percutaneous plate-electrode). These patients used Burst SCS stimulation as defined by De Ridder and also MuscleSCS (4-8Hz) twice a day for 30 min each. A crossover was possible. The patients were initially part of two clinical studies and carried on with the treatment afterwards. We now examined these patients regarding their pain, possible side effects, duration of the MuscleSCS stimulation and patient satisfaction.

Results: This is a single-center retrospective, crossover study (2/2019-4/2023). We included 65 patients and were able to evaluate 44 patients (female 49%, mean age 65.5 years). The period of MuscleSCS stimulation was: 1-12 months: n=4; 13–24 months: n=7; 25–36 months: n = 21; 37-48 months: n=12. The initial VAS was 8.37 and after treatment, it was 4.86. 74% of patients used the combined treatment. 86% of patients were still using MuscleSCS after 4 years. There were no serious adverse events. 75% of patients experienced an improvement in their back pain with MuscleSCS.

Discussion: To date, it has not been possible to adequately treat muscle pain with SCS neuromodulation [1]. However, with low-frequency stimulation of 2-8 Hertz, it is possible to reach the muscles by directly stimulating the motor neurons in the anterior horn of the spinal cord. This type of stimulation triggers a massage-like effect in the patient's muscles, which most patients describe as pleasant and pain-relieving.

Conclusions: This long-term study showed that the use of Burst SCS, as defined by De Ridder and additional MuscleSCS stimulation (4-8Hz), using a rod-electrode or a plate-electrode, could improve the outcome of patients with chronic back pain.

Supplemental Data:

References: 1. Eckermann JM, Pilitsis JG, Vannaboutathong C, Wagner BJ, Province-Azalde R, Bendel MA. Systematic Literature Review of Spinal Cord Stimulation in Patients With Chronic Back Pain Without Prior Spine Neuromodulation. 2021 Aug 18

Acknowledgements:

Learning Objectives: MuscleSCS can further improve the treatment of back pain.

Financial Disclosures: Conflict of interest: MH Morgalla has been a speaker for Abbott. The other author has no conflicts of interest to declare.

Disclosure: No significant relationships.

289

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

THE MUSCLESCS TECHNIQUE: CLINICAL TRIAL WITH MUSCLESCS AND BURST SCS STIMULATION AS DEFINED BY DE RIDDER AND PERCUTANEOUS RODE-ELECTRODES IN THE TREATMENT OF BACK PAIN

Matthias Morgalla, MD, Laura Olbrisch, MB ChB
University of Tuebingen, Neurosurgery, Tuebingen, Germany

Introduction: We did a pilot study, which showed that it is possible to create pleasant and pain-relieving muscle stimulation in the back using low-frequency SCS stimulation and we named this method the “MuscleSCS” technique. In this clinical trial, we wanted to investigate the effectiveness of this method in treating chronic lower back pain, using rod-electrodes. Our hypothesis was that the combined use of MuscleSCS and Burst SCS, as defined by De Ridder, will improve this treatment.

Materials / Methods: Patients with chronic lower back pain had previously received an SCS system (Octrode) (1-4 years ago). They were then randomly treated for two weeks each with only Burst SCS, as defined by De Ridder, or with only MuscleSCS stimulation or Burst SCS, as defined by De Ridder, combined with MuscleSCS stimulation. The patients were then treated with one of these 3 methods for another 6 weeks (crossover possible). Pain ratings (VAS) were recorded and compared. A questionnaire (PDI) was used at baseline and after 3 months.

Results: This is a prospective, single-center, single-blinded, randomized crossover study. We included 24 patients in this study (11 females, mean age 62.3 yrs.). The combined application of Burst SCS, as defined by De Ridder, with MuscleSCS stimulation (4-8Hz) was significantly better than Burst SCS, as defined by De Ridder, on its own (p=0.032) (Fig.1). No serious adverse events occurred during this study. 71.5% of the tested subjects experienced an improvement in their pain using the additional MuscleSCS stimulation.

Discussion: To date, it has not been possible to adequately treat muscle pain with SCS neuromodulation. However, with low-frequency stimulation of 2-8 Hertz it is possible to reach the muscles by directly stimulating the motor neurons in the anterior horn of the spinal cord. This type of stimulation triggers a massage-like effect in the patient's muscles, which most patients describe as pleasant and pain-relieving.

Conclusions: This study showed that the use of Burst SCS, as defined by De Ridder, and additional MuscleSCS stimulation using a rod-electrode could significantly improve the outcome of patients with chronic back pain.

Supplemental Data:

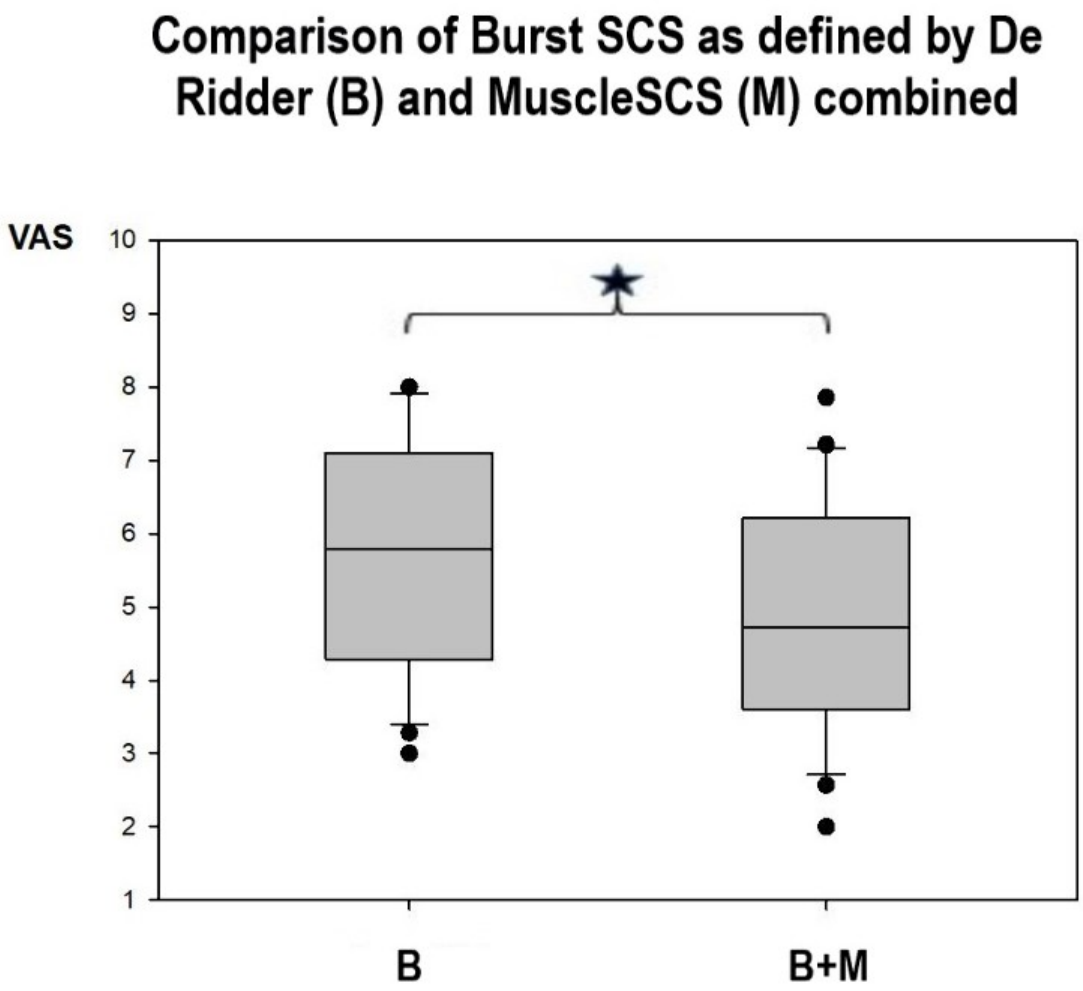


Figure 1

References: 1. Eckermann JM, Pilitsis JG, Vannaboutathong C, Wagner BJ, Province-Azalde R, Bendel MA. Systematic Literature Review of Spinal Cord Stimulation in Patients With Chronic Back Pain Without Prior Spine Neuromodulation. 2021 Aug 18

Acknowledgements:

Learning Objectives: MuscleSCS can further improve the treatment of back pain.

Financial Disclosures: Conflict of interest: MH Morgalla has been a speaker for Abbott. The other author has no conflicts of interest to declare.

Disclosure: No significant relationships.

290

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

SPINAL CORD STIMULATION IN PATIENTS WITH PAINFUL DIABETIC PERIPHERAL NEUROPATHY: A SUB-ANALYSIS FROM THE SENSE SCS STUDY

Melissa Murphy, MD[1], Andrew Will, MD[2], Velimir Micovic, MD[3], Thomas White, MD[4], Jugal Dalal, MD[5], Krishnan Chakravarthy, MD, PhD[6], Xiaoxi Sun, MA[7], Grace Santa Cruz Chavez, PhD, MSBmE[7], Louis Archila, BSc[7], Maddie Larue, PhD[7]
[1]North Texas Orthopedics & Spine Center, Grapevine, United States of America, [2]Twin Cities Pain Clinic, Minneapolis, United States of America, [3]Pain Management Consultants of Southwest Florida, Fort Myers, United States of America, [4]Procura Pain and Spine PLLC, Houston, United States of America, [5]Novant Health Spine Specialists, Winston-Salem, United States of America, [6]Coastal Research Institute, Carlsbad, United States of America, [7]Medtronic Neuromodulation, Minneapolis, United States of America

Introduction: Diabetic peripheral neuropathy (DPN) is a common neuropathic syndrome seen in 30% of patients with diabetes.[1] DPN can present with painful symptoms including bilateral stabbing or burning pain, in addition to numbness in the feet and lower legs.[1] Spinal cord stimulation (SCS) is a non-opioid therapy that has been shown to be an effective treatment for painful DPN in multiple randomized controlled trials.[2-3] A sub-analysis of real-world data collected from patients with painful DPN receiving SCS therapy was conducted utilizing a digital health platform.

Materials / Methods: The SENSE SCS (Study to Evaluate Neuromodulation Subject Experience with Contemporary Spinal Cord Stimulation Modalities for Chronic Pain) clinical trial (NCT05775510), is a prospective, multi-center, post-market, non-randomized, observational study with a hybrid decentralized model of execution. Subjects are electronically consented via a custom mobile application that also collects electronic patient reported outcomes (ePROs) at baseline, before, during, and after SCS trial, and after implantation of a permanent SCS system through 12 months. Subjects were trialed with commercially available SCS systems with a variety of programming types. The PROMIS-29 profile measure assesses seven domains (pain interference, ability to participate in social roles and activities, sleep disturbance, fatigue, depression, anxiety and physical function) and pain intensity. Higher PROMIS symptom scores reflect worse symptom burden, and higher PROMIS function scores reflect better functioning. PROMIS-29 domains, and pain intensity (0-10 numeric rating scale via PROMIS- 29 questionnaire) post-trial will be compared with baseline.

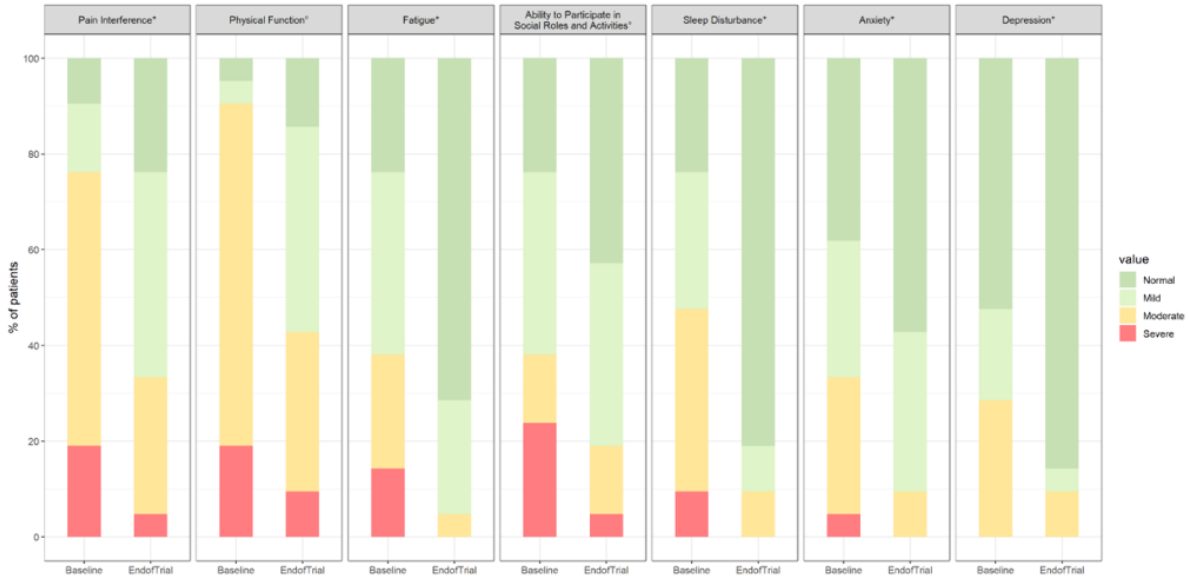
Results: The study was initiated at 6 US sites. Between April 26, 2023 and March 13, 2024, 31 subjects with painful DPN were enrolled. The study is currently in a Pilot phase, and enrollments are currently ongoing. Patient demographics to-date are presented in Table 1. PROMIS-29 domains were characterized pre- and post-trial (Figure 1) with improvements observed in all seven domains.

Discussion:

Conclusions: This sub-analysis of patients with painful DPN who underwent SCS trial demonstrates clinically important quality of life improvements in most PROMIS-29 domains. Findings from this analysis suggest SCS can be an effective therapy for painful DPN that should be considered when treating this patient population. Additionally, this study supports the use of digital health technology to allow for rapid and robust ePRO collection.

Supplemental Data:

Figure 1: PROMIS-29 Domains at Baseline and End of SCS Trial (N=21)



° Defined as: Normal (≥45), Mild (40-45), Moderate (30-40) and Severe (<30)

* Defined as: Normal (<55), Mild (55-60), Moderate (60-70) and Severe (≥ 70)

Table 1: Subject Characteristics

Age (Years), median (min – max) [N=31]	**62 (40-84)**
Sex Female n, (%) [N=31]	**11 (35.5%)**
Baseline NRS from PROMIS-29 median, (min – max) [N=27*]	**7 (4 – 10)**
Pain Duration, [N=28*]	
< 12 months, n (%)	**3 (11.1%)**
1-3 years, n (%)	**6 (22.2%)**
> 3 years, n (%)	**19 (70.4%)**
Baseline EQ-5D-5L, mean (± SD) [N=27*]	**0.343 (± 0.380)**
Pain Medication Usage – n (%) [N=27*]**	**23 (85.2%)**

***Out of 31 enrolled subjects, 28 have completed the baseline pain assessment at time of writing**
****Number of subjects taking at least one pain medication at baseline for pain that the SCS device is intended to treat**

References: 1. Sloan G, et al. The treatment of painful diabetic neuropathy. Current Diabetes Reviews. 2022;18(5):e070721194556. 2. de Vos CC, et al. Spinal cord stimulation in patients with painful diabetic neuropathy: a multicentre randomized clinical trial. Pain. 2014;155(11):2426-31. 3. Slangen R, et al. Spinal cord stimulation and pain relief in painful diabetic peripheral neuropathy: a prospective two-center randomized controlled trial. Diabetes Care. 2014;37(11):3016-24.

Acknowledgements: This study was sponsored by Medtronic.

Learning Objectives: 1) The attendee will understand the impact of a digital health platform on the execution of pain clinical trials. 2) The participant will recognize the positive impact that spinal cord stimulation therapy has on a real-world population of patients with diabetic peripheral neuropathy. 3) The attendee will evaluate the utility of holistic measurements of health, such as PROMIS-29, as a key outcome of treatment success.

Financial Disclosures: Melissa Murphy: Consultant, Medtronic, Relievant Andrew Will: None Thomas White: Consultant, Speaker, Medtronic Velimir Micovic: Speaker, Medtronic Jugal Dalal: None Krishnan Chakravarthy: Consultant, Vertos Medical, Medtronic, Mainstay Medical; Stock Options, Neuronoff, Higgs Boson Health, Rune Labs; Owner, NXTSTIM INC., Accufix Medical. Xiaoxi Sun, Rupinder Bharmi, Grace Santa Cruz Chavez, and Louis Archila: Employees, Medtronic.

Disclosure: No significant relationships.

291

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

TREATMENT OF PAINFUL POLYNEUROPATHIES IN REAL-WORLD PATIENTS USING PRECISION DOSE CONTROL CLOSED-LOOP SCS: A CASE-SERIES

Harold Nijhuis, MD[1], Lars Elzinga, MD[2], Willem-Jan Hofsté, MD[3]
[1]St. Antonius Hospital, Anesthesiology, Nieuwegein, Netherlands, [2]Bravis Hospital, Roosendaal, Netherlands, [3]St. Antonius Hospital, Nieuwegein, Netherlands

Introduction: The most common type of diabetic peripheral neuropathy is distal symmetric polyneuropathy[1] which accounts for approximately 75% of all diabetic neuropathies[2,3]. Treatment options include antidepressants, gamma-aminobutyric acid (GABA) analogs, opioids, and topical analgesics, which are intended to alleviate pain and symptoms of neuropathy, but limited data are available on their efficacy. ECAP-controlled (evoked compound action potential) closed-loop (CL) spinal cord stimulation (SCS) provides better pain control than conventional "open-loop" SCS by ensuring consistent and accurate activation of the spinal cord[4]. Here we present a retrospective case series on painful polyneuropathy patients who were candidates for ECAP-controlled CL SCS in routine commercial practice.

Materials / Methods: Patients (n=9; 2 sites) with peripheral polyneuropathy with chronic intractable pain were considered as candidates for an ECAP-controlled CL SCS were included in this case-series. Informed consent was obtained from all patients. Patients with complete 6-month data were included in this analysis. Patient-reported outcomes include pain relief [Numerical Rating Scale (NRS)], and satisfaction (four options ranging from "very satisfied" to "very unsatisfied").

Results: Baseline demographics and clinical characteristics are presented in Table 1. A total of 9 patients underwent permanent implantation of the ECAP-controlled CL SCS system. A total of 44.5% (4/9) patients had previous neuromodulation experience. Mean pain relief based on NRS at 6-months was 65%. At 6-months pain responder rate (≥50% NRS improvement) was 89% (8/9 patients) and pain high responder rate (≥80% NRS improvement) was 44% (4/9 patients). At 6-months, 100% of the patients reported being very satisfied or satisfied with their therapy, and 78% (7/9 patients) found the stimulation pleasant or were neutral to it (neither pleasant nor unpleasant).

Table 1. Baseline demographics and clinical characteristics

Characteristic	
Gender, male/female (n)	5/4
Mean±SD Pain Duration	5.5±2.9 years
Previous Neuromodulation Experience	
DRG	1
Burst and/or Conventional Open-Loop SCS	3
Pain Location	
Bilateral Foot	2
Bilateral Foot and Lower Leg	2
Bilateral Foot, Leg, Buttock and Back	2
Bilateral Foot and Hand	2
Unilateral Hand, Arm and Shoulder	1

Table 2. Overview of Patient Reported Outcomes at the 6-month visit

Pain Relief (NRS)	
Mean Pain Relief	65%
Pain responder rate (≥50% NRS improvement)	89% (8/9 patients)
Pain high responder rate (≥80% NRS improvement)	44% (4/9 patients)
Patient Satisfaction	
Satisfied or Very Satisfied with SCS Therapy	100%
Stimulation Quality	
Pleasant	3
Neither Pleasant nor Unpleasant	4
Unpleasant	2

Discussion: Results strongly suggest that ECAP-controlled CL SCS can lead to a high degree of pain relief and patient satisfaction 6-months post-implantation in real-world patients with painful polyneuropathy.

Conclusions: Preliminary real-world results associated with use of ECAP-controlled CL SCS for treating patients with painful polyneuropathy are comparable to pain relief outcomes from the controlled AVALON multi-center-study[5] and the controlled EVOKE randomized-controlled-trial[4]. The current case series documented promising outcomes in patients with painful polyneuropathy. However, the results should be interpreted with caution because the sample size was small. A prospective evaluation with longer-term follow-up is required to further validate these results.

Supplemental Data:

References: 1. Pop-Busui, R. *et al.* Diabetic Neuropathy: A Position Statement by the American Diabetes Association. *Diabetes Care* **40**, 136–154 (2017). 2. Albers, J. W. & Pop-Busui, R. Diabetic Neuropathy: Mechanisms, Emerging Treatments, and Subtypes. *Curr Neurol Neurosci Rep* **14**, 473 (2014). 3. Dyck, P. J. *et al.* Diabetic polyneuropathies: update on research definition, diagnostic criteria and estimation of severity. *Diabetes Metab Res Rev* **27**, 620–628 (2011). 4. Mekhail, N. A. *et al.* ECAP-controlled closed-loop versus open-loop SCS for the treatment of chronic pain: 36-month results of the EVOKE blinded randomized clinical trial. *Reg Anesth Pain Med* (2023) doi:10.1136/rapm-2023-104751. 5. Brooker, C. *et al.* ECAP-Controlled Closed-Loop Spinal Cord Stimulation Efficacy and Opioid Reduction Over 24-Months: Final Results of the Prospective, Multicenter, Open-Label Avalon Study. *Pain Practice* (2021).

Acknowledgements:

Learning Objectives: 1. Distal symmetric polyneuropathy which accounts for approximately 75% of all diabetic neuropathies is challenging to treat using traditional open-loop SCS 2. ECAP-controlled closed-loop SCS delivers precise and consistent neural activation of the target responsible for pain inhibition 3. ECAP-controlled closed-loop SCS appears to be a promising treatment option for patients with painful peripheral polyneuropathy

Financial Disclosures: Harold Nijhuis, Saluda Medical, Consultant/Advisory Board, 18,000 Lars Elzinga has no relevant conflicts of interest to disclose Willem-Jan Hofsté, Saluda Medical, Consultant/Advisory Board, 800

Disclosure: No significant relationships.

292

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

POSTURAL VARIATION AFFECTS DOSING ACCURACY IN CONVENTIONAL, FIXED-OUTPUT, OPEN-LOOP SCS SYSTEMS

Kiran Patel, MD[1], Johnathan Goree, MD[2], Dave Mugan, BSc (Hons)[3], Jonathan Scott, MD[4], Peter Single, BSc (Hons)[3]
[1]Lenox Hill Hospital, New York, United States of America, [2]University of Arkansas for Medical Sciences, Little Rock, United States of America, [3]Saluda Medical, Sydney, United Kingdom, [4]University of Waikato, Hamilton, New Zealand

Introduction: Fixed-output open-loop (OL) spinal cord stimulation (SCS) systems cannot automatically account for large variations in neural activation induced by physiological activity and movement. This results in variable inhibition of pain processing pathways and suboptimal therapy[1]. According to recent FDA guidance, accurate and consistent therapy delivered using physiologic closed-loop controlled (PCLC) devices can minimize human error and enhance medical care[2]. Evoked compound action potential (ECAP) controlled closed-loop (ECAP-CL) spinal cord stimulation (SCS) is PCLC-based technology that auto adjusts 4+ million times per day to deliver precise and consistent neural activation of the target responsible for pain inhibition[3]. ECAPs provide a direct measure of dorsal column activation and the relationship between stimulation intensity and ECAP amplitude can be presented in an 'activation plot' (AP)[4]. In this experiment we use such APs to compare the extent of posture-dependent variation on dorsal column recruitment (neural activation) in OL and ECAP-CL SCS.

Materials / Methods: AP measurements (Figure 1) in different postures were analysed geometrically. Activation is calculated as the stimulation current divided by the threshold current for each posture[5]. Activation at current can be written algebraically
as

Activation at current I can be written algebraically as

$$A = \frac{I}{I_T} - 1$$

Where I_T is the ECAP threshold current.

Posture-dependent ECAP threshold is calculated by extrapolating the activation plot to the point where the recorded ECAP is 0V. For OL stimulation the ECAP threshold has been shown to closely correlate with the perception threshold[6,7].

Results: Programming an OL system to ECAP threshold in sitting position will result in stimulation being above discomfort threshold in the supine position (Figure 1). Additionally for an OL system, there is no current setpoint that is therapeutic in all postures i.e., between perception and discomfort thresholds all the time. With CL SCS a 100uV target, for a patient programmed while sitting, activation decreases by 13% and 35% in sitting, and supine postures,
respectively.

***Figure 1**: Comparison of open- and closed-loop therapies using activation plots for different postures. For this patient, sitting is the least sensitive posture and supine is the most sensitive posture. Open-loop stimulation is represented by the blue line and closed-loop stimulation by the orange line. Each plot terminates at the discomfort threshold.*

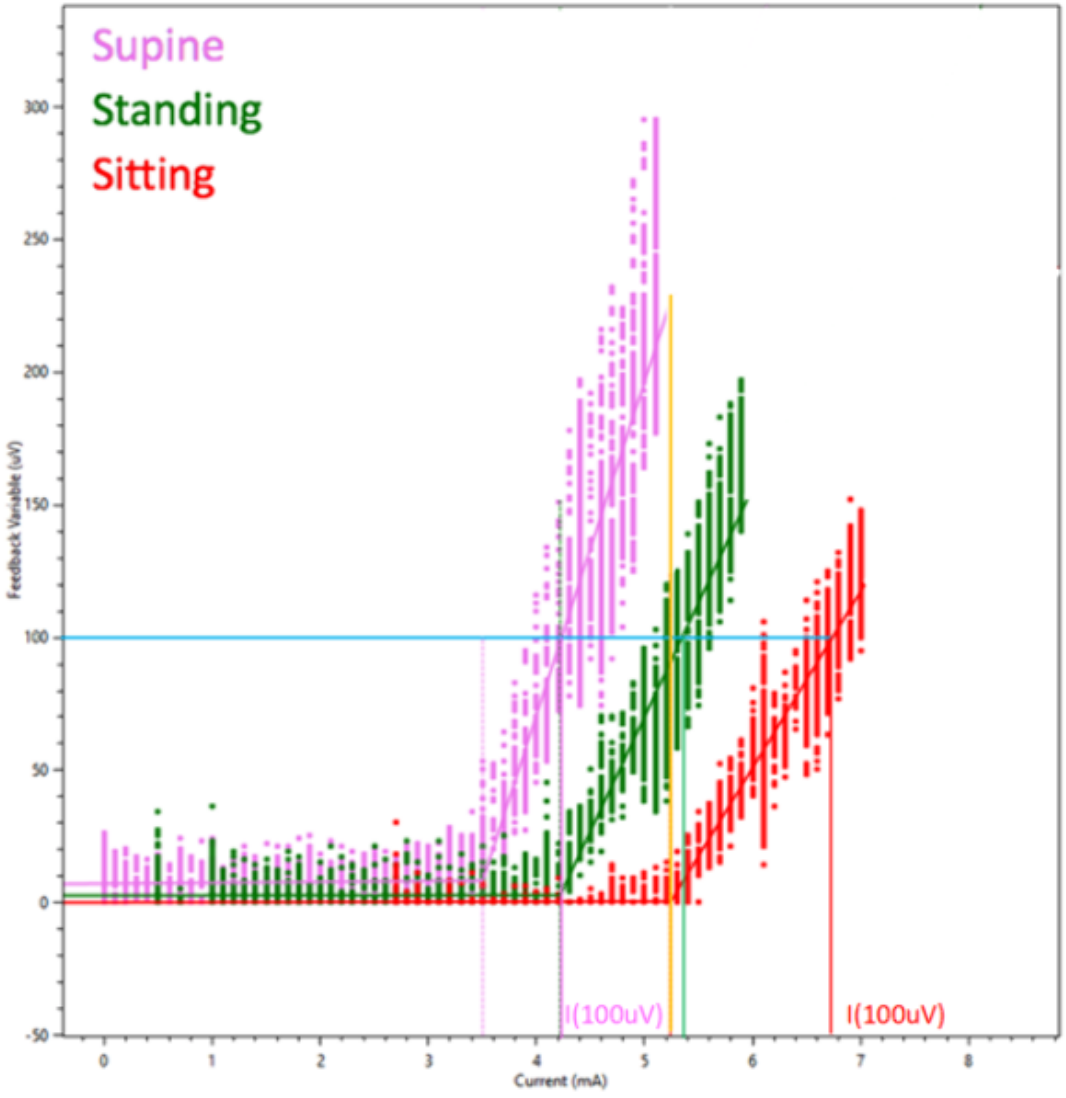


Table 1: Table 1 shows the threshold, maximum current and current required for 100uV ECAP and activation for each posture calculated using the geometric method.

	Posture		
Parameter	Supine	Standing	Sitting
Threshold (mA)	3.5	4.2	5.2
Maximum current (mA)	5.1	5.9	7.0
Current (mA) for 100uV ECAP	4.2	5.35	6.8
Activation in closed-loop for 100uV target	0.2	0.27	0.31
Variation in activation for closed-loop	-35%	-13%	0%
Activation for current = 6.7mA (ECAP=100uV when sitting) in open-loop	0.942	0.619	0.31
Variation in activation for current = 6.7mA in open-loop	+204%*	+99.7%*	0%

* Above the patients maximum comfort level.

Discussion: Using measured neural activation, a CL system can maintain therapeutic stimulation irrespective of postural changes. The change in activation thresholds as the patient changes to more sensitive postures results from the variation in distance between the ECAP recording electrode and the dorsal column for which the loop over-corrects.

Conclusions: Here, we illustrate that ability of CL-SCS in providing consistent and accurate therapeutic stimulation irrespective of posture. Conventional OL therapy delivers a constant stimulus current and requires manual adjustment to allow for posture changes to maintain effective therapy. This could potentially lead to suboptimal clinical outcomes and explants due to loss of efficacy[4].

Supplemental Data:

References: 1. Ross E, Abejón D. Improving patient experience with spinal cord stimulation: implications of position-related changes in neurostimulation. Neuromodulation. 2014;17(S1):36-41. 2. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/technical-considerations-medical-devices-physiologic-closed-loop-control-technology 3. Mekhail, N. A. et al. ECAP-controlled closed-loop versus open-loop SCS for the treatment of chronic pain: 36-month results of the EVOKE blinded randomized clinical trial. Reg Anesth Pain Med (2023) doi:10.1136/rapm-2023-104751. 4. Parker, J., Karantonis, D. & Single, P. Hypothesis for the mechanism of action of ECAP-controlled closed-loop systems for spinal cord stimulation. *Healthc Technol Lett* **7**, 76–80 (2020). 5. Holsheimer, J. Which Neuronal Elements are Activated Directly by Spinal Cord Stimulation. *Neuromodulation* **5**, 25–31 (2002). 6. Pilitsis, J. G. *et al.* The Evoked Compound Action Potential as a Predictor for Perception in Chronic Pain Patients: Tools for Automatic Spinal Cord Stimulator Programming and Control. *Frontiers in Neuroscience* 881 (2021). 7. Gmel, G. E. *et al.* The Effect of Spinal Cord Stimulation Frequency on the Neural Response and Perceived Sensation in Patients With Chronic Pain. *Front. Neurosci.* **15**, 625835 (2021).

Acknowledgements: Trial sponsored by Saluda Medical.

Learning Objectives: Conventional open-loop spinal cord stimulation (SCS) therapy delivers a constant stimulus current and requires manual adjustments to allow for posture changes to maintain

effective therapy. Evoked compound action potential (ECAP) controlled closed-loop SCS uses physiologic closed-loop controlled (PCLC)-based technology that auto adjusts 4+ million times per day ECAP-controlled closed-loop SCS improves consistency and accuracy of therapeutic stimulation during posture changes

Financial Disclosures: Kiran Patel, Saluda Medical, Consultant/Advisory Board, $500-$5000 USD Johnathan Goree, Saluda Medical, Education/Research, $20,001-$100,000 Dave Mugan, Saluda Medical, Employee, > $100,000 USD Jonathan Scott has no relevant conflicts of interest to disclose Peter Single, Saluda Medical, Employee, > $100,000 USD

Disclosure: Administrative support to authors funded by Saluda Medical.

293

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

SPINAL CORD STIMULATION AS A HOLISTIC TREATMENT FOR PAINFUL DIABETIC PERIPHERAL NEUROPATHY (PDPN): OUTCOMES FROM THE INSPIRE STUDY

Jose Paz Solis, MD[1], Cristian Rizea, MD[2], Rafael Martínez-Marín, MD[2], Javier Díaz De Terán, MD[2], María Román De Aragón, MD[1], Beatriz Mansilla, MD[1], Heleen Scholtes, MSc[3], Que Doan, BSc (Hons)[3], Ismael Huertas, PhD[3]
[1]University Hospital La Paz, Neurosurgery, Madrid, Spain, [2]University Hospital La Paz, Neurology, Madrid, Spain, [3]Boston Scientific, Neuromodulation, Valencia, United States of America

Introduction: There is an ongoing effort in neuromodulation to raise awareness on the use of Spinal Cord Stimulation (SCS) to effectively treat painful diabetic peripheral neuropathy (pDPN). Because of their condition, these patients commonly suffer from pain and many other complications in metabolic, cardiovascular and neurological (peripheral and autonomic) functions. In this communication, we introduce the currently ongoing INSPIRE study aiming to in-depth investigate the effects that SCS could holistically exerts in pDPN.

Materials / Methods: Patients with classical “stocking and glove” pDPN pain affecting their lower (primarily) and upper limbs are being treated with SCS: 4-port system and percutaneous leads at thoracolumbar (T10-T12) and, if necessary, cervical (C5-T1) levels (WaveWriter-Alpha, Boston Scientific). Holistic assessments are performed pre- and post-SCS (3-, 6- and 12-months), including: i) standard questionnaires related to pain (e.g. VRS, NPSI), quality-of-life, sleep and dysautonomia (BASQ); and ii) objective tests examining: a) neurological function: EMG, nerve conduction, sensorimotor exam (UENS), skin conductance (ESC), limbs thermography, and small-fiber density quantification (IENFD); b) gait (6MWT with sensors); c) cardiovascular function: peripheral perfusion (tcpO2, ABI) and hemodynamics (deep-breath, Valsalva, Tilt-test); and d) metabolic function: extensive blood-markers panel.

Results: To date, 18 pDPN subjects have been enrolled and 9 implanted and activated. Significant relief of pain and neuropathic symptoms have been observed in both lower limbs (VRS from 8.6 to 1.7) and upper limbs (from 6.2 to 1.1) at last follow-up (mean of ~4.6 months). Stimulation programming relies on low-frequency (50-90Hz) sub-perception paradigm. A generalized improvement in neurological function of distal nerves (both small and large fibers), is being observed, as evidenced by a meaningful relief in neuropathic symptoms (e.g. NPSI from 73 to 7), EMG recordings, sensory function (e.g. UENS from 17 to 4), limbs temperature (e.g. from 33º to 29º) and sudomotor tests (ESC from 29 to 58 µS in feet). IENFD results are still inconclusive. This is accompanied by improvements in other domains, such as sleep, QoL, autonomic symptoms and diabetes-related biomarkers (e.g. HbA1c from 6.8 to 5.1%). Group-results will be reported at the conference.

Discussion: Our early outcomes indicate that SCS can effectively treat pain and other complications in pDPN, such as autonomic, cardiovascular and metabolic dysfunctions. Our study aims to holistically treat pDPN, including thorough patient phenotyping and personalized lead placement and stimulation paradigms.

Conclusions: Specific approaches to SCS can effectively treat peripheral and autonomic neuropathy in pDPN

Supplemental Data:

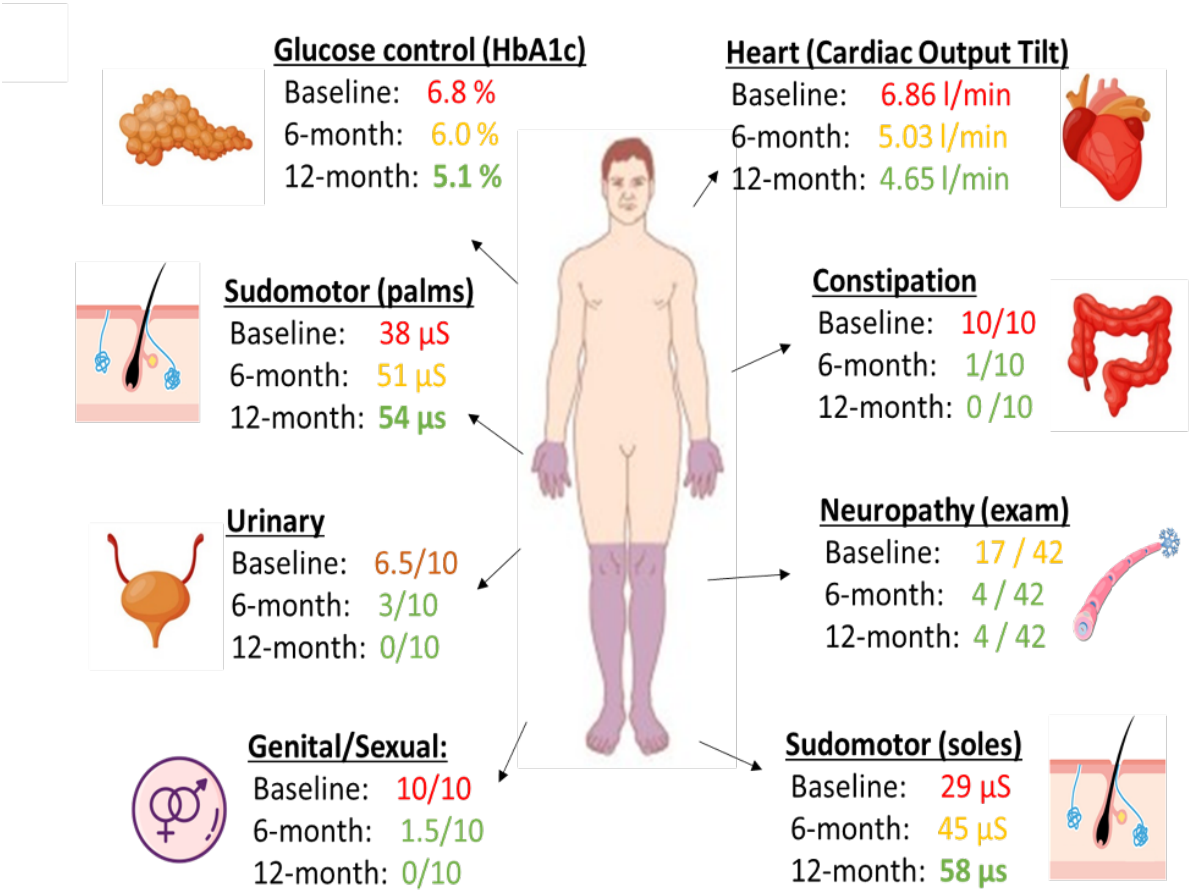


Figure 1. Holistic Outcomes of first INSPIRE pDPN subject reaching the 12-months post-SCS

References:

Acknowledgements: The support of Boston Scientific for this project is gratefully acknowledged.

Learning Objectives: (1) To ascertain SCS approach(es) to effectively treat painful neuropathy in upper and lower extremities in pDPN (2) To assess the effects of SCS in peripheral and autonomic neuropathy in pDPN (3) To investigate in-depth potential physiological changes induced by SCS in pDPN at multiple levels

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

294

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

QUALITY-OF-LIFE AND HBA1C CONTINUE TO IMPROVE AT 4 YEARS POST-IMPLANT IN PATIENTS WITH PAINFUL DIABETIC NEUROPATHY TREATED WITH 10KHZ SPINAL CORD STIMULATION

Erika Petersen, MD[1], Shawn Sills, MD[2], Thomas Stauss, MD[3], Judith White, MD[4], Michael Creamer, MD[5], Rose Azalde, MSBmE[6], Sarah Banducci, PhD[7], Michael Jaasma, PhD[8], David Caraway, MD[9]
[1]University of Arkansas for Medical Sciences, Department Of Neurosurgery, Little Rock, United States of America, [2]Touchstone Interventional Pain Center, Pain Management, Medford, United States of America, [3]Advanced Pain Management, Pain Management, Greenfield, United States of America, [4]AES Compass Orlando, Medical Affairs, Orlando, United States of America, [5]Central Florida Pain Relief Centers, Pain Management, Orlando, United States of America, [6]Nevro Corp., Clinical Research, Redwood City, United States of America, [7]Nevro Corp, Clinical Affairs, Redwood City, United States of America, [8]Nevro Corp., Clinical Affairs, Redwood City, United States of America, [9]Nevro Corp., Medical Affairs, Redwood City, United States of America

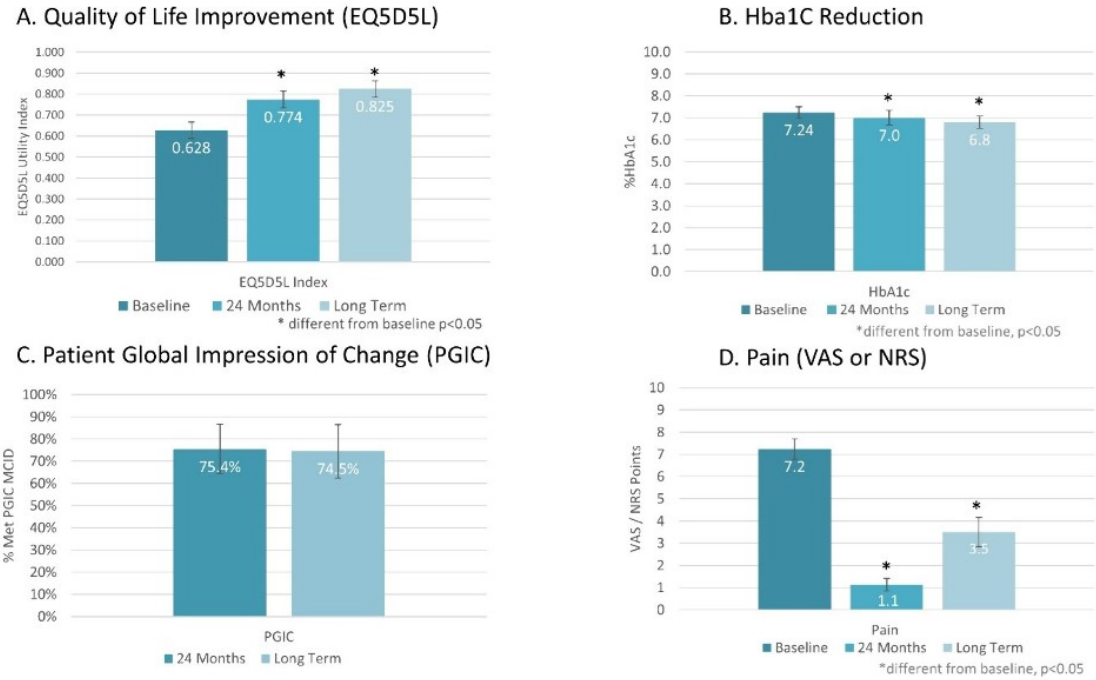
Introduction: Long-term data outside of the controlled clinical trial environment is needed to assess the treatment of painful diabetic neuropathy (PDN) with spinal cord stimulation (SCS). A multicenter PDN RCT has recently demonstrated 24-month durable outcomes with 10kHz SCS to treat PDN[1]. This study further evaluates the durability of 10kHz therapy by assessing a series of patients who had completed the PDN RCT and returned to the real-world health care environment.

Materials / Methods: All patients who completed 24 months follow-up in a large multicenter RCT (PDN RCT) were contacted by phone at approximately 2 years post-study to assess patient's status in terms of PDN related pain of the lower limbs, impression of change, quality of life, HbA1c, and weight. Validated questionnaires were administered including numerical rating scare (NRS) to assess pain, patient global impression of change (PGIC, MCID "Better" or "A Great Deal Better"), and the health-related quality of life questionnaire (EQ-5D-5L). First, we analyzed if there were differences between the patients who responded to this remote survey versus those who did not. Next, in the surveyed population we analyzed how patient status compared to their pre-therapy baseline and to the last study follow-up at 24 months.

Results: The remote survey successfully contacted and assessed 57 patients of the 141 who completed the PDN RCT 24-month follow-up. The 84 patients who were not successfully contacted, were not significantly different compared to those who answered the survey at their 24-month end of study visit in terms of EQ-5D-5L index, PGIC, and weight, but their HbA1c (7.55±1.4 vs 7.00±1.1, p =0.032) and pain (1.7±2.0 vs 1.1±1.0 points, p = 0.041) were slightly higher. Analyzing the survey results, the 57 patients were assessed an average of 4.1±0.5 (2.8 to 5.0) years post 10 kHz SCS implant. Their EQ-5D-5L index was significantly higher at long term follow-up than at the 24-month study assessment (Figure 1A, p = 0.039). The percent of patients who met the PGIC MCID stayed constant (Figure 1B). The NRS was an average 3.8 pt reduction from baseline (Figure 1C). Weight was no different compared to the 24-month study assessment, but HbA1C was statistically lower (Figure 1D, p =0.011). There were no explants due to inefficacy in the contacted

population.

Figure 1.



Discussion: Analysis shows patients continue to experience improvements in quality of life and over-all health at over 4 years post SCS implant.

Conclusions: Patients with PDN treated with 10kHz SCS maintain clinically important durable pain relief.

Supplemental Data:

References: 1. Petersen EA, Stauss TG, Scowcroft JA, et al. Long-term efficacy of high-frequency (10 kHz) spinal cord stimulation for the treatment of painful diabetic neuropathy: 24-Month results of a randomized controlled trial. *Diabetes Res Clin Pract*.

Acknowledgements:

Learning Objectives: 1) Patients with PDN treated with 10kHz SCS maintain clinically important pain relief and continue to experience improvements in quality of life and over-all health at over 4 years post SCS implant.

Financial Disclosures: Erika A. Petersen has received consulting fees from Abbott Laboratories, Biotronik, Boston Scientific, Medtronic Neuromodulation, Nalu Medical, Neuros Medical, Nevro Corp, Presidio Medical, Saluda, and Vertos Medical, research support from Mainstay, Medtronic Neuromodulation, Nalu Medical, Neuros Medical, Nevro Corp, ReNeuron, Saluda, and SPR, and stock options from neuro42 and SynerFuse. Author Thomas G. Stauss has received research support from Nevro Corp. Author Judith L. White has received consulting fees from California Institute for Biomedical Research and Eli Lilly and research support from Nevro Corp. Author Michael J. Creamer has received research support from Nevro Corp. Rose Azalde, Michael Jaasma, Sarah Banducci, and David Caraway are employees of Nevro Corp.

Disclosure: Rose Azalde is an employee of Nevro Corp.

295

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

IMPORTANCE OF BODY MEASUREMENTS IN DEVELOPMENT AND TREATMENT OF CHRONIC PAIN

Frank Trujillo, BS[1], Hannah Thomas, BS[2], Deepak Berwal, PhD[2], Nikhil Rajulapati, BS[2], Marisa Dimarzio, PhD[2], Julie Pilitsis, MD, PhD[2]
[1]Albany Medical College, Neurosurgery, Albany, United States of America, [2]Florida Atlantic University School of Medicine, Neurosurgery, Boca Raton, United States of America

Introduction: Body mass index (BMI) has been shown to negatively correlate with outcomes in Spinal Cord Stimulation (SCS). However, hip and waist circumference (HC and WC respectively) have become recognized as more accurate measurements of body fat. In order to determine how these measurements affect outcomes with SCS, it is first necessary to define normal ranges in patients with chronic pain. Further to ensure that all genders, races and ethnicities receive therapy for chronic pain, it is necessary to obtain a representative sample from across U.S. We used the NIH-sponsored All of Us database to determine the relationship of waist and hip circumference and chronic pain across groups.

Materials / Methods: We investigated waist circumference (WC), hip circumferences (HC) and the waist/hip ratio (WHR) across different cohorts categorized by sex, race, ethnicity and presence of chronic pain. All participants were further divided into four cohorts (total, without chronic pain, those with mild/moderate chronic pain (numeric rating scale (NRS) <7), and those with severe chronic pain NRS $\geq$ 7.

Results: A total of 204,013 participants aged between 18 and 100 years were included. 25.22% of the total cohort had chronic pain diagnoses with 80% described as either chronic pain not otherwise specified or fibromyalgia. In all cohorts, females had significantly greater HC while males had greater WC and WHR. Race and ethnicity also had a significant effect on HC and WHR. WC, HC, and WHR were significantly greater in the severe pain group as compared to the mild moderate pain group (<0.001).

Discussion: These data suggest that when assessing hip and waist circumference demographic variables need to be considered. Patients with severe pain have higher values in all groups and this should be considered when assessing outcomes with SCS or any pain therapy.

Conclusions: When offering treatment to patients with chronic pain, it is important to holistically manage patients.

Supplemental Data:

References: 1.Akresh I. R. (2008). Overweight and obesity among foreign-born and U.S.-born Hispanics. Biodemography and social biology, 54(2), 183–199. https://doi-org.elibrary.amc.edu/10.1080/19485565.2008.9989141 2. All of Us Research Program Investigators, Denny, J. C., Rutter, J. L., Goldstein, D. B., Philippakis, A., Smoller, J. W., Jenkins, G., & Dishman, E. (2019). The "All of Us" Research Program. The New England journal of medicine, 381(7), 668–676. https://doi-org.elibrary.amc.edu/10.1056/NEJMsr1809937 3. Centers for Disease Control and Preventions. Body Mass Index: Considerations for Practitioners Retrieved July 24, 2023, from https://www.cdc.gov/obesity/downloads/BMIforPactitioners.pdf. 4. Brady, S. R. E., Mousa, A., Naderpoor, N., de Courten, M. P. J., Cicuttini, F., & de Courten, B. (2018). Adipsin Concentrations Are Associated with Back Pain Independently of Adiposity in Overweight or Obese Adults. Frontiers in physiology, 9, 93. https://doi-org.elibrary.amc.edu/10.3389/fphys.2018.00093 5. Cameron, A. J., Magliano, D. J., Shaw, J. E., Zimmet, P. Z., Carstensen, B., Alberti, K. G., Tuomilehto, J., Barr, E. L., Pauvaday, V. K., Kowlessur, S., & Söderberg, S. (2012). The influence of hip circumference on the

relationship between abdominal obesity and mortality. International journal of epidemiology, 41(2), 484–494. https://doi-org.elibrary.amc.edu/10.1093/ije/dyr198 6. Chen, X., Tang, H., Lin, J., & Zeng, R. (2022). Causal relationships of obesity on musculoskeletal chronic pain: A two-sample Mendelian randomization study. Frontiers in endocrinology, 13, 971997. https://doi-org.elibrary.amc.edu/10.3389/fendo.2022.971997

Acknowledgements: N/A

Learning Objectives: 1. Understand that increased hip and waist circumferences are seen in chronic pain patients 2. Understand that pain should be looked at in a holistic manner when treatment is offered 3. Understand that demographical variables may also influence chronic pain symptoms in patients

Financial Disclosures: Dr. Pilitsis receives grant support from Medtronic, Boston Scientific, Abbott, NIH 2R01CA166379, NIH R01EB030324, NIH Blueprint 3U54EB015408, and NIH U44NS115111.

Disclosure: No significant relationships.

296

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

DOES MENOPAUSE EFFECT DEVELOPMENT AND TREATMENT OF CHRONIC PAIN?

Adam Ricker, BS[1], Nicole Farley, BS[1], Lisa Goudman, PhD[2], Deepak Berwal, PhD[1], Marisa Dimarzio, PhD[1], Ilknur Telkes, MSN, PhD[1], Julie Pilitsis, MD, PhD[1], Candy Wilson, PhD[1]
[1]Florida Atlantic University, Boca Raton, United States of America, [2]Laarbeeklaan 103, Stimulus Research Group, Jette, Belgium

Introduction: There is mounting evidence that females and males differ in how they experience pain and how they respond to spinal cord stimulation (SCS). Whether the responses females have changes after menopause has not been defined. In order to determine how these measurements affect outcomes with SCS, it is first necessary to define normal ranges in patients with chronic pain. Further to ensure that all genders, races and ethnicities receive therapy for chronic pain, it is necessary to obtain a representative sample from across U.S. We used the NIH-sponsored All of Us database to determine the relationship of menopause with pain intensity across groups.

Materials / Methods: We identified participants in the database with a diagnosis of chronic pain and who had numeric rating scale (NRS) data available. Severe pain was defined as NRS ≥7. Among those with chronic pain, cohorts were divided into females ≥51 years who were presumed to be menopausal, females 18-50 years who were considered pre-menopausal, and age matched male cohorts. Menopausal status was required to be present in the female cohort to be included.

Results: The 53,289 participants were separated into four cohorts by age and sex: females 18-50 (10,269), females ≥51 (20,182), males 18-50 (4,989), and males ≥51 (17,849). NRS scores between the four cohorts differed significantly ($H = 99.71$, $p < 0.001$). Post Hoc testing with Dunn's tests indicated significantly higher pain intensity scores in females 18-50 compared to females $\geq$ 51 and compared to males $\geq$ 51 ($p < 0.001$). The scores of females $\geq$ 51 were significantly lower compared to males 18-50 and significantly higher compared to males $\geq$ 51 ($p < 0.001$). Scores of males 18-50 were significantly higher than those of males $\geq$ 51 ($p < 0.001$). In white, black, and non-hispanic patients, older males and females had lower mean NRS scores as a group compared to younger patients ($p < 0.001$).

Discussion: When offering treatment to patients with chronic pain, it is important to holistically manage patients. These data suggest that menopause impacts the intensity of pain in women. Further, when assessing age, demographic variables need to be considered.

Conclusions: These factors should be considered when assessing outcomes with SCS or any pain therapy.

References: 1. Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. *Pain*. Sep 1 2020;161(9):1976-1982. doi:10.1097/j.pain.0000000000001939 2. Gibson CJ, Li Y, Huang AJ, Rife T, Seal KH. Menopausal Symptoms and Higher Risk Opioid Prescribing in a National Sample of Women Veterans with Chronic Pain. *J Gen Intern Med*. Oct 2019;34(10):2159-2166. doi:10.1007/s11606-019-05242-w 3. Mills SEE, Nicolson KP, Smith BH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. *Br J Anaesth*. Aug 2019;123(2):e273-e283. doi:10.1016/j.bja.2019.03.023 4. Schiller JS, Lucas JW, Ward BW, Peregoy JA. Summary health statistics for U.S. adults: National Health Interview Survey, 2010. *Vital Health Stat 10*. Jan 2012;(252):1-207. 5. Dahlhamer J, Lucas J, Zelaya C, et al. Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults - United States, 2016. *MMWR Morb Mortal Wkly Rep*. Sep 14 2018;67(36):1001-1006. doi:10.15585/mmwr.mm6736a2 6. Institute of Medicine Committee on Advancing Pain Research C, Education. The National Academies Collection: Reports funded by National Institutes of Health. *Relieving Pain in America: A Blueprint for Transforming Prevention,*

Care, Education, and Research. National Academies Press (US) Copyright © 2011, National Academy of Sciences.; 2011. 7. Zelaya CE, Dahlhamer JM, Lucas JW, Connor EM. Chronic Pain and High-impact Chronic Pain Among U.S. Adults, 2019. *NCHS Data Brief*. Nov 2020;(390):1-8.

Acknowledgements: N/A

Learning Objectives: 1. Learn that menopause impacts intensity of pain in women 2. Understand that when treating patients with chronic pain, demographic variables should be considered. 3. Understand that it is important to holistically treat patients with chronic pain

Financial Disclosures: Dr. Pilitsis receives grant support from Medtronic, Boston Scientific, Abbott, NIH 2R01CA166379, NIH R01EB030324, NIH Blueprint 3U54EB015408, and NIH U44NS115111. She is the medical advisor for Aim Medical Robotics and has stock equity. Dr. Telkes receives grant support from NIH R00NS119672 and Micro-Leads (NIH U44NS115111). Dr. Goudman is a postdoctoral research fellow funded by the Research Foundation Flanders (FWO), Belgium (project number 12ZF622N).

Disclosure: No significant relationships.

297

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

LONG-TERM OUTCOMES IN SAME DAY OBJECTIVE SCS TRIAL RESPONDERS: INTERIM RESULTS

Jason Pope, MD[1], Chau Vu, MD[1], Harjot Bhandal, MD[1], Philip Shumsky, MD[1], Abeer Khurram, BSE, MS[2], Ian Gould, MSc, PhD[2], Dean Karantonis, MSBmE, MSBmE[2]
[1]Evolve Restorative Center, Santa Rosa, United States of America, [2]Saluda Medical, Macquarie Park, Australia

Introduction: Traditional Open-Loop (OL) spinal cord stimulation (SCS) trials typically last 3-7 days, and success is defined by 50% reduction in pain symptoms based on subjective patient feedback. Prolonged OL-SCS trials may expose patients to higher risk of infections[1], lead migrations[2], and increase associated patient burden. Prognostic value and cost-effectiveness of SCS trials have also been questioned[3,4]. The TRIAL-STIM RCT showed there was no evidence that a screening trial provides superior patient outcomes[4]. Evoked compound action potential (ECAP)-controlled closed-loop (CL) SCS allows objective confirmation of therapeutic neural activation[5] immediately post-programming potentially enabling a same-day trial evaluation scenario. Herein, we report on the 3-month outcomes for same day responders whose leads were pulled on the same day as the trial procedure after experiencing physiologic ECAP-controlled CL-SCS.

Materials / Methods: Participants with chronic, intractable trunk and/or limb pain were enrolled in the prospective, multicenter ECAP study (NCT04319887). For a subset of patients, leads were pulled on the same day as the trial procedure after an objective trial evaluation was performed. During the trial evaluation, neural activation, and ability to maintain stable closed-loop therapy were objectively confirmed in addition to collection of patient-reported pain relief, functional improvement in various postures, and willingness to proceed to permanent implant. We report the 3-month outcomes of same day lead pull patients from a single center.

Results: Same day responders whose leads were pulled same-day as the trial procedure (N=11) had robust 3-month outcomes: 91% responders (≥50% VAS reduction) and 64% were high-responders (≥80% VAS reduction) with average pain reduction from baseline of 80%. Patients reported high satisfaction with therapy and pain relief (82% of patients “satisfied” or “very satisfied”), and 91% of patients reported being “improved” or “very much improved” on Patient Global Impression of Change (Table

1).

Table 1: 3-month Patient Outcomes for Same Day Lead Pulls.

3-Month Patient Outcomes for same day lead pulls	
50% Responder Rate	90.9% (10/11)
80% Responder Rate	63.6% (7/11)
Average Percent Pain Reduction	79.9% (N = 11)
Satisfaction with Therapy ("Satisfied" or "Very satisfied")	81.8% (9/11)
Satisfaction with Pain Relief ("Satisfied" or "Very satisfied")	81.8% (9/11)
Patient Global Impression of Change ("Much improved" or "Very much improved")	90.9% (10/11)

Discussion: Robust 3-month outcomes for patients whose leads were pulled after an objective trial evaluation provides confidence in same day trials and highlight the potential of same day trials conducted with physiologic ECAP-controlled CL-SCS for predicting long-term responders.

Conclusions: Same day trials may be beneficial for patients using anti-coagulants and for reducing trial complication rates associated with extended trials. Physiologic ECAP-controlled CL may provide objective data to improve prognostic ability of traditional SCS trials in predicting outcomes and reducing associated patient burden.

Supplemental Data:

References: 1. North, R. *et al.* Postoperative Infections Associated With Prolonged Spinal Cord Stimulation Trial Duration (PROMISE RCT). *Neuromodulation J. Int. Neuromodulation Soc.* **23**, 620–625 (2020). 2. Jenkinson, R. H., Wendahl, A., Zhang, Y. & Sindt, J. E. Migration of Epidural Leads During Spinal Cord Stimulator Trials. *J. Pain Res.* **15**, 2999–3005 (2022). 3. Provenzano, D. Spinal Cord Stimulation Trialing: Is Trialing Predictive of Short, Intermediate, and Long-term Pain Outcomes? in *ASRA Pain Medicine Conference 2022*. 4. Eldabe, S. *et al.* Does a Screening Trial for Spinal Cord Stimulation in Patients With Chronic Pain of Neuropathic Origin Have Clinical Utility (TRIAL-STIM)? 36-Month Results From a Randomized Controlled Trial. *Neurosurgery* **92**, 75 (2023). 5. Mekhail, N. *et al.* Durability of Clinical and Quality-of-Life Outcomes of Closed-Loop Spinal Cord Stimulation for Chronic Back and Leg Pain: A Secondary Analysis of the Evoke Randomized Clinical Trial. *JAMA Neurol.* **79**, 251–260 (2022)

Acknowledgements: Trial sponsored by Saluda Medical.

Learning Objectives: 1. The prognostic value and cost utility of traditional open-loop spinal cord stimulation (SCS) trials is debatable 2. ECAP-controlled closed-loop SCS allows objective confirmation of therapeutic neural activation 3. ECAP-controlled closed-loop SCS may provide objective data to improve prognostic ability of traditional SCS trials in predicting outcomes and reducing associated patient burden

Financial Disclosures: Jason Pope, Saluda Medical, Consultant/Advisory Board, >$100,000 USD Chau Vu, Saluda Medical, Consultant/Advisory Board, $1 - $500 USD Harjot Bhandal, Saluda

Medical, Consultant/Advisory Board, $500-$5000 USD Philip Shumsky, Saluda Medical, Consultant/Advisory Board, $500-$5000 USD Abeer Khurram, Saluda Medical, Employee, > $100,000 USD Ian Gould, Saluda Medical, Employee, > $100,000 USD Dean Karantonis, Saluda Medical, Employee, > $100,000 USD

Disclosure: Administrative support to authors funded by Saluda Medical.

298

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

SPINAL CORD STIMULATION IN VARIOUS CHRONIC PAIN SYNDROMES – REAL-WORLD-DATA FOR PAIN AND OPIOID-REDUCTION IN 129 PATIENTS FROM A RETROSPECTIVE SINGLE-CENTER EVALUATION

Dirk Rasche, MD, PhD
University of Luebeck, Department Of Neurosurgery, Lübeck, Germany

Introduction: Epidural spinal cord stimulation (SCS) is an invasive pain treatment option and is performed for more than 50 years. Besides the primary effect of pain reduction, also a lot of additional effects can be evaluated and have a certain impact on the patient's quality of life.

Materials / Methods: In this retrospective analysis 129 patients with various chronic refractory pain syndromes were evaluated (67 women, 62 men, mean age 53.5 years). All patients were implanted with a tonic SCS between 2008-2019 at the institution. Evaluation up to one year postoperative was focused on pain reduction, opioid-intake and correlation with final position of the lead.

Results: Overall, a pain reduction of mean 46.6% was achieved. About 47.5% of patients documented a pain reduction of at least 50% ($p<0.05$). In 18/129 patient's opioid-intake was completely stopped, a mean reduction of the daily dosage of opioids of 46% was evaluated in this patient sample. Even in the evaluation at 9-12 months postoperatively this effect was continuous. Individual analysis demonstrated that in some cases SCS lead to a significant pain reduction and a significant opioid reduction, but in other patients a significant opioid reduction of > 60% was evaluated, but pain reduction was not significant. Evaluation of the anatomical lead position (x-ray) demonstrated no significant correlation or effect on individual pain reduction and opioid consumption.

Discussion: In this evaluation and analysis of a single-center patient cohort a significant reduction of chronic refractory pain and opioid intake was evaluated. Correlation of the anatomical lead position and pain reduction or opioid intake was not significant.

Conclusions: Criteria for SCS effectiveness on pain reduction of at least 50% should be discussed critically as other effects like opioid intake or sleep quality etc. need to be considered as substantial improvement of individual patient's quality of life and success of the SCS therapy.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: SCS in chronic refractory pain Pain reduction and opiod intake Patient´s quality of life

Financial Disclosures: Honorary and travel grants from: Abbott Boston Scientific Curonix Esteve Medtronic Nevro

Disclosure: No significant relationships.

299

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

REAL-WORLD PAIN RELIEF OUTCOMES IN PATIENTS USING FAST-ACTING SUB-PERCEPTION THERAPY (FAST-SCS): A MULTICENTER EUROPEAN STUDY

Simon Bayerl, MD[1], Jose Paz Solis, MD[2], Philippe Rigoard, MD[3], Georgios Matis, MD[4], Jan Willem Kallewaard, MD[5], M. Angeles Canos-Verdecho, MD[6], Jan Vesper, MD[7], Jose Llopis-Calatayud, MD[8], Lilly Chen, MD[9], Virginie Van Belleghem, MSc[9], Edward Goldberg, MD[9]
[1]Charité Universitätsmedizin Berlin, Neurosurgery, Berlin, Germany, [2]University Hospital La Paz, Neurosurgery, Madrid, Spain, [3]Poitiers University, Spinal Neurosurgery, Neuromodulation, Poitiers, France, [4]University Hospital Cologne, Neurosurgery, Cologne, Germany, [5]Rijnstate, Anesthesiology, arnhem, Netherlands, [6]University and Polytechnic Hospital La Fe, Pain Management, Valencia, Spain, [7]University Medical Center, Heinrich Heine University, Functional Neurosurgery And Stereotaxy, Duesseldorf, Germany, [8]University Hospital La Ribera, Pain Unit, Valencia, Spain, [9]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: Traditional Spinal Cord Stimulation (SCS) modalities that achieve sub-perception analgesia (e.g.,~ 1-10 kHz, burstDR) require patients to often wait hours or even days until pain relief is fully realized. A recent study however has demonstrated that quicker analgesic onset is possible using a new subthreshold-based SCS modality called Fast-Acting Sub-perception Therapy (FAST).[1] Achieving rapid onset of pain relief offers a substantial advantage for patients and providers alike when using FAST-SCS in the real-world clinical setting. Here, we report the outcomes of real-world patients who preferred FAST-SCS for chronic pain in a European-based, multicenter, observational study.

Materials / Methods: This is an international, multicenter, observational case-series of patients permanently implanted with a Fast-Acting Sub-perception Therapy (FAST)-enabled SCS system (Boston Scientific, Marlborough, MA USA) to treat chronic pain as part of an ongoing assessment of real-world outcomes of SCS for chronic pain based on retrospective chart review (Clinicaltrials.gov identifier: NCT01550575). All analyzed patients were programmed using novel FAST (i.e., biphasic-symmetric waveform at 90 Hz; pulse width: 160-260 µs). Demographic information, pain location, surgical history, medical history were collected for all subjects. In addition, Numeric Rating Scale (NRS) scores and Percent Pain Relief (PPR) were collected as part of the chart review.

Results: To date, 71 patients have been assessed out to a mean follow-up duration of 465 ± 375 days. Baseline mean NRS pain score in this current cohort was determined to be 7.8±1.4. A 5.1 ± 2.6-point improvement ($p<0.0001$) in overall pain was reported at mean last follow-up (n = 71). Seventy-two percent of those had a pain score of 3 or less. A 5-point improvement was noted (7.8 ⇒ 2.8, n=35) in patients with baseline and 1-year follow-up. Similarly, a 5.4-point improvement at 2-year was noted (7.6 ⇒ 2.1, n = 17). Assessment of quality of life (EQ-5D-5L) and Disability (Oswestry Disability Index) demonstrated substantial improvement compared to baseline measurements. Additional data to be presented.

Discussion: A methodology that allows for near immediate pain relief following activation of neurostimulative treatment represents an advancement that may further improve the outcomes and experience of patients who desire to use sub-perception-based SCS for relief of their chronic pain.

Conclusions: Data from this multicenter, real world, observational, clinical case series demonstrate improvement of chronic pain in patients utilizing and who preferred FAST-SCS up to mean last follow up of 1.3 years. Among the subset of patients with data available up to 2-years, a similar trend was noted (5.5-point improvement).

Supplemental Data:

References: 1. Metzger CS, Hammond MB, Paz Solis JF, Newton WJ, Thomson,SJ, Pei Y, Jain R, Moffitt M, Annecchino L, Doan QA novel fast acting sub perception spinal cord stimulation therapy enables rapid onset of analgesia in patients with chronic pain. Expert Rev Med Devices 2021 Mar 18(3) 299-306.

Acknowledgements:

Learning Objectives: This study will seeks to assess the following in patients using FAST-SCS for chornic pain at follow-up: 1) Pain relief 2) Quality of Life 3) Disability

Financial Disclosures: Drs. Bayerl, Paz-Solis, Matis, Kallewaard, and Vesper have consulting agreements with Boston Scientific. a) Boston Scientific b) consultant c) 5-20k

Disclosure: This study is sponsored by Boston Scientific. Lilly Chen, Virginie Van Belleghem, and Ed Goldberg are employees of Boston Scientific.

300

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

IMPROVED PAIN OUTCOMES AND THERAPY LONGEVITY AFTER SALVAGE USING NOVEL SCS SYSTEMS: EUROPEAN EXPERIENCE

Philippe Rigoard, MD[1], Renaud Bougeard, MD[2], Jose Llopis-Calatayud, MD[3], Sylvie Raoul, MD[4], Georgios Matis, MD[5], Hayat Belaid, MD[6], Jan Vesper, MD[7], M. Angeles Canos-Verdecho, MD[8], Sarah Love Jones, MBBS BSc FRCA FFPMRCA EDPM[9], Adam Williams, MD[10], Virginie Van Belleghem, MSc[11], Yu Pei, MPA[11], Edward Goldberg, MD[11]
[1]Poitiers University, Spinal Neurosurgery, Neuromodulation, Poitiers, France, [2]Clinique de la Sauvegarde, Pain Management, Lyon, France, [3]University Hospital La Ribera, Pain Unit, Valencia, Spain, [4]University Hospital Nantes, Neurosurgery, Nantes, France, [5]University Hospital Cologne, Neurosurgery, Cologne, Germany, [6]Fondation Adolphe de Rothschild, Neurosurgery, Paris, France, [7]University Medical Center, Heinrich Heine University, Functional Neurosurgery And Stereotaxy, Duesseldorf, Germany, [8]University and Polytechnic Hospital La Fe, Pain Management, Valencia, Spain, [9]Southmead Hospital, Pain Medicine, Bristol, United Kingdom, [10]Southmead Hospital, Neurosurgery, Bristol, United Kingdom, [11]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: Spinal Cord Stimulation (SCS) is an effective therapy for chronic neuropathic pain, with its long-term efficacy well-established. However, some patients experience loss of efficacy (LoE) over time and become refractory over the course of follow-up.[1] Providing various waveforms and programming options in novel SCS systems can facilitate more customized delivery of analgesic neurostimulation to chronic pain patients implanted with an SCS device. However, technologies that offer such optimization capabilities are not accessible to long-term implanted patients using older devices, some of whom may experience loss or attenuation in therapeutic efficacy over time. These patients therefore may elect to undergo a "conversion" to a different SCS system that possesses these capabilities.

Materials / Methods: This is a real-world, multicenter retrospective study of patients who were previously implanted with an SCS system (commercially-available device) who went on to convert to a new device (Boston Scientific) capable of multiple modality stimulation and/or combination therapy via an applicable device adaptor and new implantable pulse generator (IPG). Pain relief and other associated outcomes using both the previously-implanted SCS system and the newly connected device IPG are being collected.

Results: Fifty-eight patients (mean age = 58.3 years) have been assessed to date. A mean baseline overall pain (NRS) score of 7.8 ± 1.9 (n = 47) was reported prior to receiving SCS. Seventy-one percent of patients (N = 41) chose to convert for better pain relief followed by the need to access multiple programs (34%) and/or to get coverage of new areas of pain (33%). Previous SCS devices represent a range of different manufacturers. Among all patients (regardless of reasons for conversion), a pain score of 3.1 was noted at last follow-up and sustained improvement was noted up to 3.4 years with current systems. In patients for whom the conversion was performed to “rescue” suboptimal outcomes with the previous system (N=49), a mean 3.9-point improvement with the current system was noted at last follow-up (3.6 years post-implant, 7.3 ⇒ 3.4, $p<0.0001$).

Discussion: When experiencing problems with SCS device longevity and/or loss of efficacy, some previously-implanted patients may be able to obtain better outcomes using more advanced neuromodulation systems that offer a range of waveforms and programming options to address their chronic pain.

Conclusions: Significant improvement was noted in overall pain in patients who converted to a new SCS device capable of providing multiple device programming options including anatomically guided paresthesia based stimulation, combination therapy, and novel sub-perception modalities.

Supplemental Data:

References: 1. Deer TR, Mekhail N, Provenzano D, et al Neuromodulation Appropriateness Consensus Committee The appropriate use of neurostimulation avoidance and treatment of complications of neurostimulation therapies for the treatment of chronic pain Neuromodulation Appropriateness Consensus Committee. *Neuromodulation* 2014 Aug 17 6 571-97. discussion 597-8.
2. Kumar K, Hunter G, Demeria D Spinal cord stimulation in treatment of chronic benign pain challenges in treatment planning and present status, a 22-year experience. *Neurosurgery* 2006 Mar 58 3 481 96 discussion 481-96.

Acknowledgements:

Learning Objectives: 1. To assess pain relief outcomes (including long-term outcomes) in an SCS-implanted population (with sub-optimal pain relief) who have replaced their older generation SCS batteries with a newer generation device that provides multiple modalities.
2. To assess the reasons for conversion in patients who converted to newer SCS systems.
3. To evaluate the programs that are most preferred by patients who have converted to a newer SCS system.

Financial Disclosures: Drs. Rigoard, Raoul, Matis, and Vesper have consulting agreements with Boston Scientific. a) Boston Scientific b) consultant c) 5-20k

Disclosure: This study is sponsored by Boston Scientific. Lilly Chen, Virginie Van Belleghem, and Edward Goldberg are employees of Boston Scientific.

301

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

PAIN RELIEF OUTCOMES USING PERIPHERAL NERVE FIELD STIMULATION (PNFS) COMBINED WITH SPINAL CORD STIMULATION IN CHRONIC PAIN

Philippe Rigoard, MD[1], Paolo Maino, MD[2], Eva Koetsier, MD[2], Simon Bayerl, MD[3], Jose Llopis-Calatayud, MD[4], Sylvie Raoul, MD[5], Lilly Chen, MD[6], Virginie Van Belleghem, MSc[6], Edward Goldberg, MD[6]
[1]Poitiers University, Spinal Neurosurgery, Neuromodulation, Poitiers, France, [2]Pain Management Center, Neurocenter of Southern Switzerland, Pain Management, Lugano, Switzerland, [3]Charité Universitätsmedizin Berlin, Neurosurgery, Berlin, Germany, [4]University Hospital La Ribera, Pain Unit, Valencia, Spain, [5]University Hospital Nantes, Neurosurgery, Nantes, France, [6]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: Peripheral Nerve Field Stimulation (PNFS) and Spinal Cord Stimulation (SCS) are treatment options for patients with chronic pain. Combining localized stimulation using PFNS along with SCS may have potential to treat areas of pain not previously covered with SCS alone. To address this question, we undertook an observational, multicenter study of patients using PNFS together with SCS implanted with a device that allows for precise customized programming of therapeutic neurostimulation parameters and settings.

Materials / Methods: This is a multicenter, observational case-series of patients implanted with a neuromodulation system (Precision™, Precision Spectra™, Spectra WaveWriter™, Boston Scientific, Marlborough, MA, USA) conducted as part of an on-going retrospective chart review evaluation of real-world outcomes for chronic pain (Clinicaltrials.gov: NCT01550575). Patients were diagnosed with chronic pain and treated with PNFS as an "add on" therapy to SCS. Assessments collected include baseline characteristics (demographics, medical history, pain diagnosis) and pre- and post-implant outcomes (NRS pain score).

Results: To date, a total of 33 patients (22 Female, mean age 57.3 ± 12.2 years) who received both SCS and PNFS for the treatment of their pain were analyzed. At baseline, a mean overall pain score of 7.8 ± 1.4 (NRS) was reported which reduced to 3.1 ±1.3 (Δ= 4.9) out to 24-months follow-up. This represents a 62% reduction in overall pain versus baseline. Data collection and analysis is still ongoing, and updated, new results will be presented.

Discussion: Neuromodulation systems capable of providing various stimulation waveforms, parameters, and programming settings that can be used in a selective, individual manner by patients utilizing PNFS and SCS in combination can elicit effective analgesic outcomes.

Conclusions: Results of this observational case-series so far demonstrate that patients who use PNFS along-with SCS for treatment of chronic pain can achieve significant and clinical meaningful pain relief. Additional study is needed.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. To assess the baseline pain of patients who use SCS combined with PNFS for treatment of chronic pain.
2. To assess pain relief (at the last follow-up visit) in patients who use SCS combined with PNFS for treatment of chronic pain.

3. To track the pain relief over 6-months and 2-years follow-up in patients who use SCS combined with PNFS for treatment of chronic pain.

Financial Disclosures: Drs. Rigoard, Bayerl, and Raoul have consulting agreements with Boston Scientific. a) Boston Scientific b) consultant c) 5-20k

Disclosure: This study is sponsored by Boston Scientific. Lilly Chen and Edward Goldberg are employees of Boston Scientific.

302

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

CASE REPORT: 10KHZ STIMULATION FOR INTRACTABLE PAIN IN BRACHIAL PLEXUS AVULSION

Beatriz Mansilla, MD, María Román De Aragón, MD, Jose Paz Solis, MD
University Hospital La Paz, Neurosurgery, Madrid, Spain

Introduction: Brachial plexus injuries are devastating for the person who suffers from them and their environment. The most common etiology is traumatic. Although Tonic Spinal Cord Stimulation (SCS) has shown standard results in the treatment of this pathology, it has been shown that High frequency stimulation has superior results in both pain relief and quality of life than this type. of patients.
This abstract presents a case of a patient with pain due to deafferentation of the left brachial plexus, caused by multiple trauma in 2017. After several surgeries, she presents with chronic neuropathic pain, and is referred to our service for subsequent pain control.
In the consultation we propose implantation of a 10Khz SCS or a DREZ, which destroys the aberrant transmission, reducing pain through multiple thermal RF lesions in the posterolateral sulcus.
Patient implanted in the test phase for 10 days with a High Frequency spinal stimulator (10KHz) with a 50% reduction in VAS and subsequently implanted with the Omnia HFX stimulation system whose VAS reduction is 80%.

Materials / Methods: 47-year-old man, with complete postganglionic section C5, C6 and C7, with preganglionic avulsion C7 and complete preganglionic avulsion C8 and T1, referred to my office for the control of his chronic pain.VAS 10/10. Patient presents neuropathic pain that implies an additional deterioration in the patients' quality of life, added to the motor, sensory and autonomic deficit. The avulsion is a preganglionic lesion, where central and peripheral mechanisms are involved. A High Frequency SCS is implanted, reducing VAS to 3/10, with programming according to protocol between C2/C3.

Results: The day after the electrode implantation, the patient reports better control of his pain, in addition to being able to sleep more than 4 hours straight. In the following check-ups prior to the generator implantation, the patient reported more pain relief, reaching 4/10 VAS, more than 50% pain relief, especially in pain intensity.

Discussion: Over the past few years, there have been new modalities of SCS that have been shown to be more effective than classic tonic stimulation. Most of them have been based on frequency changes.

Conclusions: In this Case Report, we present a patient with a pathology that is complicated to treat due to the different types of pain that can coexist: nociceptive, peripheral neuropathic, central neuropathic and complex regional pain syndrome, where High Frequency stimulation (10,000Hz) has greater pain reduction than systems with tonic or sub-threshold stimulation, in addition to better seizure control.

Supplemental Data:

References: 1. Dorsal Root Entry Zone Lesioning for Brachial Plexus Avulsion Injuries: Case Series and Literature Review. PMID: 35295454 PMCID: PMC8915773 DOI: 10.3389/fpain.2021.749801 2. Daniela Floridia, Francesco Cerra, Giuseppe Guzzo, Silvia Marino, Nunzio Muscarà, Francesco Corallo, Alessia Bramanti, Antonino Chillura, Antonino Naro. Treatment of pain post-brachial plexus injury using high-frequency spinal cord stimulation. PMID: 30568480 PMCID: PMC6267358 DOI: 10.2147/JPR.S168031 3. Sayed D, Salmon J, Khan TW, Sack AM, Braun T, Barnard A, Rotte A. Retrospective Analysis of Real-World Outcomes of 10 kHz SCS in Patients with Upper Limb and Neck Pain. J Pain Res. 2020 Jun 15; 13:1441-1448. doi: 10.2147/JPR.S257071. eCollection 2020. PMID:

32606910 4. Sayed D, Kallewaard JW, Rotte A, Jameson J, Caraway D. Pain relief and improvement in quality of life with 10 kHz SCS therapy: summary of clinical evidence. CNS neuroscience & therapeutics 2020;26(4):403-415. 5. Kasra Amirdelfan, Ricardo Vallejo, Ramsin Benyamin, Steven Rosen, Peter Kosek, David Caraway, Anand Rotte & Abram Burgher. Pain relief and opioid usage in upper limb and neck pain patients after 10-kHz spinal cord stimulation treatment: subanalysis of USA studies. Accepted for publication: 30 October 2020; Published online: 13 November 2020. Future Medicine. 6. Angeles Canós-Verdecho, David Abejón, Ruth Robledo, Rosa Izquierdo, Ara Bermejo, Elisa Gallach, Pilar Argente, Isabel Peraita-Costa, María Morales-Suárez-Varela. Randomized Prospective Study in Patients with Complex Regional Pain Syndrome of the upper Limb with High-Frequency Spinal Cord Stimulation (10-kHz) and Low-Frequency Spinal Cord Stimulation. Neuromodulation December 2020. DOI: 10.1111/ner.13358.

Acknowledgements:

Learning Objectives: Is there any superior High Frecuency SCS

Financial Disclosures: No significant relationships'.

Disclosure: No significant relationships.

303

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

PROSPECTIVE, MULTICENTER STUDY OF MULTIPHASE SPINAL CORD STIMULATION WITH REMOTE DEVICE MANAGEMENT: 12-MONTH SAFETY AND EFFECTIVENESS RESULTS

Marc Russo, MBBS[1], James Yu, MD[2], Kasra Amirdelfan, MD[3], Leonardo Kapural, MD[4], Paul Verrills, MBBS[5]
[1]Hunter Pain Specialists, Broadmeadow, Australia, [2]Sydney Spine and Pain, Hurstville, Australia, [3]Boomerang Healthcare, Pain Management, Walnut Creek, United States of America, [4]Carolinas Pain Institute, Winston-Salem, United States of America, [5]Monash House Private Hospital, Metro Pain Group, Clayton, Australia

Introduction: The ongoing, long-term BENEFIT-03 study (NCT04683718) is evaluating an implantable spinal cord stimulation (SCS) system featuring a proprietary multiphase stimulation paradigm, which demonstrated significant pain relief in a short-term trial.[1] The SCS system also enables proactive care by offering automatic, objective, daily remote monitoring and remote programming.[2] Here, we present effectiveness and safety outcomes from BENEFIT-03 through 12 months.

Materials / Methods: BENEFIT-03 is a prospective, single-arm, multicenter study ongoing in Australia with Human Research Ethics Committee approval in consenting participants with chronic low back and/or leg pain. Post-implant follow-up consists of in-office visits (3, 6, 12, and 24 months) and remote visits that may be initiated by participants, investigators, proactive triggers (based on automatic daily device monitoring), or patient-reported outcomes (PROs). Primary endpoints are responder rate (at least 50% overall pain relief, VAS) and freedom from device-related complications at 6 months. Additional outcomes include daily at-home PROs (pain intensity, sleep quality), Oswestry Disability Index (ODI), opioid usage, and Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29).

Results: As of this March 2024 interim analysis, 25 of 31 implanted participants had 12-month follow-up data available for analysis. Responder rates (at least 50% relief, VAS) at 12 months were 84.0% (overall pain), 79.2% (back pain) and 90.9% (leg pain). Mean overall pain intensity (VAS) at 12 months was 18.4mm versus 78.3mm at baseline, and mean overall percentage pain relief (PPR) was 76.5%. Trends in daily at-home PROs were similar to in-clinic results: mean at-home daily pain intensity (NRS) was 2.2 at 12 months versus 7.3 at baseline, and mean at-home PPR was 69.3%. ODI scores substantially improved, with 80.0% of participants reporting minimal/moderate disability at 12 months (baseline=4.0%). Additionally, of baseline opioid users, 68.8% reduced opioid dose by at least half and 62.5% fully eliminated use by 12 months. Regarding safety, one device- or procedure-related serious adverse event (AE) was reported (lead anchor failure resolved by surgical replacement).

Discussion: Participants reported substantial pain relief both in-clinic and at-home, along with less severe disability. Most participants on opioids at baseline eliminated or substantially reduced dose, and serious device- or procedure-related AEs were rare.

Conclusions: BENEFIT-03 12-month results provide evidence of the long-term safety and effectiveness of an SCS system with multiphase stimulation, remote device management, and proactive care.

Supplemental Data: None

References: 1. Kapural L, Patterson D, Li S, et al. Multiphase Spinal Cord Stimulation in Participants With Chronic Back or Leg Pain: Results of the BENEFIT-02 Randomized Clinical Trial. *Neuromodulation*. 2023;26(7):1400-1411. 2. Russo M, Yu J, Mohabbati V, et al. An Implantable

SCS System With Automated Daily Remote Monitoring and Remote Programming: First-in-Human Experience [ASIPP poster]. Pain Physician. 2023;26:E293.

Acknowledgements: BIOTRONIK sponsors the study and funded writing/editorial support.

Learning Objectives: 1. To distinguish the features of the spinal cord stimulation system being evaluated in BENEFIT-03: multiphase stimulation, remote device management, and proactive care 2. To identify key safety and effectiveness outcomes of BENEFIT-03, including the 6-month responder rate (at least 50% pain relief) and freedom from complications at 6 months 3. To summarize results supporting the benefits of therapy demonstrated in BENEFIT-03, including substantial improvements in disability and opioid use

Financial Disclosures: Marc Russo: SPR Therapeutics, historical stockholder <1%; Saluda Medical, stock options <0.5%; and Presidio Medical, stock options <0.5%. **James Yu:** Abbott, consultant; Nevro, consultant, research; Medtronic, consultant, research; Boston Scientific, consultant, research; Saluda, research; Biotronik, research; and Nalu, research. **Kasra Amirdelfan:** Medtronic, consultant; Boston Scientific, consultant; Nevro, consultant; Biotronik, consultant; and Nalu, consultant, stock options. **Leonardo Kapural:** Nevro, consultant, research; Abbott, consultant; Medtronic, consultant, research; Nalu, consultant; Saluda, consultant, research; Biotronik, consultant, research; Gimer Medical, research; Neuros, research; and SPR Therapeutics, research. **Paul Verrills:** Presidio, consultant, research, $500 – $5,000; Biotronik, consultant, research, $1 - $500; Saluda, consultant, $5,000 - $20,000; and Nalu, consultant, $1 – $500.

Disclosure: Jacob Hicks is an employee at Biotronik INC.

304

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

NOVEL AUTOMATED SCS PROGRAMMING PLATFORM: FEASIBILITY STUDY RESULTS

Marc Russo, MBBS[1], Charles Brooker, MB ChB[2], Rebecca Martin, MD[2], Dean Karantonis, MSBmE, MSBmE[3], Daniel Parker, BSc (Hons)[3], Paul Verrills, MBBS[4]
[1]Hunter Pain Specialists, Broadmeadow, Australia, [2]Royal North Shore Hospital Pain Management and Research Centre, St Leonards, Australia, [3]Saluda Medical, Macquarie Park, Australia, [4]Metro Pain Group, Melbourne, Australia

Introduction: Despite advances in Spinal Cord Stimulation (SCS) technology, programming open-loop (OL) devices is a subjective, trial-and-error process. OL-SCS programs are manually optimized by company representatives based on patients' verbal feedback. Here, we report the feasibility of using a novel Automated Evoked compound action potential (ECAP) controlled closed-loop (CL) SCS Programming (AEP) platform leveraging a big ECAP database, next-generation artefact rejection filter technology, and automated measurement routines integrating direct patient input on the programmer and objective neural responses to predict the optimal therapeutic dose. The Signal to Noise Ratio (SNR) is a clinically relevant CL SCS programming metric that quantifies the degree to which noise (i.e., artefact) impacts the ability of the control loop to maintain consistent neural activation. Optimization of program parameters for SNR is desirable, and is rapidly achieved through automation. Here, we also characterize the AEP's SNR.

Materials / Methods: The Freshwater study (NCT04662905) investigated the feasibility of the AEP platform (n=34 patients). Outcomes collected immediately post-AEP programming include stimulation quality, patient satisfaction with stimulation quality, and patient comfort (AEP program vs. Manual Program).

Results: The AEP successfully and automatically generated a closed-loop program in 91% of patients (n=31/34). The human programmer was able to generate the CL program in the remaining 3 patients. · 87.1% of patients either rated AEP stimulation quality as pleasant or were neutral (Figure 1). · 83.8% of patients were very satisfied or satisfied with AEP stimulation quality (Figure 2). · 86.7% of patients found AEP programming experience as more comfortable or similar vs. manual programming (Figure 3). · Average SNR improvement of 50% (3.5 dB) vs. manual program. · 67% (14/21) of patients received an AEP program with a higher SNR vs. manual program.

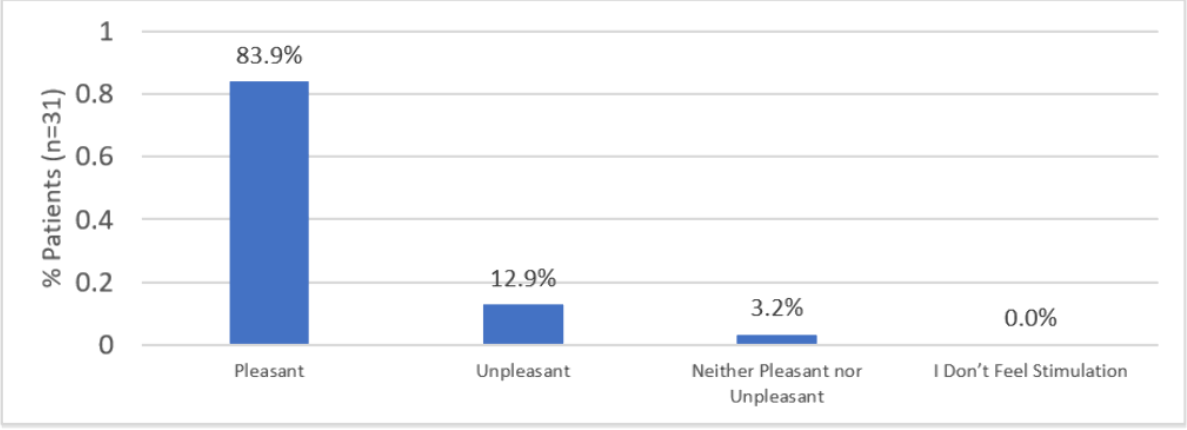


Figure 1: Stimulation quality of Program generated by Automated Programming System.

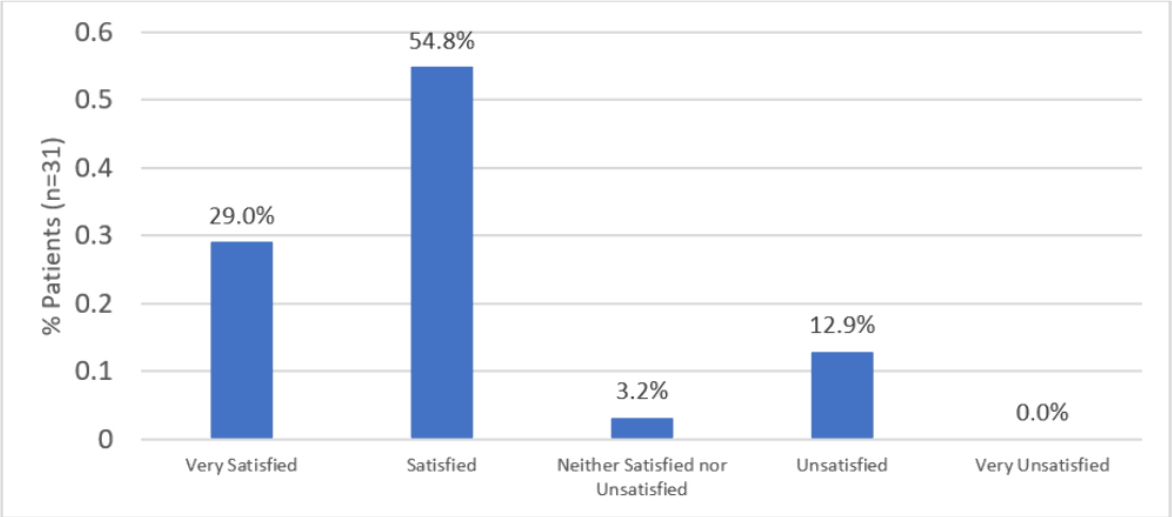


Figure 2: Patient satisfaction with Stimulation Quality.

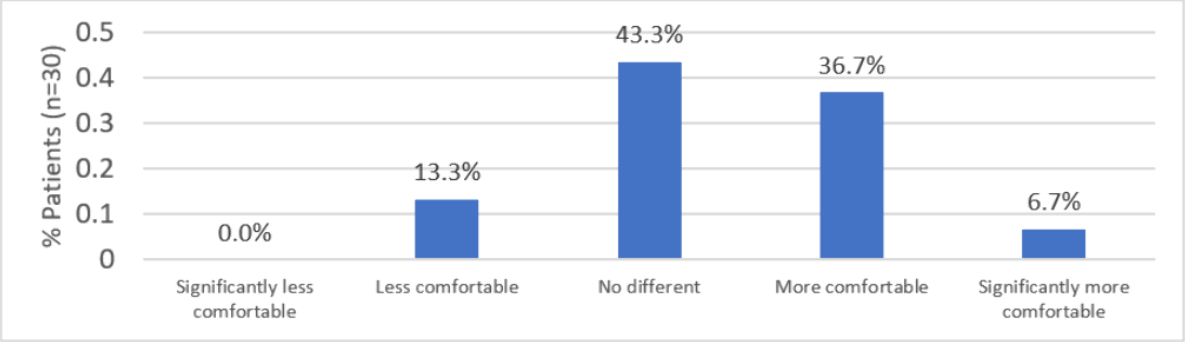


Figure 3: Patient comfort: Program generated by Automated Programming System vs. Conventional Closed-loop programming.

Discussion: Automated programming is a novel clinical utility based on an expert system developed using big ECAP data to predict the precise therapeutic dose. ECAPs combined with reduced reliance on verbal patient input is a novel concept in neuromodulation resulting in enhanced patient satisfaction with the potential to improve patient outcomes compared to manual programming. Average SNR is also higher when compared to manual programs.

Conclusions: Pilot study results demonstrate high rates of successful closed-loop calibration, and improved patient experience with potential to improve patient outcomes.

Supplemental Data:

References:

Acknowledgements: Trial sponsored by Saluda Medical.

Learning Objectives: 1. Automated programming is a novel clinical utility based on an expert system developed using big ECAP data to predict the precise therapeutic dose. 2. Automation of therapy configuration and setup for SCS has the potential to play an important role in reducing cognitive overload, minimizing human error, providing higher quality care, and filling resource gaps in healthcare settings. 3. Automation and an objective biomarker of SCS therapy can monitor for optimal therapy and therapy adherence in a complex chronic pain condition.

Financial Disclosures: Marc Russo, Saluda Medical, Stock Options, >$100,000 Charles Brooker has no relevant conflicts of interest to disclose Rebecca Martin has no relevant conflicts of interest to disclose Dean Karantonis, Saluda Medical, Employee, > $100,000 USD Daniel Parker, Saluda

Medical, Employee, > $100,000 USD Paul Verrills, Saluda Medical, Speaker Program, $5,001-$20,000 USD, Consultant/Advisory Board, $5,001-$20,000 USD, Education/Research, $500-$5000 USD

Disclosure: Administrative support to authors funded by Saluda Medical.

305

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

PASSIVE DISCHARGE BURST STIMULATION IN THE DORSAL ROOT GANGLION FOR FOOT PAIN – A CASE REPORT

John Salmon, MBBS
PainCare Perth, Pain Medicine, Perth, Australia

Introduction: Intractable chronic foot pain, is a common therapeutic challenge. Dorsal root ganglia (DRG) stimulation has been shown to be a very target specific dorsal column stimulation technique with very promising clinical outcomes with most sensory innervation to the foot derived from L5 and S1 dermatomes.[1]Passive discharge burst stimulation (BurstDR) has been shown to be superior to conventional tonic stimulation and whilst improving the psychological effects associated with chronic pain.[2] Here, we present a case of stimulating the DRG with passive discharge burst for the treatment of foot pain.

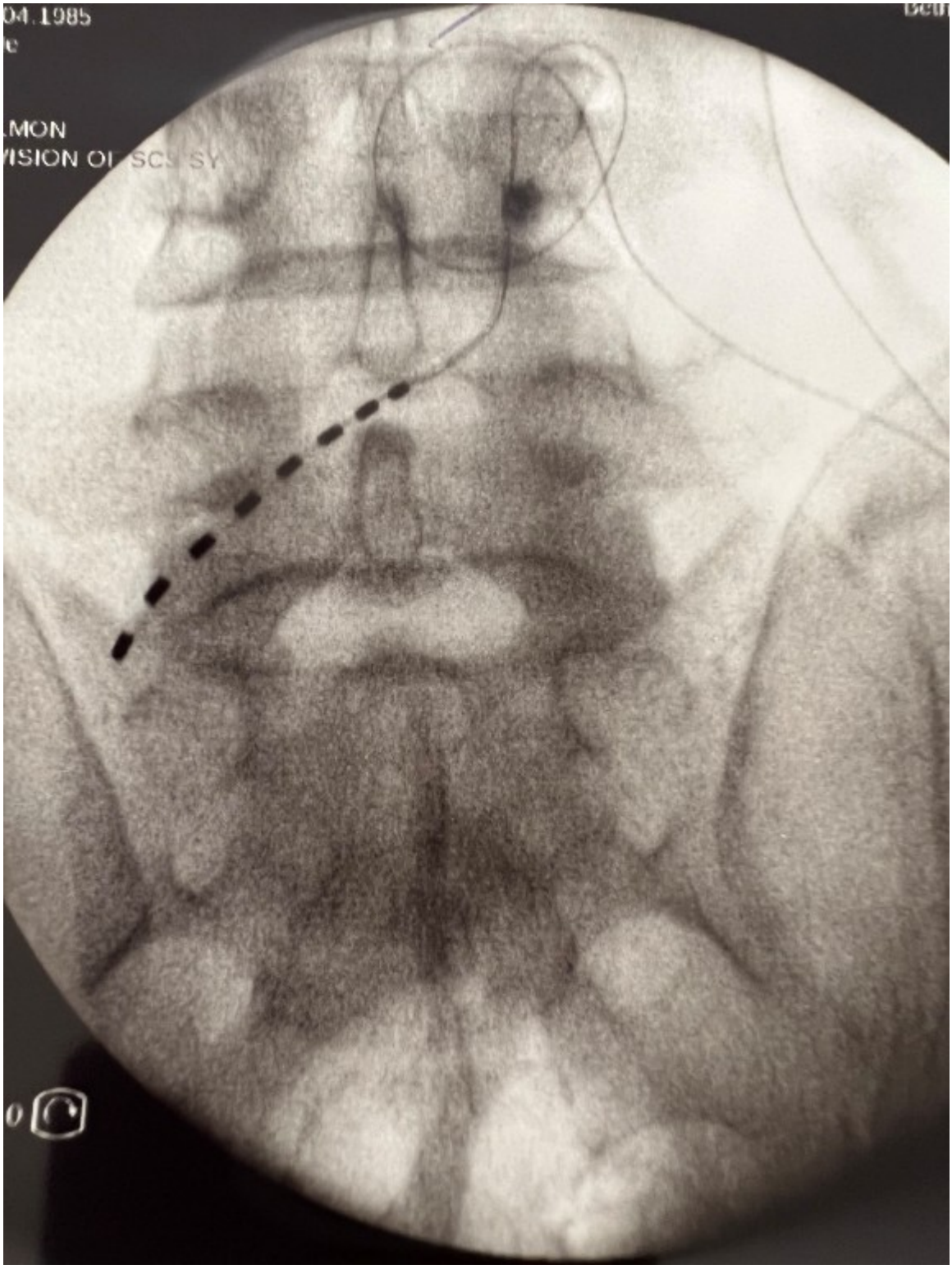
Materials / Methods: A 38-yo male presented with a two year history of chronic neuropathic pain in his left foot following a motor vehicle accident, which markedly restricted weight-bearing and prevented him from returning to work of any kind. After failure of conservative management including nerve block interventions, specialised physiotherapy, multidisciplinary pain management and multiple analgesics he received a spinal cord stimulation system implant. Electrode placement consisted of two percutaneous 8-contact leads, one positioned midline across T10/11 which provided stimulation coverage into the left leg and foot, the other lead was inserted retrograde from L4 to stimulate the left L5 nerve dorsal root ganglion in the foramen.

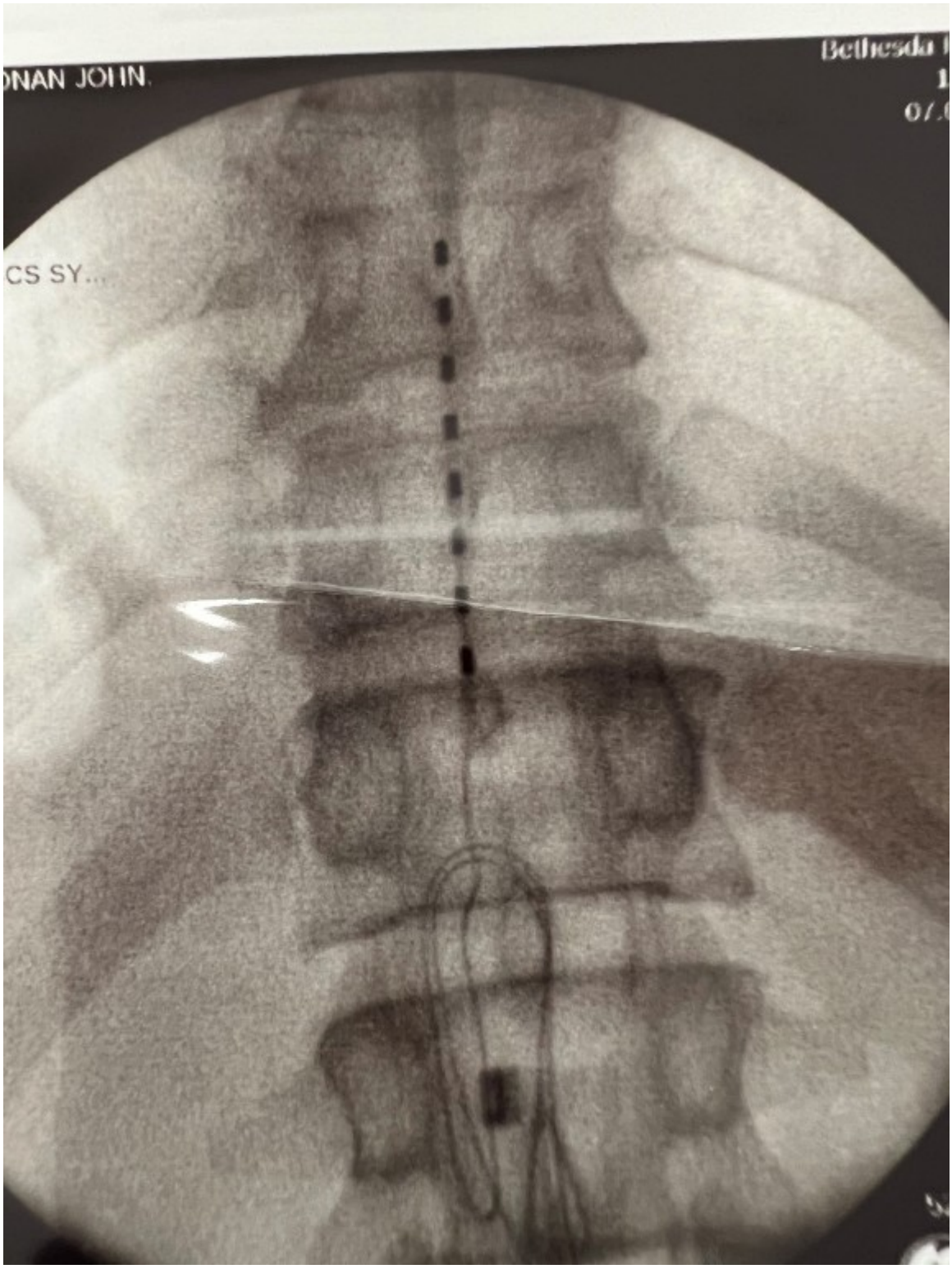
Results: During the initial 3 weeks post implant, only the DRG lead was activated (contact-2 [-], contact-3 [+]) resulting in pain relief of 60% was reported. For the following 3-6 weeks, both DRG and T10/T11 leads were activated using BurstDR at 0.25mA with no paraesthesia, pain relief improved to 70%. During these initial weeks after implantation, the patient was able to weight bear and walk much more comfortably and is preparing for a graduated return to work as a social worker. He has ceased taking all routine analgesic medication.
At 6 months post implant the patient is reporting in the region of 60% pain reduction and markedly improved walking and activity tolerances and capacity to return to light work. He has a preference for utilising the L5 DRG stimulating electrode only.

Discussion: Neuropathic/CRPS foot pain can be difficult to manage with spinal cord stimulation utilising a variety of waveforms and on occasion tonic DRG stimulation may also fail. This patient is currently reporting a good outcome utilising burst DR stimulation via a retrograde L5 DRG stimulating electrode.

Conclusions: This single case study reports on the improved pain state of a patient with foot pain treated with L5 DRG lead placement using BurstDR stimulation maintained at 6 month follow-up.

Supplemental Data:


04.1985
MON



References: Deer TR, Levy RM, Kramer J, et al. Dorsal root ganglion stimulation yielded higher treatment success rate for complex regional pain syndrome and causalgia at 3 and 12 months: a randomized comparative trial. Pain. 2017 Apr;158(4):669-681. Dirk De Ridder, Tim Vancamp, Steven M. Falowski & Sven Vanneste (2020) All bursts are equal, but some are more equal (to burst firing): burstDR stimulation versus Boston burst stimulation, Expert Review of Medical Devices, 17:4, 289-295

Acknowledgements:

Learning Objectives: Novel placement of 8-contact percutaneous lead for stimulating the DRG with passive discharge burst waveform

Financial Disclosures: John Salmon is a consultant for Abbott, Nevro, and Saluda.

Disclosure: No significant relationships.

306

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

OBJECTIVE NEUROPHYSIOLOGICAL INSIGHTS USING ECAP-CONTROLLED CLOSED-LOOP SCS IN A PATIENT WITH MULTIPLE SCLEROSIS AND NEUROPATHIC PAIN

Björn Carsten Schultheis, MD
Neuwerk Hospital, Medical Director Interventional Pain Therapy, Neuwerk, Germany

Introduction: Multiple sclerosis is a chronic demyelinating autoimmune disease associated with widespread neurological symptoms and functional limitations[1]. Chronic pain is one of the most common symptoms associated with multiple sclerosis[2,3,4]. Patients also suffer from neuropathic pain as a result of neuronal demyelination[2,3,4]. Unfortunately, these pain symptoms are refractory to pharmacological treatments[2,3,4]. In addition, spasticity occurs in more than 80% of patients[5]. Recently, a novel spinal cord stimulation (SCS) system has been developed and investigated that can measure spinal cord neural responses in the form of real-time evoked compound action potentials (ECAPs) and use this information to automatically adjust stimulation intensity[6,7].

Materials / Methods: A 62-year-old man formerly diagnosed with multiple sclerosis developed neuropathic lower extremity pain and sensory disturbances. The patient was permanently implanted with a cervical and thoracic lead on 27 January 2023 after a successful trial period (Fig.1A-D). Patient-reported outcomes and electrophysiological data from the first patient with the Evoke® SmartSCS™ (Saluda Medical, Australia) at 9-months are presented here.

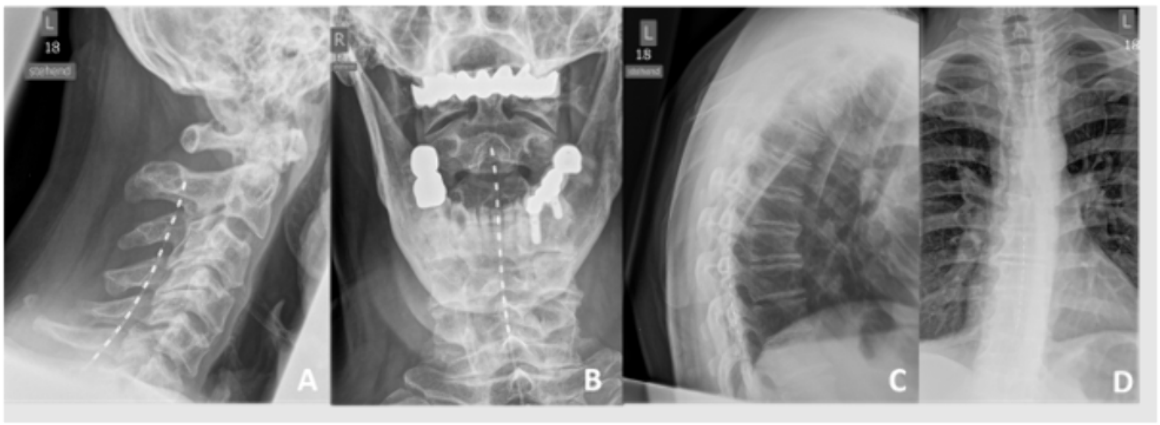


Figure 1: X-ray of cervical and thoracic electrode placement.

Results: Six-months after permanent implantation, the patient reported that the frequency of seizures in his legs decreased by 70% compared to baseline. Sleep also improved by 50% compared to baseline. Nine-months after permanent implantation, the patient still reported that the frequency of seizures in his legs had decreased and that he would do this surgery again anytime. The Physical and Mental Composite Score also revealed improvement (Veterans-Rand-12) at 6- and 9-months, as did Depression-Anxiety-Stress Scale (Fig.2). The Pain Disability Index decreased by 11.4 points after 6-months and by 10.4 points after 9-months and can be considered as a real change in pain-related disability[8] (Fig.2). Mean (±SEM) conduction velocities in the orthodromic and antidromic propagation directions were recorded during pleasant stimulation at the cervical lead. After 1-month the average conduction velocity was 68.26±1.46m/s orthodromic and 64.57±1.08m/s antidromic; after 6-months 62.60±11.30m/s orthodromic and 66.09m/s antidromic; and after 9-months 83.97±3.16 m/s orthodromic and 57.09m/s antidromic, indicating that large, myelinated fibers were activated (N1 peak position in time or latency;[9,10] (Fig.3)).

	Questionnaire	6-months	9-months
DASS (Change from Baseline)	DASS Anxiety Scale (0-42)	-4.0	-4.0
	DASS Depression Scale (0-42)	-6.0	-6.0
	DASS Stress Scale (0-42)	0.0	-4.0
Veteran-12 (Change from Baseline)	PCS (0-80)	+5.4	+4.4
	MCS (0-80)	+0.2	-1.8
PDI (Change from Baseline)	PDI score (0-70)	-11.4	-10.2

Figure 2: Patient reported outcomes after 6- and 9-months. DASS = Depression-Anxiety-Stress-Scale; PCS = Physical Composite Score; MCS = Mental Composite Score; PDI = Pain Disability Index

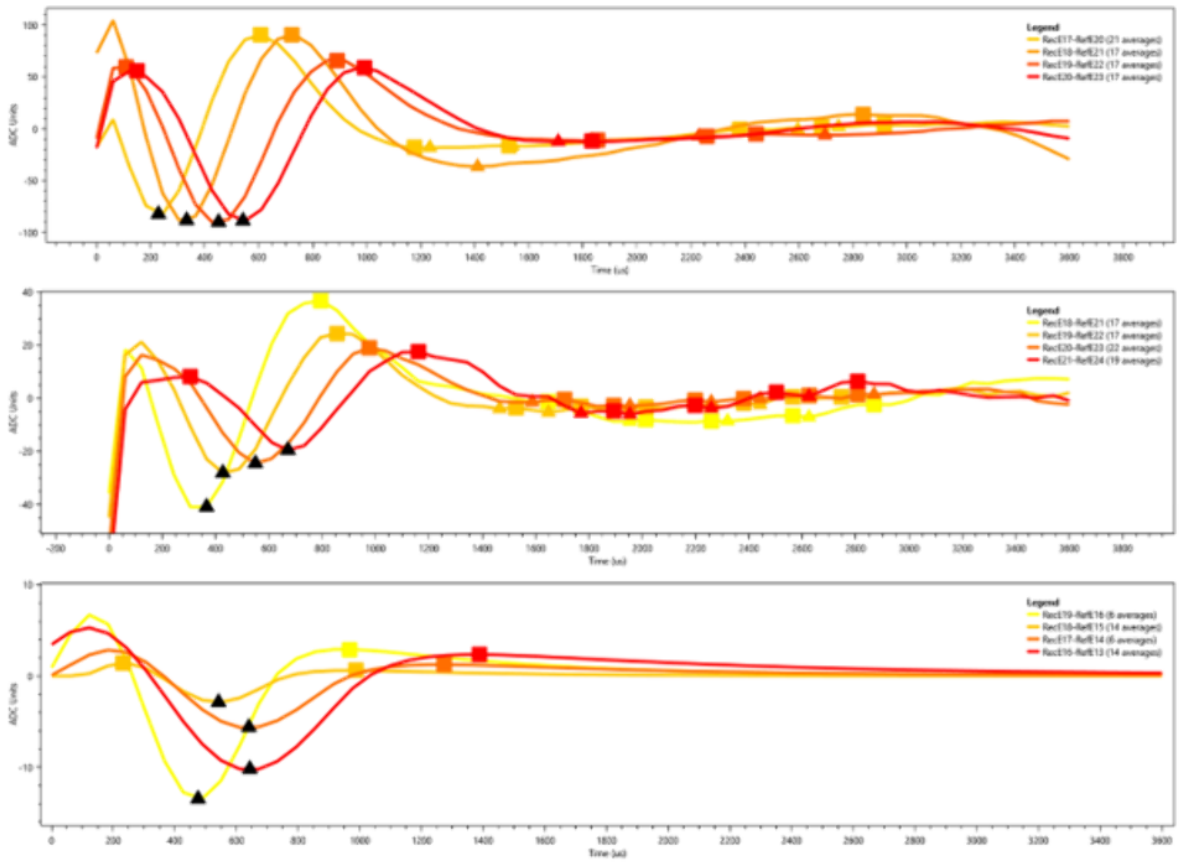


Figure 3: Conduction velocities after 1-, 6- and 9-months.

Discussion: To date, this is the first case report of the use of ECAP-controlled SCS for pain management in patients with multiple sclerosis. Average conduction velocity was on the higher end of normal range in general population[9,10].

Conclusions: ECAP-controlled SCS appears promising for the treatment of multimodal symptoms associated with multiple sclerosis. Further research and a longer follow-up period are needed.

Supplemental Data:

References: 1. Ghasemi N, Razavi S, Nikzad E. Multiple sclerosis: pathogenesis, symptoms, diagnoses and cell-based therapy. Cell J. 2017;19:1–10. 2. Solaro C, Trabucco E, Messmer Uccelli M. Pain and multiple sclerosis: pathophysiology and treatment. Curr Neurol Neurosci Rep 2013;13:320. 3. Brichetto G, Messmer Uccelli M, Mancardi GL, Solaro C. Symptomatic medication use in multiple sclerosis. Mult Scler 2003;9:458–460. 4. Provenzano D.A., Williams J.R., Jarzabek G., DeRiggi L.A., Scott T.F. 2016. Treatment of Neuropathic Pain and Functional Limitations Associated With Multiple Sclerosis Using an MRI-Compatible Spinal Cord Stimulator: A Case Report With Two Year Follow-Up and Literature Review. Neuromodulation 2016; 19: 406–413. 5. Urits, I., Adamian, L., Fiocchi, J., Hoyt, D., Ernst, C., Kaye, A. D., & Viswanath, O. (2019). Advances in the understanding and management of chronic pain in multiple sclerosis: a comprehensive review. Current pain and headache reports, 23, 1-11. 6. Brooker, C., Russo, M., Cousins, M. J., Taylor, N., Holford, L., Martin, R., ... & Parker, J. (2021). ECAP-Controlled Closed-Loop Spinal Cord Stimulation Efficacy and Opioid Reduction Over 24-Months: Final Results of the Prospective, Multicenter, Open-Label Avalon Study. Pain Practice. 7. Mekhail, N., Levy, R. M., Deer, T. R., Kapural, L., et al. (2020). Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial. The Lancet Neurology, 19(2), 123-134. 8. Beemster, T., Van Bennekom, C., van Velzen, J., Reneman, M., & Frings-Dresen, M. (2018). The interpretation of change score of the pain disability index after vocational rehabilitation is baseline dependent. Health and quality of life outcomes, 16, 1-9. 9. Kandel, E. R., J. H. Schwartz, Jessell, T. M., S. A. Siegelbaum, and A. J. Hudspeth, Principles of Neural Science, Fifth Edition. McGraw Hill Professional, 2013. 10. E. St. J. Smith and G. R. Lewin, “Nociceptors: a phylogenetic view,” J Comp Physiol A, vol. 195, no. 12, pp. 1089–1106, Dec. 2009, doi: 10.1007/s00359-009-0482-z.

Acknowledgements:

Learning Objectives: 1. To learn that ECAPs are used to adjust stimulation levels in real-time to maintain consistent activation of the spinal cord. 2. To show that ECAP-controlled SCS can be used for pain management in patients with multiple sclerosis. 3. To provide that conduction velocities can be recorded in a multiple sclerosis patient.

Financial Disclosures: Björn Carsten Schultheis, Saluda Medical, Consultant/Advisory Board, 1800

Disclosure: No significant relationships.

307

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

ENHANCED FOCAL STIMULATION: THE ADVANTAGE OF THE NEW DIRECTIONAL MULTICOLUMN PERCUTANEOUS LEAD

Konstantin Slavin, MD[1], Maria Celeste Cantone, MSc[2], Omar Caspani, MSc[2], Matteo Saini, MSc[2], Federica Montrone, MSc[2], Sandro Ferrari, PhD[2], Valentina Ferpozzi, PhD[2], Alessandro Dario, MD[3]
[1]University of Illinois at Chicago, Neurosurgery, Chicago, United States of America, [2]WISE Srl, Cologno Monzese, Italy, [3]ASST Settelaghi-Insubria University, Neurosurgical Clinic, varese, Italy

Introduction: In recent years, Spinal Cord Stimulation (SCS) technology has seen advancements, coinciding with the expansion of medical indications for this therapeutic approach. To enhance the SCS effectiveness, the ideal SCS lead should possess the capability to deliver focal current with directionality, optimizing the current delivery to the dorsal columns while conserving battery energy. Responding to this medical need, an innovative lead was conceived, marking a significant milestone as the first multicolumn directional lead that can be percutaneously implanted. It comprises a cable with an array of electrodes distributed across two columns, situated on two wings extending from the cable; these wings are designed to rest against the dura when in place. During insertion, the wings can be conveniently coiled into a cylindrical shape within a delivery sheath. To elucidate the advantages of this lead, we present the findings of an *in vivo* neurophysiological study aimed to demonstrate that the new lead provides a more focal stimulation, allowing for a reduction of the current required to elicit response compared to a cylindrical lead with identical electrode length and inter-electrode distance.

Materials / Methods: In a porcine model, one new multicolumn (manufactured by WISE, Italy) and two cylindrical leads were surgically implanted at the L2 to L3 with electrodes of both leads positioned at the same anatomy. A stimulation protocol, consisting of a single pulse with negative polarity, a pulse width of 100µs, and a pulse frequency of 1Hz, was administered to the spinal cord using one pair of electrodes from each column of the new lead, in conjunction with the corresponding electrode pair from the cylindrical leads. The aim was to elicit a stable and consistent motor response, and to compare the stimulation intensity required to achieve this with both leads.

Results: Responses were observed in the external abdominal oblique muscles when stimulated by both the left and right dorsal columns using both leads. The latency of these responses remained consistent for each muscle, but the motor threshold intensity required for the new lead to induce a stable response was lower, ranging between one-half and one-third of the intensity required for a cylindrical lead.

Discussion: More focal stimulation delivered by the new multicolumn lead suggests its energy-saving superiority compared to the cylindrical leads.

Conclusions: The reduced stimulation intensity necessary to elicit a motor response may translate into more efficient and sustainable SCS therapy using percutaneously insertable directional multicolumn lead, holding promise for a multitude of clinical application.

Supplemental Data:

References:

Acknowledgements: This work was funded by: European Commission – European Innovation Council and SMEs Executive Agency. PercPad - GA No. 959546. MiMit - Agreements for Innovation. SCS Expert - B29J23000210005.

Learning Objectives: 1- A multicolumn directional lead delivers a focal stimulation. 2- A focal stimulation may translate into a battery savings. 3- A focal stimulation may translate into more efficient and sustainable SCS therapy.

Financial Disclosures: K. Slavin is (past and current) consultant for Abbott, Biotronik, Integer, Saluda Medical, Synergia, Epiminder, Varian and WISE. K. Slavin has also received grant/research support from Medtronic, Abbott, Neuros and Stryker. M. C. Cantone, O. Caspani, M. Saini, F. Montrone, S. Ferrari and V. Ferpozzi are employees of WISE. WISE is the manufacturer of the new multicolumn directional lead. A. Dario is consultant for WISE.

Disclosure: I am an employee of WISE. WISE is the manufacturing company that developed the multicolumn directional lead.

308

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

SPINAL CORD STIMULATION (SCS) FOR CHRONIC NEUROPATIC PAIN ASSOCIATED WITH RESTLESS LEGS SYNDROME (RLS)

Phillipp Slotty, MD[1,2], Zarela Krause Molle, MD[3], Heike Littges, RN[3], Phyllis McPhillips, RN[3], Andrea Dreyer, RN[3], Jan Vesper, MD[3]
[1]Helios Krefeld, Department Of Orthopaedics, Trauma Surgery And Hand Unit, Krefeld, Germany, [2]Heinrich-Heine University, Duesseldorf, Germany, [3]University Medical Center, Heinrich Heine University, Functional Neurosurgery And Stereotaxy, Duesseldorf, Germany

Introduction: Spinal cord stimulation (SCS) is a well-established therapy for chronic neuropathic pain syndromes, but only a few cases are published for other conditions like gait disturbances or movement disorders. Restless legs syndrome (RLS) is very common (3.9-14% prevalence) and can be very painful by itself, beside its effect on sleep and patient's quality of life. Treatment generally consists of dopaminergic medication.
Patients we treated with SCS for PSPS I and II reported that their cormobidity RLS significantly improved, additionally to their leg and back pain. We hereby present the first larger case series of patients with chronic neuropathic pain with associated RLS.

Materials / Methods: We retrospectively reviewed the charts of 19 (9m, 10f) consecutive RLS patients, who underwent SCS implantation for PSPS I or II with concomitant RLS. The lead (Octrode Abbott, Pleno) tip was placed in the midline Th7 under local anesthesia. One patient did not respond during the trial stimulation, 18 patients responded to the trial and were implanted with a permanent system.

Results: Responder rates regarding pain control were high with an improvement in overall mean VAS baseline 9 vs. 3 at 1 month follow up. Patients additionally completed the International Restless Legs Syndrome Scale questionnaire to objectively quantify the severity of their symptoms. Follow up RLS Score is available in 4 patients until now and shows an improvement under stimulation from 35 points (range 31-40) to 22 points (range 10-34) on the 40-point scale.

Discussion: To our knowledge, this is the first reported case series using SCS as a potentially long-lasting, safe, and highly effective therapy for RLS. This effect may be explained by increased inhibition from hypothalamic cells controlling dopaminergic input to the spine².

Conclusions: SCS turned out to be a potential alternative treatment for medical refractory RLS. We submit this as a late breaking aspect as we expect to present completed data sets on the RLS questionnaire for final presentation.

Supplemental Data:

References: David A Byrne 1, Christopher M Sobey 2, Jake Trahan 3rd 1, Kanika Bagai 3, Arthur Walters 3, Spinal Cord Stimulation in Patients With Chronic Pain and Restless Legs Syndrome: A Case Report, Case Reports A A Pract. 2019 Aug 1;13(3):110-113. doi: 10.1213/XAA.0000000000001007. Syed M Adil 1, Jing L Han 2, Beth A Parente 1, Patrick Hickey 3, Shivanand P Lad 4, Spinal Cord Stimulation for Restless Legs Syndrome: Case Series and Mechanistic Hypothesis, Case Reports Stereotact Funct Neurosurg, 2019;97(1):31-36. doi: 10.1159/000494737. Epub 2019 Apr 4. Marshall T Holland 1, Leigh A Rettenmaier 1, Oliver E Flouty 1, Teri R Thomsen 2, Nivedita U Jerath 2, Chandan G Reddy 3, Epidural Spinal Cord Stimulation: A Novel Therapy in the Treatment of Restless Legs Syndrome, Case Reports World Neurosurg, 2016 Aug:92:582.e15-582.e18. doi: 10.1016/j.wneu.2016.05.077. Epub 2016 Jun 3.

Acknowledgements:

Learning Objectives: 1) Many patients suffering from PSPS also suffer from RLS 2) RLS can be very painful beside its influence on sleep and QoL 3) RLS might be a new indication for SCS

Financial Disclosures: Philipp J. Slotty reveiced travel grants and reimbursement from Abbott, Boston Scientic, Uniqure, Saluda and Photonamics

Disclosure: No significant relationships.

309

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

MULTIDIMENSIONAL OUTCOMES OF SPINAL CORD STIMULATION IN PATIENTS WITH CHRONIC PAIN: RESULTS FROM A EUROPEAN PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY

Simon Thomson, MBBS
Mid & South Essex University Hospitals NHSFT, Pain And Neuromodulation Centre, Basildon, United Kingdom

Introduction: Spinal cord stimulation (SCS) has been used since the late 1960s and is a safe and effective non-opioid therapeutic alternative to manage chronic pain patients. Over the past few years, SCS devices have been equipped to provide for an array of neuromodulation modalities thereby enabling the precise optimization of treatment on a personalized basis. Here we assessed real-world outcomes from a subset of patients as derived from a European multicenter prospective study and report the effects of SCS therapy in multiple dimensions.

Materials / Methods: RELIEF (clinicaltrials.gov identifier: NCT01719055) is a global multicenter prospective single-arm observational study designed to collect real-world data for neurostimulation systems utilized for chronic pain indications by patients within standard of care clinical practice. A sub-set of patients who have been treated in European centers were analyzed. Study assessments include quality of life (EQ5D), disability (ODI/PDI), Global impression of change (P-GIC/C-GIC), percentage of pain relief (PPR), satisfaction with treatment (patient/clinician), and resource utilization inventory.

Results: To date, over 200 patients have been enrolled and implanted in European centres. In those patients who reached their 6- and 12-month follow-up visits, substantial improvements have been recorded for various patient-reported outcome measures (PROMs). At 6-month and 12-month evaluation visits, patients' function improved by over 30% per Oswestry Disability Index (ODI), and substantial improvement in quality of life measures have been reported (EQ5D). Patient Global impression of change evaluations at 6- and 12-month follow-up visits show that more than 85% patients reported improvement. RELIEF study is ongoing and these preliminary results will be updated.

Discussion: Measuring the outcomes of SCS therapy via multidimensional assessments is valuable, so that the overall impact of the treatment on patients' daily life and global health is taken into account and measured.

Conclusions: This ongoing prospective evaluation of real-world outcomes show that spinal cord stimulation using personalized therapies may provide substantial improvements in multiple domains such as quality of life, function, percent pain relief and global impression of change.

Supplemental Data:

References: none

Acknowledgements:

Learning Objectives: 1. Multidimensional assessment of patients with chronic pain 2. Impact of SCS in multiple domains 3. The value of real-world prospective data

Financial Disclosures: Simon J. Thomson: Scientific Advisory Board: Boston Scientific Neuromodulation (£10 000), Galvani Bioelectronics (£3000), Mainstay Medical (£7000), Saluda

Medical (£10 000). Scientific Research Institutional Funding: Boston Scientific Neuromodulation, Mainstay Medical, Saluda Medical Speakers Bureau: Boston Scientific Neuromodulation, Mainstay Medical, Saluda Medical Stock Holder, Stock Options, Product Royalties: None

Disclosure: I am an employee of Boston Scientific, sponsor of the Relief Study and part of the Clinical Research Team.

310

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

SINGLE CENTER EXPERIENCE WITH 10KHZ SPINAL CORD STIMULATION

José Manuel Trinidad Martin-Arroyo, MD, Gema Gómez-Benítez, MD, Diego Benítez-Pareja, MD, Javier Morales Guerrero, PhD, Antonio Pernia-Romero, MD, Jose Antonio Lopez Lopez, MD
Puerta del Mar University Hospital, Cádiz, Spain

Introduction: The use of high frequency SCS at 10 kHz (10kHz SCS) has been shown to be safe and effective in multiple pain pathologies, including Failed Back Surgery Syndrome (FBSS), Non-Surgical Refractory Back Pain (NSRBP), upper limb and neck pain, failed low-frequency SCS (LF-SCS), and Painful Diabetic Neuropathy (PDN). The decrease in VAS pain scores was consistent throughout the studies and the ºpublished literature suggests that 10kHz SCS is also linked with an improved quality of life and a reduction of the opioid consumption. The aim of this retrospective review was to document a real-world experience with 10kHz SCS.

Materials / Methods: This is a retrospective review of all patients trialed with 10 kHz SCS at our center, between November 2018 to October 2023. Sixty-nine consecutive patients were identified, of which 14,5% had previous SCS experience. The majority suffered from predominant back pain (77%), whereas suffered from predominant leg pain. The remaining 23% had pain in other areas. All patients completed a 10kHz SCS trial and were followed up as per centers' routine practice. Patients who experienced ³50% pain reduction during the stimulation trial were implanted with a permanent system (IPG). Verbal rating scores for pain (VRS), patient reported percentage pain relief, medication changes, sleep, and function improvements were analyzed.

Results: Of the 69 patients who had a 10kHz trial, 81% were successful (>50% pain relief) and had an IPG implanted. Their VRS average was reduced from 8.4 at baseline to 2.8 at end of trial, sustained at 2.9 at the last visit. At their last visit, 90% of the patients were responders, with 89% reporting functional improvement and 98% reporting improvement in sleep. All patients decreased their medication. Additionally, we evaluated patients' remote use and charge burden. On average the patients used their remote 1.4 times per week and charged 5.0 time per week, with an average duration of 40 minutes.

Discussion: After analyzing the data obtained during the last 4 years from patients implanted with 10Khz, we have verified how the pain reduction is maintained, even after more than 36 months.

Conclusions: Our experience shows that 10kHz SCS provides good pain relief in lower back and legs pain predominant, and also in visceral pain, post Mastectomy pain, arm pain, further supporting the use of 10kHz SCS as an efficacious therapy for chronic pain. Additionally, most of the patients also experienced an improvement in medication use, sleep and function reflecting an improvement in their QOL.

Supplemental Data:

References: 1. Kapural L, Yu C, Doust MW, Gliner BE, Vallejo R, Sitzman BT, et al. Novel 10-kHz high-frequency therapy (HF10 therapy) is superior to traditional low-frequency spinal cord stimulation for the treatment of chronic back and leg pain: the SENZA-RCT randomized controlled trial. Anesthesiology 2015;123(4):851-860. 2. Al-Kaisy A, Van Buyten J, Smet I, Palmisani S, Pang D, Smith T. Sustained effectiveness of 10 kHz high-frequency spinal cord stimulation for patients with chronic, low back pain: 24-month results of a prospective multicenter study. Pain Medicine 2014;15(3):347-354. 3. Al-Kaisy A, Palmisani S, Smith TE, Carganillo R, Houghton R, Pang D, et al. Long-term improvements in chronic axial low back pain patients without previous spinal surgery: a cohort analysis of 10-kHz high-frequency spinal cord stimulation over 36 months. Pain Medicine 2018;19(6):1219-1226. 4. El Majdoub F, Neudorfer C, Richter R, Schieferdecker S, Maarouf M. 10

kHz cervical SCS for chronic neck and upper limb pain: 12 months' results. Annals of clinical and translational neurology 2019;6(11):2223-2229. 5. Sayed D, Salmon J, Khan TW, Sack AM, Braun T, Barnard A, et al. Retrospective analysis of real-world outcomes of 10 kHz SCS in patients with upper limb and neck pain. Journal of Pain Research 2020; 13:1441. 6. Kapural L, Sayed D, Kim B, Harstroem C, Deering J. Retrospective assessment of salvage to 10 kHz spinal cord stimulation (SCS) in patients who failed traditional SCS therapy: RESCUE study. Journal of Pain Research 2020; 13:2861. 7. Galan V, Scowcroft J, Chang P, Li S, Staats P, Rotte A, et al. 10-kHz spinal cord stimulation treatment for painful diabetic neuropathy: results from post-hoc analysis of the SENZA-PPN study. Pain Management 2020;10(5):291-300. 8. Petersen EA, Stauss TG, Scowcroft JA, Brooks ES, White JL, Sills SM, et al. Effect of high-frequency (10-kHz) spinal cord stimulation in patients with painful diabetic neuropathy: a randomized clinical trial. JAMA neurology 2021. 9. Sayed D, Kallewaard JW, Rotte A, Jameson J, Caraway D. Pain relief and improvement in quality of life with 10 kHz SCS therapy: summary of clinical evidence. CNS neuroscience & therapeutics 2020;26(4):403-415

Acknowledgements:

Learning Objectives: - To publicize the results of High Frequency Stimulation (10Khz) in different Pathologies. - Medication reduction with 10Khz Stimulation. - Show the versatility of the High Frequency Stimulation (10Khz)

Financial Disclosures: 'No significant relationships'.

Disclosure: No significant relationships.

311

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

EFFECT OF DIFFERENTIAL TARGET MULTIPLEXED SCS ON INTRACTABLE UPPER LIMB PAIN: A 12-MONTH PROSPECTIVE STUDY

Thomas White, MD[1], Rafael Justiz, MD[2], Michael Fishman, MD[3], David Schultz, MD[4], Aaron Calodney, MD[5], Harold Cordner, MD[6], Wilson Almonte, MD[7], Yoann Millet, MD[1], Kenneth Wu, MD[1], Gennady Gekht, MD[8], Andrew Will, MD[9], Philip Kim, MD[3], Richard Bundschu, MD[10], Justin Sirianni, MD[8], Amr El-Naggar, MD[11], Mayank Gupta, MD[12], Wesley Park, MPH[13], David Cedeño, PhD[13], Ricardo Vallejo, MD, PhD[13]
[1]Procura Pain and Spine, The Woodlands, United States of America, [2]Oklahoma Pain Physicians, Oklahoma City, United States of America, [3]Center for Interventional Pain and Spine, Lancaster, United States of America, [4]Nura Research Institute, Minneapolis, United States of America, [5]Precision Spine Care, Pain Management, Tyler, United States of America, [6]Florida Pain Management Associates, Sebastian, United States of America, [7]Victoria Pain and Rehabilitation, Victoria, United States of America, [8]Coastal Orthopedics and Pain Management, Bradenton, United States of America, [9]Twin Cities Pain Clinic, Minneapolis, United States of America, [10]Coastal Orthopedics, Pain Management, Bradenton, United States of America, [11]DREZ One, Somerset, United States of America, [12]Neuroscience Research Center, Overland Park, United States of America, [13]SGX Medical LLC, Bloomington, United States of America

Introduction: Radicular upper limb pain (ULP) is a common chronic condition. When conventional medical management fails to alleviate pain, Spinal Cord Stimulation (SCS) may be considered. Treatment of chronic ULP using conventional SCS is challenging due to the possible occurrence of uncomfortable paresthesia triggered by neck motion. Differential target multiplexed SCS (DTM SCS) has proven successful for the treatment of low back and lower limb pain[1,2]. This study evaluated the safety and efficacy DTM SCS in subjects diagnosed with chronic ULP through 12-months.

Materials / Methods: This post-market, prospective, cohort, multicenter study evaluated DTM™ SCS in patients with chronic ULP. Informed, consented, eligible subjects were enrolled in 11 centers in the US. Eligibility criteria are presented in Table 1. Subjects evaluated DTM SCS during a trial phase. Successfully trialed patients were implanted with cervically placed leads and a permanent neurostimulator. Primary endpoint was ULP responder rate (percentage subjects with ≥50% relief vs. baseline) at 3-month post-device activation. Failed trials were carried forward in the analysis. Effect of DTM SCS on pain level, pain disability index (PDI), patient impression of change (PGIC), patient satisfaction, and frequency of study-related adverse events was evaluated for 12-months after device activation.

Results: Out of 52 subjects completing the trial, 46 were permanently implanted, with 43, 40, and 39 completing the 3-, 6- and 12-month visits, respectively. The responder rate for ULP was 92% at the primary endpoint, 91% at 6-months and 86% at 12-months. Average ULP relief was 81% at 3-month and 6-month, and 80% at 12-month. Mean disability (PDI) was reduced by 31 points at primary endpoint from a mean 44 point baseline, and was sustained at the completion of study. >97% of subjects felt improved by treatment and were satisfied. 14 study-related adverse events were reported by 13 subjects.

Discussion: This study indicates that DTM SCS is a feasible treatment for chronic intractable ULP. A large, long-term randomized clinical study should be conducted to confirm these findings.

Conclusions: DTM SCS can effectively reduce pain in this difficult to treat patient population.

Supplemental Data:

TABLE 1. Key eligibility criteria.

INCLUSION	EXCLUSION
• Adult (≥18 y/o) • ULP level ≥5 cm VAS-10 • Candidate for SCS as per indication* • Stable pain medication	• Contraindications for SCS system • Conditions that could interfere with evaluation of treatment • Active implanted device • Cervical stenosis, Facet spondylosis, • Mechanical instability • Previous surgery of the posterior elements of the cervical spine

*For example: Radicular pain syndrome or radiculopathies resulting in pain secondary to surgery or herniated disk, CRPS

References: 1. Fishman M, Cordner H, Justiz R, Provenzano D, Merrell C, Shah B, et al. Twelve-month results from multicenter, open-label, randomized controlled clinical trial comparing differential target multiplexed spinal cord stimulation and traditional spinal cord stimulation in subjects with chronic intractable back pain and leg pain. Pain Pract. 2021 Nov;21(8):912-923. 2. Fishman MA, Calodney A, Kim P, Slezak J, Benyamin R, Rehman A, et al. Prospective, multicenter feasibility study to evaluate differential target multiplexed spinal cord stimulation programming in subjects with chronic intractable back pain with or without leg pain. Pain Pract. 2020 Sep;20(7):761-768.

Acknowledgements: This study has been sponsored by SGX Procura (acquired by Medtronic).

Learning Objectives: 1. Understand the benefits of SCS in patients with upper limb pain. 2. Evaluate feasibility study data in support of SCS for the treatment of chronic intractable upper limb pain. 3. Investigate safety and efficacy of Differential Target Multiplexed SCS for chronic intractable upper limb pain.

Financial Disclosures: David L. Cedeno, PhD. SGX Medical, Consultant, >$100,000 Ricardo Vallejo MD, PhD, SGX Medical, Consultant, >$100,000 Ricardo Vallejo, MD, PhD, Medtronic Inc, Consultant/Advisory Board, >$100,000

Disclosure: I am an employee of Medtronic.

312

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

MULTIVENDOR TRIAL IN BURST SPINAL CORD STIMULATION – A RANDOMIZED CLINICAL TRIAL

Jan Vesper, MD, Guilherme Santos Piedade, MD, Phyllis McPhillips, RN, Andrea Dreyer, RN, Niels Stritt, medical student, Zarela Krause Molle, MD, Phillipp Slotty, MD
University Medical Center, Heinrich Heine University, Functional Neurosurgery And Stereotaxy, Duesseldorf, Germany

Introduction: The development of different waveforms and various spinal cord stimulation (SCS) systems increases the options for patients with chronic neuropathic pain. However, the choice for the used stimulation system is commonly made on an arbitrary basis. We therefore prospectively explored the influence of different providers during the temporary trial phase of burst SCS in a randomized clinical trial.

Materials / Methods: After implantation of a SCS test lead, subjects were tested in a randomized order with two external pulse generators (EPG) of two different device manufacturers (A and B). Test leads from A, the connection with the EPG from either A or B (according to random result) was made with an adapter. Tonic stimulation was used for two days. Stimulation was then switched to burst for another five days. There was a washout period of two days before the second EPG was tested with burst only for five days. After the trial, the SCS system of the provider whose stimulator produced the best pain relief was implanted. Patients were followed for 6 months. Pain was assed with VAS, PainDETECT, PCS and SF-12.

Results: Out of 50 PSPS II patients for screening, a total of 30 was included. If eligible for the study, patients underwent trial with ne SCS electrode of company A in the midline around Th7 (tip of the electrode). All patients s, all the subjects had Pain DETECT scores over 12 indicating neuropathic pain. Mean pain intensity at the baseline was 7.45 and achieved 6.94 after five days with burst stimulation from either B and 5.81 after Burst stimulation from A. Reduction in PCS was similar between the groups – from 32.21 to 22.56 points with company B and to 23.06 points with company A. The tonic stimulation phase, which was done with the system of a single company for each patient, elicited 5.63 VAS score pain relief with B and 5.99 with A consecutively. No differences were found for PCS and SF-12.

Discussion: SCS was effective in both groups. There were three trial failures (trial to perm rate 90%). Burst stimulation from company A and B seems to be both effective for chronic neuropathic pain.

Conclusions: No significant differences were found but a very high trial to perm rate. To achieve optimal stimulation results, selection of patients and close contact to the patient might be more important compared the choice of the manufacturer alone. Trial success does not depend on the chosen company

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: burst stimulation is highly effective in SCS no significant advantages amnog the compared providers patient selsction and intensive postoperative care are critical for a good outcome

Financial Disclosures: JV seves as a consultant for Boston Scientific and ABBOTT, JV, AD,, PMP, PS receives travel garnts from ABBOTT and BSCI

Disclosure: No significant relationships.

313

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

NOVEL DYNAMIC STIMULATION PATTERNS TO IMPROVE THE CLINICAL EFFECTIVENESS OF SPINAL CORD STIMULATION

Ashwin Viswanathan, MD[1], Tianhe Zhang, PhD[2], Jessica Block, MSc[2], Satya Avvaru, PhD[2], Luke Gelvoligaya, BSc[1], Rosana Esteller, PhD[2]
[1]Baylor College of Medicine, Houston, United States of America, [2]Boston Scientific Neuromodulation, Research And Development, Valencia, United States of America

Introduction: Spinal Cord Stimulation (SCS) is an established and effective neuromodulation therapy for treating medically refractory chronic pain. Current SCS technology delivers static stimulation, or waveforms with fixed, time-invariant clinical parameters. However, the unchanging nature of static stimulation limits therapy personalization and may make the therapy prone to habituation. To improve existing therapy, we aim to build upon previous preclinical and clinical assessments of novel dynamic stimulation (DS) patterns in SCS, in which a therapeutically relevant waveform parameter (amplitude, pulse width, or rate) is configured to vary in time at a specific modulation rate and depth[1,2]. DS patterns may improve pain relief versus static stimulation, customize therapy, and enhance therapy longevity by mitigating habituation[1,3]. To evaluate our hypothesis that DS will improve SCS outcomes, we will undertake a federally funded, first-in-human, randomized, controlled, double-blinded crossover clinical study using an SCS platform capable of delivering DS.

Materials / Methods: We devised a novel blocked clinical study design for a two year 43-patient blinded, cross-over, randomized controlled feasibility trial (NCT05968664). Firmware and software improvements were made to an existing SCS pulse generator (IPG) (“Boston Scientific Wavewriter Alpha®”) to facilitate chronic and direct efficacy comparisons among static SCS, intensity (amplitude/pulse width) modulated DS, and rate modulated DS for the study. Changes to the IPG included implementing: 1) Precise spatial targeting of DS patterns, 2) Automated scheduled delivery of DS patterns, and 3) Energy efficient stimulation. Furthermore, a systematic Stimulation Adjustment Protocol was developed for each therapy block to evaluate therapeutic relevance and effects of DS parameters. The primary and secondary outcomes of NRS pain score, Oswestry Disability Index, and Patient Global Impression of Change along with other biometric and exploratory outcomes will be collected and compared across paradigms during the blinded randomized phase and an open-label long-term follow-up phase.

Results: Development of device firmware and software followed appropriate US quality and regulatory requirements, included formal verification and validation, and culminated in FDA IDE approval for study use in 2023. Preclinical work, IPG modifications, and the clinical trial design will be presented in detail.

Discussion: The RCT feasibility study will evaluate the ability of DS to improve SCS efficacy and longevity along the primary and secondary outcomes.

Conclusions: Prior work provides strong rationale for IPG improvements, and the innovative study design will enable rigorous assessment of the ability of novel DS patterns to improve SCS and to reduce therapy maintenance burden.

Supplemental Data:

References: 1. Edhi, M.M., Heijmans, L., Vanent, K.N., Bloye, K., Baanante, A., Jeong, K.S., Leung, J., Zhu, C., Esteller, R. and Saab, C.Y., 2020. Time-dynamic pulse modulation of spinal cord stimulation reduces mechanical hypersensitivity and spontaneous pain in rats. *Scientific Reports*, *10*(1), p.20358. 2. Frey, R., Zhu, C., Lechleiter, K., Kaufman, H., Moffitt, M., and Esteller, R. Patterned Pulse Trains Yield Manifold Sensations Perceived by Patients during Acute Spinal Cord

Stimulation Evaluation. Poster at the 2019 International Neuromodulation Society Conference. 3. Block, J., Loudermilk, E., Frey, R., Zhu, C., Lechleiter, K., Moffitt, M., and Esteller, R. Dynamic Stimulation (DS) Patterns Produce Varied Pain Coverage During Acute Spinal Cord Stimulation Evaluation. Poster at the 2023 North American Neuromodulation Society Conference.

Acknowledgements: The authors gratefully acknowledge funding support from the US National Institutes of Health (NIH) under grant UG3NS121563.

Learning Objectives: 1. Learn the technical definition, scientific background, and potential therapeutic benefits of novel dynamic stimulation (DS) patterns for spinal cord stimulation (SCS). 2. Learn about firmware and software features for an investigational SCS device that enable sophisticated clinical delivery of DS patterns. 3. Learn about the design of a first-in-human feasibility trial intended to compare outcomes among tonic SCS, intensity-modulated DS patterns, and rate-modulated DS patterns.

Financial Disclosures: Ashwin Viswanathan, Boston Scientific, Consulting/Advisory Board, $20,001 - $100,000 Ashwin Viswanathan, Medtronic, Consulting/Advisory Board, $501-5,000 Tianhe Zhang, Boston Scientific, Company Employee, >$100,000 USD Tianhe Zhang, Boston Scientific, Stock Owner, $20,001-$100,000 USD Tianhe Zhang, Boston Scientific, Stock Options, $20,001-$100,000 USD

Tianhe Zhang, Boston Scientific, Patent Royalties, $20,001-$100,000 USD Jessica Block, Boston Scientific, Company Employee, >$100,000 USD Sandeep Avvaru, Boston Scientific, Company Employee, >$100,000 USD

Sandeep Avvaru, Boston Scientific, Stock Owner, $1-$500 Rosana Esteller, Boston Scientific, Company Employee, >$100,000 USD

Rosana Esteller, Boston Scientific, Stock Owner, $20,001-$100,000 USD Rosana Esteller, Neuropace, Stock Owner, $501 - $5000 USD

Disclosure: (Please see my author disclosures)

314

Poster on Board
POSTER ON BOARD: AS05A. SPINAL CORD: PAIN
13-05-2024 08:00 - 19:00

NURSING VISIT UTILITY PRIOR TO SCS

Alba Vivas Munoz, RN, Miriam Pérez, RN, Eva Monzón, MD, Cristina Abad, MD, Raquel Herrador, RN, Helena Diaz-Hellín, RN, Monica Fernández, RN, David Abejón, MD
University Hospital Quirónsalud, Pain Management, Madrid, Spain

Introduction: The most promising treatment for refractory chronic pain is currently neuromodulation, such as spinal cord stimulation (SCS). In accordance with the guidelines provided by the British Pain Society, patients receive care from a diverse team of professionals skilled in neuromodulation. This approach enables patients to make well-informed choices regarding their therapy and gain a complete comprehension of the treatment process and its impact on their condition.

Materials / Methods: The aim of this study is to optimize and improve long-term outcomes of electrode implantation by analyzing and improving results, identifying key factors contributing to patient satisfaction or dissatisfaction and pinpointing selection criteria failures. In our daily practice, after the medical visit, the patient is assessed and informed by an expert psychologist in chronic pain and later by a nurse in an educational training session. The session consists of a patient's anamnesis, and the assessment of their pain, expectectations, and doubts about benefits and risks that are key points of information as well as giving them a schedule of patient's visits and cares that must be followed by the nurse. A telephone survey was done on the last 20 patients who had been informed in the nurse's educational session (15 women and 5 men). Average age of 58 years who were implanted with a SCS between January 2021 and December 2022 in QuironSalud Madrid Hospital.

Results: The survey found that all patients informed were satisfied with the information provided by the nurse. Doubts and fears were resolved and there was enough time to answer the patient's questions. At the same time, the information provided during the educational session helped when making the decission to be implanted. In general, the care provided was reported as good, however the 60% of patients said that some items of the nurse's educational session should be improved: reinforce that neurostimulation does not always improve, the patient must have patience and adjustment to therapy, more comprehensive information about stimulation and how it works and explain the symptoms of overstimulation.

Discussion: The survey results suggest that the care provided in the nurse's educational sessions was satisfactory for the majority of patients, although there is still space for improvement and efforts should continue to be made to ensure patient satisfaction with spinal cord stimulation therapy.

Conclusions: Within our multidisciplinary team, nursing can play a key role prior to the intervention in the preparation and information to the patient.

Supplemental Data:

References: (1)Yang S, Zhong S, Fan Y, Zhu Y, Xu N, Liao Y, Fan G, Liao X and He S (2023) Research hotspots and trends on spinal cord stimulation for pain treatment: a two-decade bibliometric analysis. Front. Neurosci. 17:1158712. doi: 10.3389/fnins.2023.1158712 (2)Spanish group of neuromodulation spanish guidelines for neurostimulation. Guía española de neuroestimulación en el dolor crónico [Internet]. ESRA; 2005. Abailable in: https://www.esra-spain.org/web/fuentes/NEUROESTIMULACION.pdf

Acknowledgements: To Dr. Abejon's team.

Learning Objectives: 1- Neuromodulation requires a team of professionals who allow a multidisciplinary approach to improve results 2- Nursing can play a key role prior to the intervention in

the preparation and information to the patient 3- Efforts should continue to be made to improve our results in neuromodulation and to ensure patient satisfaction with spinal cord stimulation therapy

Financial Disclosures: No financial support to be disclosed.

Disclosure: No significant relationships.

315

Poster on Board
POSTER ON BOARD: AS05B . SPINAL CORD: INTRATHECAL DRUG DELIVERY FOR PAIN
13-05-2024 08:00 - 19:00

MECHANISTIC PHARMACOKINETIC STUDY OF THE INTRATHECAL DRUG DISPERSION IN THE SPINE

Ayankola Ayansiji, PhD[1], Konstantin Slavin, MD[2], Andreas Linninger, PhD[1,2]
[1]University of Illinois at Chicago, Biomedical Engineering, Chicago, United States of America, [2]University of Illinois at Chicago, Neurosurgery, Chicago, United States of America

Introduction: Intrathecal drug (IT) delivery can efficiently target regions in the central nervous system without hindering the blood-brain barrier. This delivery mode is especially promising for novel therapeutics such as enzyme replacement, gene, or antisense oligonucleotide (ASO) therapies, among others. However, there were speculations that IT delivery method confine drug locally to the injection site. We hypothesis that acute infusion, through catheter, can get the drug spread out and cover large sections of the CNS.

Materials / Methods: To test our hypothesis, we carried out realistic tracer infusion and dispersion (physical transport) experiment in a manufactured subject-specific in vitro model of human spine (in prone position) over the entire physiological range of cerebrospinal fluid (CSF) pulsation amplitudes and frequencies. With the use of high-speed camera, the evolution of the tracer was captured which was later analyzed using in-house MATLAB code. A Distributed Mechanistic Pharmacokinetic (DMPK) model, which quantifies the tracer's bio dispersion alongside uptake (lipophilicity, enzymatic decay, etc.) was then developed and used to back up the experimental data.

Results: The analysis of the obtained tracer evolution shows that tracer moves towards the cranial direction and gets to the head at about 10 min after infusion. Strong micro mixing from the micro anatomical features in the invitro spine increases the speed of the tracer towards the head. The prediction from our computational model also supports the fact that high-volume infusion of tracer can get the tracer to the brain.

Discussion: The use of subject-specific in vitro human spine is very critical to obtaining results that are close to what is obtainable in vivo. In all infusion experiments, there was steady caudocranial advancement towards the head. The DMPK model was used to estimate parameters that quantify biodistribution of tracer.

Conclusions: Our in vitro experiment supports the notion that tracers can successfully target large sections of the neuraxis even get to the brain which is valid for all molecules. The experimental data and the computational results obtained point to the fact that IT delivery method can potentially spread drug in the spine and target the brain.

Supplemental Data:

References: 1) Ayansiji A., Gehrke D., Baralle B, Nozain A, Singh M. R., Linninger AA., Determination of spinal tracer dispersion after intrathecal injection in a deformable CNS model, Frontiers in Physiology 14, 2023. DOI=10.3389/fphys.2023.1244016, 2023 2) Linninger Andreas A., Barua Dipak, Hang Yaming, Iadevaia Sergio, Vakilynejad Majid., A mechanistic pharmacokinetic model for intrathecal administration of antisense oligonucleotides, Frontiers in Physiology 14, 2023. DOI=10.3389/fphys.2023.1130925, 2023 3) Tangen K., Nestorov I., Verma A., Sullivan J., Holt R. W., Linninger A. A. (2020). *In vivo* intrathecal tracer dispersion in cynomolgus monkey validates wide biodistribution along neuraxis. *IEEE Trans. Biomed. Eng.* 67 (4), 1122–1132. doi:10.1109/TBME.2019.2930451 4) Ayansiji A. O. (2023). *Drug delivery to the central nervous system*. Chicago: University of Illinois. PhD Thesis. 5) Tangen K. M., Hsu Y., Zhu D. C., Linninger A. A. (2015). CNS wide simulation of flow resistance and drug transport due to spinal microanatomy. *J. Biomech.* 48 (10), 2144–2154. doi:10.1016/j.jbiomech.2015.02.018 6) Hsu YB, Hettiarachchi HDM,

Zhu DC, Linninger AA. 2012. The frequency and magnitude of cerebrospinal fluid pulsations influence intrathecal drug distribution: key factors for interpatient variability. Anesth. Analg. 115:386–94 7) Belov, V., Appleton, J., Levin, S., Giffenig, P., Durcanova, B., and Papisov, M. (2021). Large-volume intrathecal administrations: Impact on CSF pressure and safety implications. *Front. Neurosci.* 15, 604197. doi:10.3389/fnins.2021.604197

Acknowledgements: The funding from the National Science Foundation, the National Institutes of Health, Neurological Disorders, and Stroke and the National Institute of Aging are gratefully acknowledged. Also, Vaibhav Maheshwari, Takeda, is acknowledged for useful review comments.

Learning Objectives: 1) Drugs can be delivered to the brain intrathecally with acute injection. 2) Amplitude and frequency of pulsation of the CSF play vital role in the acceleration of biodispersion process of drug delivery intrathecally. 3) Novel experimental and computational models that can be used to quantify biodispersion in the spine

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

316

Poster on Board
POSTER ON BOARD: AS05B . SPINAL CORD: INTRATHECAL DRUG DELIVERY FOR PAIN
13-05-2024 08:00 - 19:00

DO ADJUVANTS ATTENUATE TOLERANCE DEVELOPMENT IN LONG-TERM INTRATHECAL OPIOID THERAPY?

Michael Kretzschmar, PhD[1], Lukas Fuhrmann, BSc (Hons)[2], Marcus Schwarz, PhD[3], Marco Reining, MD[1], Erdem Güresir, MD, PhD[4], Dirk Winkler, PhD[5]
[1]SRH Wald-Klinikum Gera, Pain Medcine & Palliative Care, Gera, Germany, [2]Dental practice, Weißenfels, Germany, [3]SRH Hochschule für Gesundheit, Campus Gera, Gera, Germany, [4]Universitätsklinikum Leipzig, Department Of Neurosurgery, Leipzig, Germany, [5]University Hospital Leipzig, Department Of Neurosurgery, Leipzig, Germany

Introduction: Although intrathecal drug delivery systems (IDDS) can be an effective treatment option for patients with chronic pain, there is still confusion regarding optimal dosing. Limited data on efficacy and dose-response, especially in long-term therapy, have resulted in a lack of consensus-based guidelines for IDDS dosing and for the correct management of tolerance[1, 2]. The aim of our study was to determine whether the addition of adjuvants would delay the development of tolerance to continuous intrathecal opioids for pain treatment.

Materials / Methods: A total of 87 patients suffered from chronic non-malignant pain could be analyzed. All patients underwent an efficacy test with a passaged catheter prior to pump implantation to confirm the efficacy of intrathecal opioid administration. The efficacy of the addition of adjuvants was also tested. After successful implantation of the IDDS, the effectiveness of therapy was assessed at each refill (pain intensity? withdrawal symptoms?). If necessary, the opioid dose was adjusted. The patients' average opioid dose was recorded at six-month intervals after each pump implantation. A mixed ANOVA was performed to test the hypothesis that adjuvants slowed the development of opioid tolerance. The Mauchly test and the Fisher-Yates test were used to check the homogeneity of variance and linearity of the results.

Results: The mean age of the 87 patients with implanted IDDS was 61 years, with males being younger than females. A mean duration of therapy of 6.5 years was analyzed. The average daily opioid dose required by patients on monotherapy (mean = 2.08, SD = 1.42) was significantly lower than that required by patients on adjuvant therapy (mean = 3.05, SD = 2.09). The significant increase in opioid dose over time was statistically demonstrated ($F(5,58,563,48) = 13.33$, $p < .001$, $\eta^2 = 0.12$). When testing the hypothesis of linearity of increase, values of 0.21 mg morphine/year were obtained in patients on monotherapy and 0.26 mg morphine/year in patients on combination therapy.

Discussion: The most surprising finding of our study was that patients receiving intrathecal opioid therapy with adjuvants required a higher daily dose of opioids over the long term than patients receiving monotherapy. This contradicts hypotheses previously formulated by other authors. It is also noteworthy that the difference in daily opioid requirements between the adjuvanted and nonadjuvanted groups increased steadily over time

Conclusions: Apparently, the application of adjuvants to intrathecal opioids does not slow the development of tolerance, although the possible progression of baseline pathology was not considered in this study**.**

Supplemental Data:

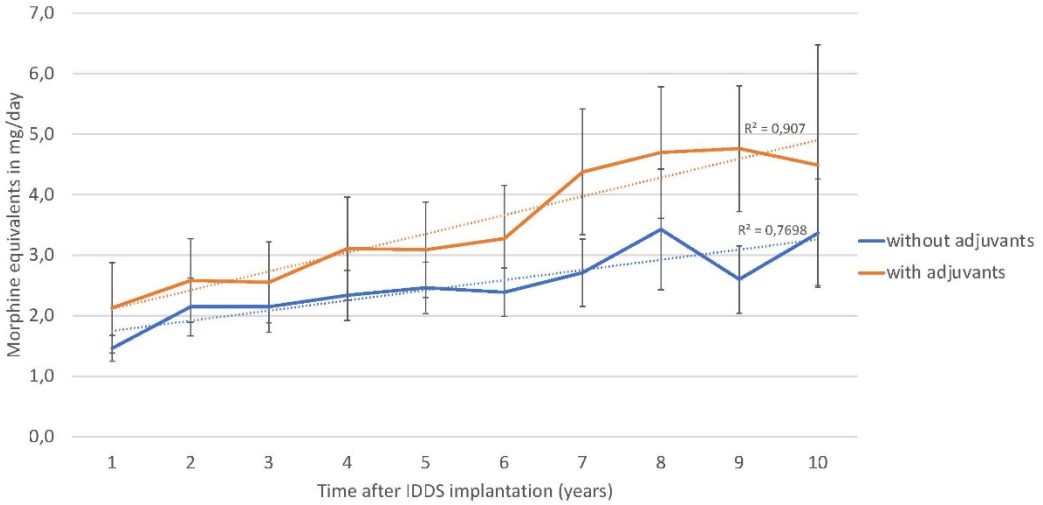


Figure 1.Opioid dose progression in 87 patients with chronic nonmalignant pain treated with pump-directed intrathecal opioid delivery (IDDS). Opioid monotherapy (blue) is compared to opioid therapy with the addition of adjuvants (local anesthetics and/or clonidine) (orange). Mean opioid doses (mg morphine equivalents per day) at 6-month intervals are shown. The dotted lines show the calculated (linear) increase in dose over the treatment period.

References: [1]Duarte RV, Raphael JH, Haque MS et al (2012) A predictive model for intrathecal opioid dose escalation for chronic non-cancer pain. Pain Physician 15(5):363-369 [2]Dumas EO, Pollack GM (2008) Opioid tolerance development: a pharmacokinetic/pharmacodynamic perspective. The AAPS journal 10(4):537-551.

Acknowledgements:

Learning Objectives: 1. Pump-directed intrathecal opioid therapy can be administered long-term to selected patients with chronic non-malignant pain.
2. However, the addition of adjuvants does not slow down the expected increase in the dose of opioids as a function of the duration of therapy.
3. Therefore, the question that needs to be addressed is whether or not these patients actually benefit from the use of adjuvants to intrathecal opioid therapy.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

317

Poster on Board
POSTER ON BOARD: AS05B . SPINAL CORD: INTRATHECAL DRUG DELIVERY FOR PAIN
13-05-2024 08:00 - 19:00

LOW-DOSE ZICONOTIDE AS FIRST-LINE INTRATHECAL MONOTHERAPY: A CASE SERIES WITH 42 MONTHS FOLLOW-UP

Georgios Matis, MD
University Hospital Cologne, Neurosurgery, Cologne, Germany

Introduction: The use of ziconotide in intrathecal analgesia (ITA) has been limited by dose-related side effects. We present our experience with ziconotide as first-line intrathecal monotherapy in patients with chronic pain and present our low and slow dosing algorithm aimed at reducing side effects and appropriately managing pain in these patients.

Materials / Methods: Six patients (mean age 64.5 years (55-78); four (67%) men and two (33%) women; one (17%) with multifocal pain syndrome and five (83%) with persistent spinal pain syndrome (PSPS). All six had mixed forms of pain (a combination of neuropathic and nociceptive pain). Treatment was started with ziconotide when the pain was ≥7 (mean 8.5) on the visual analog scale (VAS). The initial dose was 0.6 µg/day in six patients. After two and four days, the dose was increased by an additional 0.6 µg. Provided that pain relief (even minimal) was perceived after the initial titration on day six at a dose of 1.8 µg/day and no bothersome side effects occurred, a gas pressure-operated pump was implanted in four patients and a battery-operated programmable pump in two patients. A further dose increase was performed with the internal pump. Response to ziconotide was assessed at 1, 6, 12, 24, and 42 months after dose titration.

Results: All patients could be evaluated as responders. They showed a 20% (at 4 weeks, VAS1M), 30% (at 6 and 12 months, VAS6M, 12M), 33% (at 2 years, VAS24M), and 31% (at 42 months, VAS42M) improvement in pain intensity (VAS). Mean pain reduction: VAS1M=6.7 (5.6-8), VAS6M=5.9 (5-7), VAS12M=6 (5.2-7), VAS24M=5.7 (4.9-6.6), and VAS42M=5.9 (5-7). Mean daily dose: 1M=3.6µg (2.4-4.8), 6M=5.1µg (4.2-6), 12M=6.4µg (5.4-7.6), 24M=7.6µg (6.6-8.8), and 42M=7.9µg (7.2-8.8).Two patients (34%) described a perception of a strange taste and one patient (17%) reported nausea during the first three months. No psychiatric abnormalities were observed and one reported mild cognitive impairment. Two patients had elevated serum creatinine kinase levels. None of the patients had discontinued treatment after 42 months.

Discussion: We present our experience with low and slow ziconotide ITA as first-line monotherapy, which had no or moderate side effects. The advantages of the drug are no respiratory depression, no endocrinological disturbances and no development of tolerance.

Conclusions: A conservative dosing strategy can effectively treat chronic pain patients.

Supplemental Data:

References: Georgios Matis, Pasquale De Negri, Denis Dupoiron, Rudolf Likar, Xander Zuidema, Dirk Rasche. Intrathecal pain management with ziconotide: Time for consensus? Brain Behav. 2021 Mar;11 Suppl 1(Suppl 1):e02055. doi: 10.1002/brb3.2055.

Acknowledgements:

Learning Objectives: 1. Raising awareness about ziconotide as an on-label alternative to morphine in the context of the intrathecal therapy. 2. Underlying the necessity of a "start low, go slow" dosing principle. 3. Raising awareness about extent of pain relief and possible side effects.

Financial Disclosures: Esteve Germany - Consultant agreement - $501 - $5,000 USD

Disclosure: No significant relationships.

318

Poster on Board
POSTER ON BOARD: AS05B . SPINAL CORD: INTRATHECAL DRUG DELIVERY FOR PAIN
13-05-2024 08:00 - 19:00

UPDATE ON 2ND EDITION MOBILE APP OF THE 2024 POLYANALGESIC CONSENSUS CONFERENCE (PACC)® GUIDELINES

Gladstone McDowell, MD
Integrated Pain Solutions, Columbus, United States of America

Introduction: The PACC app was first released in 2017 in response to requests from providers for a more readily accessible way to review the published 2016 **P**oly**A**nalgesic **C**onference **C**onference (**PACC**)® panel recommendations. Our goal was to make it easy to reference and integrate the recommendations at medical practices. The first iteration of the app involved not only the algorithms and text descriptions, but also verbal reading of the text and algorithms.

Materials / Methods: For our second edition, the 2024 Polyanalgesic Consensus Conference panel recommendations, charts and references are presented in an easy-to-visualize format. The second edition incorporates many new features such as the ability to zoom, access hyperlinked references, isolate and print desired content, with a new color scheme and modern interactive graphics.

Results: N/A

Discussion: The PACC was convened with INS members worldwide chosen for their recognized clinical expertise, familiarity with the peer-reviewed literature, research capabilities, and previous publications. The world's literature in English was searched to identify and compile the evidence for neuromodulation therapies for the treatment of pain. Peer-reviewed literature was evaluated using the United States Preventive Services Task Force (USPSTF) criteria for quality of evidence modified for neuromodulation studies and consensus points, supported by evidence, created for each major section or topic by the PACC.

Conclusions: The 2017 PACC App has been well received nationally and internationally; utilized to provide a quick review of the information published in the 2016 main PACC article. In response to requests from providers we have updated the app with the 2024 published information, with improvements in functionality and appearance.

Supplemental Data:

References: 1. Deer TR, Pope JE, Hayek SM, Bux A, Buchser E, Eldabe S, De Andrés JA, Erdek M, Patin D, Grider JS, Doleys DM, Jacobs MS, Yaksh TL, Poree L, Wallace MS, Prager J, Rauck R, DeLeon O, Diwan S, Falowski SM, Gazelka HM, Kim P, Leong M, Levy RM, McDowell G II, McRoberts P, Naidu R, Narouze S, Perruchoud C, Rosen SM, Rosenberg WS, Saulino M, Staats P, Stearns LJ, Willis D, Krames E, Huntoon M, Mekhail N. The Polyanalgesic Consensus Conference (PACC): Recommendations on Intrathecal Drug Infusion Systems Best Practices and Guidelines. Neuromodulation. 2017 Feb;20(2):96-132. doi: 10.1111/ner.12538
2. Hayek, SM, et. al., (in press) The Polyanalgesic Consensus Conference (PACC): Intrathecal Drug Delivery Guidance on Safety and Therapy Optimization 2024. *Neuromodulation: Technology at the Neural Interface.*

Acknowledgements:

Learning Objectives: 1. Review the 2024 PACC guidelines and apply recommendations for intrathecal therapy. 2. Understand the process and approach of the Polyanalgesic Consensus Conference in reviewing publications and expert opinions and developing consensus to create guidelines. 3. Utilize the PACC guidelines to assist with decisions when considering appropriate medications, concentrations, dosing, titration, monitoring outcomes and avoiding complications.

Financial Disclosures: The International Neuromodulation Society has received a grant from TerSera Therapeutics to underwrite the technical aspects of the App development.

Disclosure: The International Neuromodulation Society has received a grant from TerSera Therapeutics to underwrite the technical aspects of the App development.

319

Poster on Board
POSTER ON BOARD: AS05B . SPINAL CORD: INTRATHECAL DRUG DELIVERY FOR PAIN
13-05-2024 08:00 - 19:00

THE USE OF VIRTUAL REALITY DURING INPATIENT INTRATHECAL PUMP REFILLS IN CHILDREN

Lisa Goudman, PhD[1], Ann De Smedt, MD[2], Maxime Billot, PhD[3], Manuel Roulaud, MSc[3], Philippe Rigoard, MD[4], Maarten Moens, MD[1]
[1]Vrije Universiteit Brussel, Stimulus Research Group, Jette, Belgium, [2]Universitair Ziekenhuis Brussel, Stimulus Research Group, Jette, Belgium, [3]CHU de Poitiers, Neurosurgery Departement/prismatics Lab, Poitiers, France, [4]Poitiers University, Spinal Neurosurgery, Neuromodulation, Poitiers, France

Introduction: Virtual Reality has proven to be an effective approach to decrease pain in acute settings, both in adults and children. Children who have been implanted with an intrathecal pump are dependent from regular refill procedures at the hospital, which could be accompanied by experiences of fear and pain in relation to the usage of needles for a refill procedure. The aim of this study is to evaluate whether Virtual Reality (VR) could reduce pain during an intrathecal pump refill procedure in children receiving intrathecal drug delivery, compared to a standard refill procedure.

Materials / Methods: This is a prospective experimental single center three-arm crossover randomized controlled trial, evaluating the effect of VR on pain in children undergoing an intrathecal pump refill compared to a standard refill and a refill with distraction (watching a video). Only children with cerebral palsy between 8 and 16 years old who received intrathecal baclofen delivery through an implanted pump were eligible to participate. Pain was evaluated using the Wong-Baker Faces Scale. Secondary outcomes were procedural pain, fear, state anxiety, the incidence of adverse events and satisfaction.

Results: Six children participated in this study, whereby all children underwent the three conditions. Five children indicated an equal of lower pain score during VR, compared to a standard refill. This finding of an equal or lower pain intensity score for the VR condition compared to the control condition was also revealed by the ratings of the parents, physician and the researcher. The influence of VR on anxiety and fear seem to be in line with the influence of watching a video. In terms of satisfaction, all children and parents agreed with the statement that they would like to use VR again for a next refill.

Discussion: Due to the lack of adverse events, the high degree of satisfaction of children with VR and the decreased pain levels after a refill with VR, physicians may aim to explore the implementation of VR during intrathecal pump refill procedures in children, in a daily clinical routine care setting.

Conclusions: Children prefer to have their next intrathecal pump refill with a VR goggle; no adverse events were observed, an equal or lower pain score was revealed and for most of the children, lower degrees of anxiety and fear were observed. Therefore, it may be suggested that VR could be used to facilitate the refill procedure in children who are regularly undergoing an intrathecal pump refill in the hospital.

Supplemental Data:

References: Goudman L, Jansen J, De Smedt A, Billot M, Roulaud M, Rigoard P, Moens M. Virtual Reality during Intrathecal Pump Refills in Children: A Case Series. J Clin Med. 2022 Oct 5;11(19):5877. doi: 10.3390/jcm11195877.

Acknowledgements:

Learning Objectives: 1) To gain insight in non-invasive technologies (e.g., VR, video) to reduce pain during intrathecal pump refill procedures 2) To gain insights in the practical execution of pump refills

with VR in children 3) To know the evidence about the use of VR for intrathecal pump refills in children

Financial Disclosures: Lisa Goudman is a postdoctoral research fellow funded by the Research Foundation Flanders (FWO), Belgium (project number 12ZF622N). Philippe Rigoard reports grants and consultant fees from Medtronic, Abbott and Boston Scientific, outside the submitted work. Maarten Moens has received speaker fees from Medtronic, Nevro and Saluda Medical. There are no other conflicts of interest to declare.

Disclosure: No significant relationships.

320

Poster on Board
POSTER ON BOARD: AS05B . SPINAL CORD: INTRATHECAL DRUG DELIVERY FOR PAIN
13-05-2024 08:00 - 19:00

INTRATHECAL DRUG DELIVERY FOR CHRONIC NON-CANCER PAIN WHEN ELECTRICAL NEUROMODULATION HAS FAILED

Marc Russo, MBBS[1,2,3], Brendan Moore, MBBS[4], James O'Callaghan, MBBS[4], Murray Taverner, MBBS[5], John Monagle, MBBS[6], Danielle Santarelli, PhD[2]
[1]Hunter Pain Specialists, Broadmeadow, Australia, [2]Genesis Research Services, Broadmeadow, Australia, [3]University of Newcastle, School Of Biomedical Sciences And Pharmacy, College Of Health, Medicine And Wellbeing, Callaghan, Australia, [4]Axxon Pain Medicine, Brisbane, Australia, [5]Frankston Pain Management, Frankston, Australia, [6]Berwick Pain Management, Berwick, Australia

Introduction: Modern day intrathecal drug therapy practice for chronic noncancer pain is unclear due to advances made in spinal cord, dorsal horn, and dorsal root ganglion stimulation. One can hypothesise that after one or more failed trials of electrical neuromodulation, intrathecal drug delivery therapy may be more effective than pursuing further trials of electrical neuromodulation. Therefore, a pilot study was envisaged to evaluate the outcomes of low dose targeted drug delivery (TDD) therapy when chosen after negative trial(s) of spinal cord stimulation (SCS). We present the available data and make recommendations around methodology for larger scale trials.

Materials / Methods: This was a prospective, multicentre, investigator-initiated study. Eligible patients with chronic primary back pain who had “failed” SCS therapy were enrolled in the study. “Failed” was defined as an inadequate response to SCS therapy at the trial stage or after permanent implant, or loss of efficacy post-implant. Patients must have failed SCS therapy at least twice or failed once and deemed unsuitable for subsequent SCS intervention. An opioid taper to achieve ≤20mg morphine equivalent dose (MED) was directed pre-implant if required. Patients were implanted with a SynchroMed II infusion system (Medtronic), with or without prior infusion or bolus therapy trial. Intrathecal morphine sulphate or hydromorphone dose started at 0.2mg/day MED and adjusted as needed following the Control Workflow for TDD (Medtronic). Follow-up visits occurred at 1-, 4-, 6-, and 12-months post-implant. Outcome measures included pain VAS, Brief Pain Inventory, quality-of-life (EQ-5D-5L), 36-Item Short Form (SF-36) health survey, and adverse events.

Results: Nine patients were enrolled and four withdrew post-4-month visit. At 4-months, three patients reported ≥50% pain relief. At 12-months, three of five remaining patients reported ≥50% pain relief and all reported ≥30% pain relief. Due to low recruitment numbers, the data could not be analysed as planned.

Discussion: Whilst the concept for this study was sound and the need to re-evaluate the place for intrathecal drug delivery in chronic noncancer pain remains, it became clear that more implanting sites are required to achieve a sufficient sample size for analysis. A 25% dropout rate should be expected.

Conclusions: A multinational study may be required to provide definitive trial outcomes. In the absence of such a study, patients should be counselled that some, but certainly not all, patients can be salvaged with TDD.

Supplemental Data:

References:

Acknowledgements: We thank the study site staff for their contributions to the study.

Learning Objectives: Objective 1: Readers should be able to describe a clinical scenario in which intrathecal drug therapy may be an appropriate option for the management of chronic noncancer pain. **Result:** Intrathecal drug therapy may be capable of rescuing pain relief in patients with chronic noncancer pain who have failed spinal cord stimulation. **Objective 2:** Readers should be able to list methods for achieving sufficient participant numbers in future clinical trials of intrathecal drug therapy. **Result:** High number of implanting sites (>5), recruit top implanters, international sites may be required. A 25% dropout rate should be expected. **Objective 3:** Readers should be able to list the various variables studied as part of documenting the pain experience. **Result:** Pain VAS, Brief Pain Inventory, quality-of-life (EQ-5D-5L), 36-Item Short Form (SF-36) health survey, and adverse events.

Financial Disclosures: The clinical trial was supported by the Medtronic External Research Program (ERP-2018-11566).

Disclosure: Dr Russo discloses non-paid consultancies to and research activities for Boston Scientific, Mainstay Medical, Medtronic, Nevro, Presidio Medical, and Saluda Medical.

321

Poster on Board
POSTER ON BOARD: AS05C. SPINAL CORD: SPASTICITY
13-05-2024 08:00 - 19:00

SPASTICITY MORE THAN PAIN WAS IMPROVED IN THREE PATIENTS WITH TRAUMATIC SPASTIC PARAPARESIS AND NEUROPATHIC PAIN TRATED BY SPINAL CORD STIMULATION

Juan Carlos M. Andreani, MD, Guillermo Larrarte, BChir, Félix Barbone, BChir
Ministery of Public Health- Pcia de Buenos Aires - Argentina, Provincial Program Of Neuromodulation, Avellaneda, Argentina

Introduction: Refractory Spasticity and Pain are common complications in Paraplegia and their treatment by Spinal Cord Stimulation (SCS) have been extensively reported in the international Bibliography (1,2). Nevertheless, in despite Pain is present in 57 % of the cases of Spastic Paraplegia (3), little has been described about their independent evolution when treated by SCS (4). The objective of this presentation is to show preliminary results in three cases of an ongoing clinical trial.

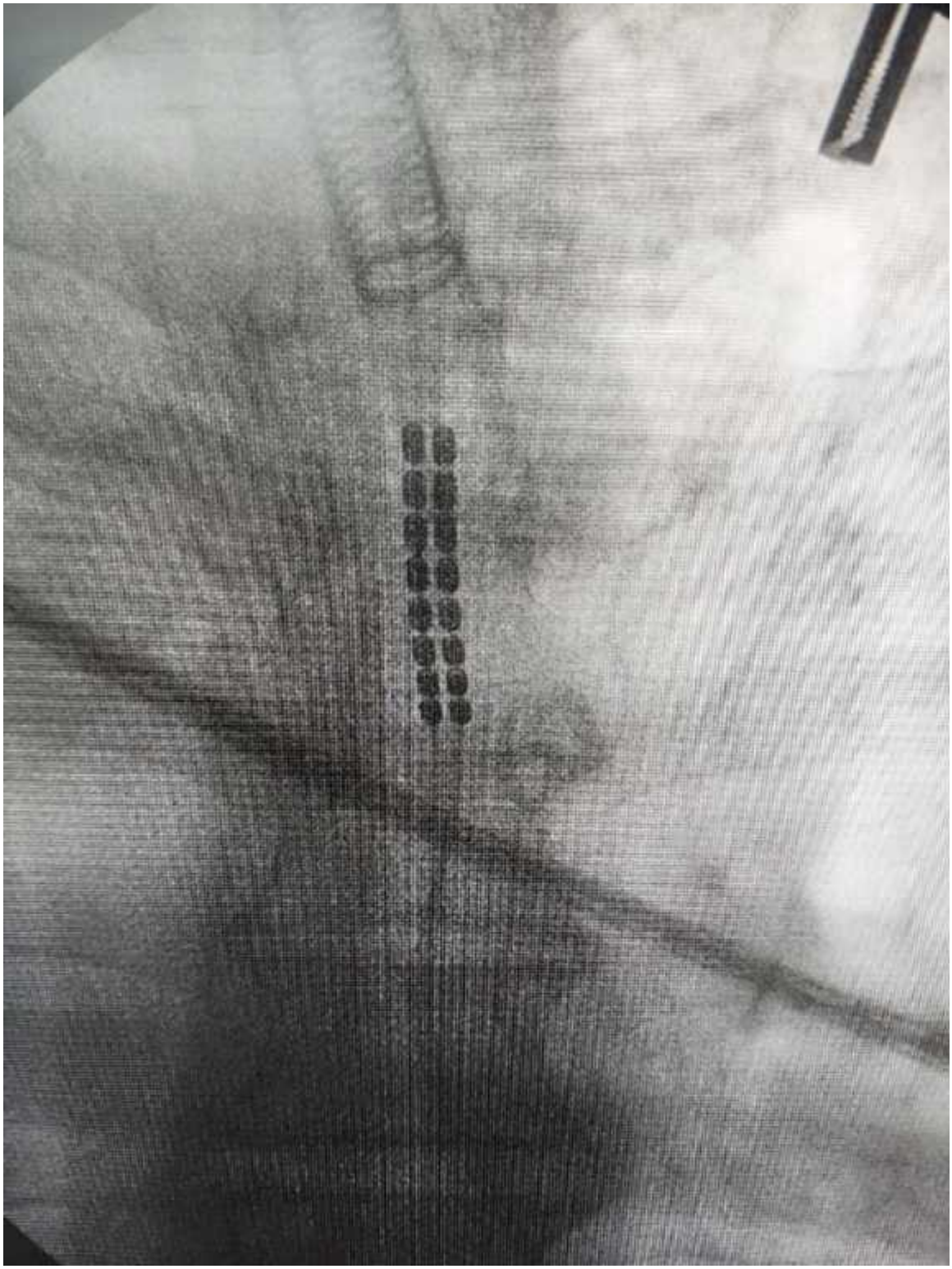
Materials / Methods: Three male patients with Spastic traumatic paraparesis (2 cases Asia C and 1 ASIA D Scale) at lower dorsal spinal level with Pain (Table 1) were treated by dorsal spinal cord stimulation (figure 1(a) and (b)). Pre and post interventional Ashworth and Penn scales assessments, as well as Visual Analogue Scale (VAS) were monthly performed, 3 months before and after surgeries.

Results: Pre and post interventional Ashworth and Penn scales assessments showed significant improvement (Table 2) while VAS showed mild or no improvement during the post operative evaluations (Table3), Two patients (1 and 2) regained some walking capacity in reason of the diminishon of the severity of Spasticity and spasms

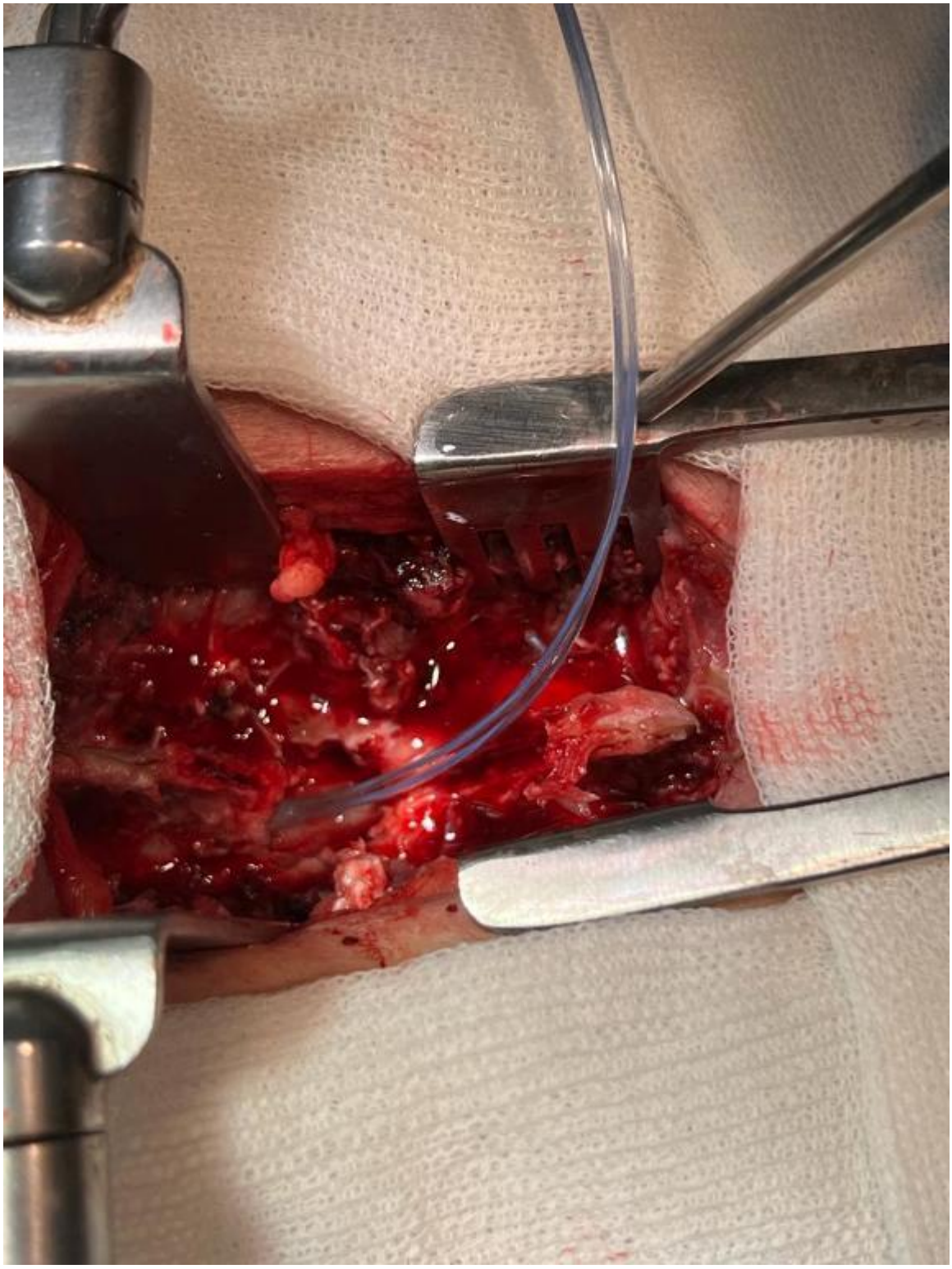
Discussion: We have found in our 3 cases, a more favorable evolution of spasticity and the frequency of spasms than in the improvement of pain. Improvement in neurpathic pain has been described in isolated cases of complete paraplegia (ASIA A)(5). A recent extensive review (6) describes the high prevalence of neuropathic pain in tetraplegics and below the lession. Other authors (7,8) focusing in Spasticity have extensively described described the Pathophysiology of both. There are also authors who have extensively described the benefits and complications of Spinal Cord Stimulation (SCS) in refractory spasticity (9, 10, 11). However,none of those works provide data on the parallel evolution of both neurological signs.

Conclusions: While spasticity was strongly and rapidy improved in our cases, pain showed a unparalell mild positive reults

Supplemental Data:



Topographyc electrodes´s placement



Fg ure 1(b). Surgica electrodes placement **TABLES 1 -2 - 3**

	Level of spinal injury	Ethiology	Clinical picture	Level of spinal electrode implant
Patient 1 Male, 73 y.o.	T9	Gunshot Impact at vertebra D11. Contussive lession over Spinal Cord, no penetration 10 years before implant	Neuropathic, Bilateral, shooting Pain crisis. Distal bilateral Spasticity (more manifest at right), Spasms preventing gait	T5-7
Patient 2 Male, 51 y.o.	T8	Gunshot impact at vertebra D12, parasagital penetration 12 years before implant	Neuropathic, both legs, shooting crisis, whole legs bilateral Spasticity, frequent spasms	T5-7
Patient 3 Male, 48 y.o.	T11 + Radicular avulsion L4-5	Shotgun wound with pellets, Spinal penetration at vertebra 12, bullet remaining in Spinal canal, additional lesion at lower lumbar vertebrae	Right unilateral leg bilateral shooting pain, frequent spasms distal segmental spasticity related to left foot and ankle	T7-9

	Mean Pre-operative Penn scale value (3 monthly assessments prior to IPG implant	Mean Post-operative Penn scale value (monthly assessments after IPG implant	Mean Pre-operative Ashworth scale value on hip, knee, ankle and toes (3 monthly bilateral assessments prior to IPG implant	Mean Post-operative Ashworth scale value on hip, knee, ankle and toes (monthly bilateral assessments prior to IPG implant
Patient 1 Male, 73 y.o.	3,3	2,1 (8 monthly evaluations)	3,2	1,8 (8 monthly evaluations)
Patient 2 Male, 51 y.o.	3,66	1,9 (11 monthly evaluations)	3,8	2 (11 monthly evaluations)
Patient 3 Male, 48 y.o.	3	1,8 (14 monthly evaluations)	3,1	2,1 (14 monthly evaluations)

	Mean Pre-operative Penn scale value (3 monthly assessments prior to IPG implant	Mean Post-operative Penn scale value (monthly assessments after IPG implant	Mean Pre-operative Ashworth scale value on hip, knee, ankle and toes (3 monthly bilateral assessments prior to IPG implant	Mean Post-operative Ashworth scale value on hip, knee, ankle and toes (monthly bilateral assessments prior to IPG implant
Patient 1 Male, 73 y.o.	3,3	2,1 (8 monthly evaluations)	3,2	1,8 (8 monthly evaluations)
Patient 2 Male, 51 y.o.	3,66	1,9 (11 monthly evaluations)	3,8	2 (11 monthly evaluations)
Patient 3 Male, 48 y.o.	3	1,8 (14 monthly evaluations)	3,1	2,1 (14 monthly evaluations)

References: 1) Cioni B, Meglio M, Pentimalli L, Visocchi M.Spinal cord stimulation in the treatment of paraplegic pain 2) Nagel SJ, Wilson S, Jhonson M, et al. Spinal cord stimulation for Spasticity: Historical approaches, Current Status, and Future Directions. Neuromodulation 2017;20: 307-32. 3) Priebe MM, Sherwood AM, Thornby JI, Kharas NF, Markowski J. Clinical assessment of spasticity in spinal cord injury: a multidimensional problem. Arch Phys MedRehabil1996;77: 713–6. 4) Pain severity and mobility one year after spinal cord injury: a multicenter, cross-sectional study. 4) Marcondes BF, Sreepathi S, Markowski J, Nguyen D, Stock SR, Carvalho S, Tate D, Zafonte R, Morse LR, Fregni .Pain severity and mobility one year after spinal cord injury: a multicenter, cross-sectional study..Eur J Phys Rehabil Med. 2016 Oct;52(5):630-636. 5) Reck TA, Landmann G.Successful spinal cord stimulation for neuropathic below-level spinal cord injury pain following complete paraplegia: a case report. Spinal Cord Ser Cases. 2017 Aug 10;3:17049. 6) Burke D, Fullen BM, Stokes D, Lennon O. Neuropathic pain prevalence following spinal cord injury: A systematic review and meta-analysis. Eur J Pain 2016; 24: 905. 7) Billington Z.J., Henke A.M., Gater D.R. Spasticity management after spinal cord injury: The here and now. J. Pers. Med. 2022;12:808. 8) Guest J , Datta N, Jimsheleishvili G, Gater DR. Pathophysiology, Classification and Comorbidities after Traumatic Spinal Cord Injury.J Pers Med. 2022 Jul 11;12(7):1126. 9) Dones I, Levi V. Spinal Cord Stimulation for Neuropathic Pain: Current Trends and Future Applications. Brain Sci. 2018 Jul 24;8(8):138. 10) Dekopov AV, Shabalov VA, Tomsky AA, Hit MV, Salova EM. Chronic Spinal Cord Stimulation in the Treatment of Cerebral and Spinal Spasticity. Stereotact Funct Neurosurg. 2015;93(2):133-139. 11) Mayr W, Krenn M, Dimitrijevic MR. Epidural and transcutaneous spinal electrical stimulation for restoration of movement after incomplete and complete spinal cord injury. Curr Opin Neurol. 2016 Dec;29(6):721-726

Acknowledgements:

Learning Objectives: 1) To determine the different outcomes of Spasticity and Pain in Paraplegia. 2) To assess the isolated outcomes of Spasticity and Pain in Paraplegic patients whenever clinically associated. 3) To study the Pathophysiological relationships of Pain and Spasticity in Paraplegia

Financial Disclosures: No conflicts of interest

Disclosure: No significant relationships.

322

Poster on Board
POSTER ON BOARD: AS05C. SPINAL CORD: SPASTICITY
13-05-2024 08:00 - 19:00

UTILITY OF BACLOFEN, INTRATHECALLY ADMINISTERED BY BOLUS IN THE TREATMENT OF SPASTICITY

Sue Copley, MSc[1], Sam Eldabe, FRCA[2], Maria-Luisa Rosato, RN[3], Jeanine Le Berre, RN[3], Vaishali Wankhede, MD[3], Massimo Allegri, MD[3], Eric Buchser, MD[3]
[1]South Tees Hospitals NHS Foundation Trust, Pain Management, Middlesbrough, United Kingdom, [2]James Cook University Hospital, Department Of Pain Medicine, MIDDLESBROUGH, United Kingdom, [3]EHC Hopital de Morges, Pain And Neuromodulation Centre, Morges, Switzerland

Introduction: Intrathecal baclofen has been used for the treatment of spasticity of cerebral or spinal origin for a number of decades with an established record of effectiveness and safety. [1-3] Most studies report the administration of intrathecal baclofen (ITB) by continuous infusion. Few studies have reported on the use of boluses of baclofen with some degree of success for the treatment of refractory spaticity. [4-6]

Materials / Methods: We present a retrospective review of the outcomes of 15 adult patients treated with boluses of baclofen for the treatment of spasticity over a duration of 192 years. Diagnoses included hypoxic brain injury, spinal cord injury and degenerative disease processes. Doses, including permitted frequency and size of bolus, plus how many doses were self-administered between refills were recorded. Pain scores, self-reported improvement (when available), and clinically relevant adverse events were noted.

Results: Most patients received baclofen, 4 patients received baclofen and clonidine. The median (IQR) duration of therapy was 14.3 years (9.8, 16.5). Median (IQR) baclofen dose was 183µg (125, 275). Number of bolus doses available to patients ranged from 1 to 20 per day with a median (IQR) dose of 15µg (12.2, 28.3). Bolus per day use was median (IQR) 0.8 (0.16, 1.8). Median (IQR) (NRS) scores (n=15) were 4.2 (1.9, 5.0). Reported improvement (n=12) was 70% (60%, 80%). Only 3 clinically relevant adverse effects were noted from the patient records. One patient had a blocked catheter, followed by catheter fracture and pump failure which presented with increased spasticity. The second patient presented with increased spasticity prior to the expected refill date; their pump was empty despite a 7mL expected discard. It is likely they had a partial pocket fill with no noted ill effects at the time of pump refill.

Discussion: Dosing regime varied between patients, with some patients having larger and more frequent bolus available, whereas others had small doses or few boluses available. Patients rarely used the full amount of bolus doses, and the three adverse effects related to baclofen treatment were not due to patient overdose, but to an unexpected withdrawal of the treatment. When reported in the notes, patient improvement was high.

Conclusions: Intrathecal baclofen administered by bolus, has the potential to reduce spasticity that may not respond to baclofen continuous infusion. Our findings confirm the reports of others that boluses of baclofen are safe and may improve the efficacy of ITB in selected patients.

Supplemental Data:

References: 1. Coffey JR, Cahill D, Steers W, et al. Intrathecal baclofen for intractable spasticity of spinal origin: results of a long-term multicenter study. *J Neurosurg.* 1993;78(2):226-232. 2. Hoving MA, van Raak EP, Spincemaille GH, et al. Safety and one-year efficacy of intrathecal baclofen therapy in children with intractable spastic cerebral palsy. *Eur J Paediatr Neurol.* 2009;13(3):247-256. 3. Schiess MC, Eldabe S, Konrad P, et al. Intrathecal Baclofen for Severe Spasticity: Longitudinal Data From the Product Surveillance Registry. *Neuromodulation.* 2020. 4. Heetla HW, Staal MJ, van Laar T. Tolerance to continuous intrathecal baclofen infusion can be reversed by pulsatile bolus

infusion. *Spinal Cord.* 2010;48(6):483-486. 5. Hoving MA, van Raak EP, Spincemaille GH, Palmans LJ, Sleypen FA, Vles JS. Intrathecal baclofen in children with spastic cerebral palsy: a double-blind, randomized, placebo-controlled, dose-finding study. *Dev Med Child Neurol.* 2007;49(9):654-659. 6. Clearfield JS, Nelson ME, McGuire J, Rein LE, Tarima S. Intrathecal Baclofen Dosing Regimens: A Retrospective Chart Review. *Neuromodulation.* 2016;19(6):642-649.

Acknowledgements: N/A

Learning Objectives: 1 To show that ITB effective for spasticity: desired result to inform other clinicians that this may be a more effective therapy for their patients where continuous infusion is not providing sufficient relief. 2 . Animal studies have shown larger distribution of baclofen in CSF by bolus administration: this may indicate why this method of treatment in these patients has an improved result. 3. ITB boluses may be an effective long term solution clinically: therefore this may provide more acceptable care for patients, enabling them to manage their own pain releif needs more effectively.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

323

Poster on Board
POSTER ON BOARD: AS05C. SPINAL CORD: SPASTICITY
13-05-2024 08:00 - 19:00

SUCCESSFUL SPASTICITY MANAGEMENT VIA INTRATHECAL BACLOFEN IN A PATIENT WITH ALS

Alexandra Moreira, MD
University of Miami/JMH, Miami, United States of America

Introduction: A 41 year old female with a past medical history of Amyotrophic lateral sclerosis (ALS) (HCC) presenting to clinic after Baclofen pump implantation for management of spasticity. She was first diagnosed 2 years prior after noticing a gradual onset of progressively worsening symptoms. Initially, she experienced had left-hand weakness followed by slowing of her speech. Her gait became slower and stiffer. A month later, she noticed right hand weakness affecting her dexterity and causing her difficulty while doing ADLs. Months later her disease process progressed involving bilateral lower extremity weakness (L>R) and dysphagia. Her limitations with swallowing food led to a significant weight loss and nutritional decline. Within months, she developed dyspnea and orthopnea as well and was evaluated worked up by neurology. She was referred to pain clinic for spasticity management. She underwent successful baclofen trial and underwent implantation of intrathecal baclofen pump implant six months later. Since implantation, her pain has improved and care giver burden has decreased significantly. Patient is currently taking Riluzole for her disease progression, gabapentin for neuropathic pain, and magnesium for muscle cramping.

Materials / Methods: Setting: Outpatient Physical Medicine and Rehabilitation Clinic

Results: Patient was weaned off of orals and successfully managed via intrathecal baclofen pump for her spasticity without major complications.

Discussion: ALS is a degenerative motor neuron disease characterized by severe movement disorders. The disease progressively results in respiratory insufficiency, spasticity and painful muscle which limits quality of life. ALS is a progressive neurodegenerative disorder. Baclofen, an agonist of γ-amino butyric acid, is one of the most effective drugs in the treatment of spastic movement disorders. However, higher oral dosages required for sufficient spasticity control are related to intolerable central side effects3. The use of intrathecal baclofen in treating amyotrophic lateral sclerosis has not been commonly studied.

Conclusions: This report highlights a rare case of successful spasticity management via intrathecal Baclofen pump implantation in a patient with ALS.

Supplemental Data:

References: 1. Elman LB et al. Clinical features of amyotrophic lateral sclerosis and other forms of motor neuron disease. Uptodate. Updated Feb 13, 2023. Accessed June 2, 2023. 2. McClelland S 3rd, Bethoux FA, Boulis NM, Sutliff MH, Stough DK, Schwetz KM, Gogol DM,Harrison M, Pioro EP. Intrathecal baclofen for spasticity-related pain in amyotrophic lateral sclerosis: efficacy and factors associated with pain relief. Muscle Nerve. 2008 Mar;37(3):396-8. doi: 10.1002/mus.20900. PMID: 178943583. 3. Marquardt G, Seifert V. Use of intrathecal baclofen for treatment of spasticity in amyotrophic lateral sclerosis. Journal of Neurology, Neurosurgery & Psychiatry 2002;72:275-276. 4. Norris FH, Sang U K, Sachais B, Carey M. Trial of Baclofen in Amyotrophic Lateral Sclerosis. Arch Neurol. 1979;36(11):715–716. doi:10.1001/archneur.1979.00500470085019

Acknowledgements:

Learning Objectives: 1. Identifying successful strategies for management of refractory spasticity in patients with ALS. 2. Describe intrathecal baclofen pump therapy for this unique subset population of

ALS patients. 3. Increase awareness of ALS spasticity treatment options for familiies and clinicians/pain providers.

Financial Disclosures: Alexandra Moreira, MD (Role: Primary Author) Nicole Pontee, MD (Role: Co-Author) Kaitlyn Brunworth, MD (Role: Co-Author) No significant relationships.

Disclosure: No significant relationships.

324

Poster on Board
POSTER ON BOARD: AS05D. SPINAL CORD: FUNCTIONAL RESTORATION
13-05-2024 08:00 - 19:00

NEUROIMAGING INSIGHTS INTO THE MECHANISMS OF NON-INVASIVE SPINAL CORD TRANSCUTANEOUS STIMULATION FOR FUNCTIONAL RECOVERY AFTER SPINAL CORD INJURY

Nabila Brihmat, PhD[1], Mehmed Bayram, PhD[1], Fan Zhang, PhD[1], Soha Saleh, PhD[2], Guang Yue, PhD[3], Gail Forrest, PhD[1]
[1]Kessler Foundation, Tim And Caroline Reynolds Center For Spinal Stimulation, West Orange, United States of America, [2]Department of Rehabilitation and Movement Sciences, School of Health Professions, Department Of Neurology, Robert Wood Johnson Medical School (rwjms), Newark, United States of America, [3]Center for Mobility and Rehabilitation Engineering Research, Kessler Foundation, West Orange, United States of America

Introduction: Non-invasive spinal cord transcutaneous stimulation (scTS) is a neuromodulatory intervention that has the potential to enhance the therapeutic effects of activity-based training (ABT) on upper extremity (UE) function recovery after a spinal cord injury (SCI). The beneficial effects of scTS on function recovery are thought to be due to spinal and supraspinal plasticity mechanisms. Here, we present findings on supraspinal and corticospinal changes related to scTS-based training in SCI individuals.

Materials / Methods: Neuroimaging and functional data were obtained from 7 participants with chronic, cervical, complete, and incomplete SCI, in the context of an ongoing 3-arm, multicenter, open-label RCT. The protocol consists of a baseline assessment, 60 sessions of intervention, and re-assessment post-intervention. During the interventions, each participant received UE ABT with or without continuous targeted scTS applied depending on participants tolerability and deficits. UE sensorimotor function was assessed using the GRASSP scale scores. Functional MRI was acquired to examine changes in resting-state functional connectivity (FC). Using the Conn v12 toolbox, regression analysis was performed to explore the relationship between SMN FC and the GRASSP scores at baseline, and paired t-tests were used to investigate Pre-to-Post changes in SMN FC. Five of the participants additionally underwent fNRIS and TMS assessment during one of their sessions to investigate respectively, real-time cortical and neurophysiological modulation induced by a single session of scTS-based training.

Results: No serious side effects have been observed or reported. The participants showed different level of sensorimotor impairments at baseline that were associated with increased FC between regions of the SMN and decreased FC between SMN regions and visual associative and cerebellar regions, mainly within the left hemisphere. By the end of the scTS-based training, UE sensorimotor function increased in all participants (ΔGRASSP = +25.9 ± 10.2). The functional improvements were associated with reorganization in FC within SMN and between SMN regions and the rest of the brain. The findings also highlight effects of single-session interventions on real-time SMN activity and intracortical inhibition.

Discussion: The results confirm the involvement of supraspinal and corticospinal processes in the effects of scTS-based training on function in chronic SCI individuals; processes that seem to already appear after single session intervention.

Conclusions: Understanding spinal and supraspinal underlying mechanisms of scTS would help future optimization of scTS-based rehabilitation after CNS injury. Neuroimaging findings could be used as markers of scTS intervention efficacy.

Supplemental Data:

References: None

Acknowledgements: The study received funding from the Tim Reynolds Foundation. The authors would like to acknowledge the center research team and the participants for their involvement in the study.

Learning Objectives: 1. Single session of scTS-based training induces visible cortical and corticospinal changes in SCI participants. 2. Repeated sessions of scTS-based rehabilitation training improve upper-extremity sensorimotor function in individuals with complete and incomplete SCI. 3. Functional changes in the brain involve regions outside the sensorimotor network, such as those pertaining to the prefrontal and visual cortices.

Financial Disclosures: No significant financial relationships.

Disclosure: No significant relationships.

325

Poster on Board
POSTER ON BOARD: AS05D. SPINAL CORD: FUNCTIONAL RESTORATION
13-05-2024 08:00 - 19:00

MULTISYSTEMS NEURO-MODULATION THROUGH EPIDURAL ELECTRICAL STIMULATION IN A CHRONIC COMPLETE SPINAL CORD INJURY PATIENT: FROM MOTOR CONTROL TO AUTONOMIC FUNCTIONS

Alessandro Dario, MD[1], Franco Molteni, MD[2], Elena Guanziroli, PhD[2], Alessandro Specchia, PhD[2], Maurizio Cazzaniga, MD[2], Giulio Gasperini, MD[2]
[1]ASST Settelaghi-Insubria University, Neurosurgical Clinic, varese, Italy, [2]Valduce Hospital, Villa Beretta Rehabilitation Center, Costamasnaga, Italy

Introduction: Spinal cord injury (SCI) alters the equilibrium between inhibition and excitement signals that are essential to enable functional states of spinal circuits. Epidural electrical stimulation (EES) of the lumbar tract is one of the possible strategy to stimulate the pathways disrupted by the injury and the most common application is for chronic pain control. The therapeutic effect of EES may improve motor, autonomic and bladder control after spinal cord injury. The aim of this work is to verify if epidural electrical stimulation of the lumbar tract for chronic pain control with a proper stimulation configuration setting can produce a multisystem (motor and autonomic functions) neuro-modulation in a chronic complete thoracic spinal cord injury patient.

Materials / Methods: A complete chronic motor complete spinal cord injury at T6, classified according to American Spinal Injury Association Impairment Scale as level A was enrolled in the study. A 16-electrode array was implanted 4 years after the acute event for pain control. sEMG of lower limbs muscles during an overground gait training with a powered wearable exoskeleton, autonomic nervous system evaluation and urodinamic bladder evaluation were collected with the EES off and with EES with different electrode configuration and current frequency and intensity.

Results: sEMG data shows that lower limb muscular activation induced by overground exoskeleton gait training alone is able to induce muscular activation ,that is influenced by the exoskeleton setting in a complete spinal cord injury patient. The combination of exoskeleton overground gait training, with proper Ekso setting , in combination with EES is able to further modulate modify the lower limb muscular pattern improving muscles activation in terms of intensity and timing. EES changes autonomic regulatory system was measured with more physiological responses related to postural changes and termic stimulation provided during autonomic nervous system evaluation. During EES we don’t found increasing in bladder pressure.

Discussion: In this study an unique EES configuration with different current intensity is able to drive rhythmic motor circuitry during gait supported by wearable powered robotic eksoskeleton and to provide a modulation of the autonomic nervous system causing vasoconstriction an ergogenic effect during tilt up test, and a consequent increase in blood pressure and vasoconstriction venous return, without increasing bladder pressure was defined.

Conclusions: The SCS could restore several functions lost in praplegic patients

Supplemental Data:

References: None

Acknowledgements: none

Learning Objectives: 1. evaluate the SCS use in paraplegic patients 2. valuate the current output to obtain functional improvements 3. clarify the spinal mechanisms of this improvement

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

326

Poster on Board
POSTER ON BOARD: AS05D. SPINAL CORD: FUNCTIONAL RESTORATION
13-05-2024 08:00 - 19:00

ELECTROPHYSIOLOGICAL CHANGES IN PATIENTS WITH CHRONIC COMPLETE PARAPLEGIA THAT ARE SUBJECT TO EPIDURAL SPINAL CORD STIMULATION

Dimitrios Peios, MD[1], Georgios Matis, MD[2], Antonis Kerasnoudis, MD[3], Aikaterini Kyriakidou, MD[3], Christina Ble, MD[1], Ioannis Moralis, MD[4], Nikolaos Psarras, MD[4], Konstantinos Kontogiannis, MD[4], Ilias Kopatzidis, MD[1], Athanasios Koulousakis, MD[5]
[1]St Luce's Hospital, Panorama Thessaloniki, Functional Neurosurgery, Thessaloniki, Greece, [2]University Hospital Cologne, Neurosurgery, Cologne, Germany, [3]St Luce's Hospital, Panorama Thessaloniki, Neurology, Thessaloniki, Greece, [4]St Luce's Hospital, Neurosurgery, Thessaloniki, Greece, [5]Kunibertsklinik, Cologne, Germany

Introduction: Spinal Cord Injury (SCI) is a condition that requires long effort, time and resources to rehabilitate and retrain the patient and the damaged nervous system. For the chronic paraplegic seeks continuously new techniques, medications and interventions that may enhance and accelerate the recovery process. Assistance to the evaluation for the efficacy of such measures is the neurophysiological investigation in specific time intervals. We report the findings from 3 of our patients' investigations in one-year follow-up of their rehabilitation progress after an implantation of an epidural spinal cord stimulator (eSCS).

Materials / Methods: We implanted SCSs in 3 patients with SCI. All have been operated in the spine with various forms of fusion, have undergone treatment at rehabilitation centers and have been stable with complete motor and complete or incomplete sensory paralysis with sphincter dysfunction. The lead was implanted at T11-T12 with laminectomy of L1 or T12, according to the level of conus medullaris. A surgical 16 electrodes lead was used in all cases. Various programs were tested at frequencies from 15 to 200 Hz, pulse width up to 450ms and intensity being set according to presentation of pain, local spasticity or tremor. Investigations were performed every 3 months with the stimulator on and off.

Results: Applying separated stimulating programs for the left and right side and upper (trunk, thigh) and lower (tibia, foot) parts of the legs during exercise produced more constant responses to electrophysiology and electromyographic recordings. In 3 of our patients, there was total absence of electrical dynamics at the time of implantation that remained fairly unchanged for over next 3 months. At 6 months, significant changes were seen with the appearance of Motor Unit Potentials (MUPs) that were recorded even with the stimulator off.Best Potentials without triggering spasticity were recorded at 15hz.

Discussion: Neurophysiological studies are important to measure outcomes and indicate the need to alter the stimulation settings in patients with complete paraplegia, since most of the time these patients cannot provide feedback that will help the attending physician improve the stimulation parameters.

Conclusions: There is an enormous interest at the momment for the use of electrical stimulation of the spinal cord for the treatment of SCI. Techniques that monitor the neurophysiology are essential to apply stimulating programs as reproducibly as possible with less complicated processes and less burden to an already damaged nervous system.

Supplemental Data:

References: Korupolu R, Stampas A, Singh M, Zhou P, Francisco G. Electrophysiological Outcome Measures in Spinal Cord Injury Clinical Trials: A Systematic Review. Top Spinal Cord Inj Rehabil. 2019; 25(4):340-354 Dorrian RM, Berryman CF, Lauto A, Leonard AV. Electrical stimulation for the treatment of spinal cord injuries: A review of the cellular and molecular mechanisms that drive

functional improvements. Front Cell Neurosci. 2023;17:1095259. Hachmann J et al. Epidural spinal cord stimulation as an intervention for motor recovery after motor complete spinal cord injury. J Neurophysiology 2021; 126(6): 1843-1859 Seáñez, I., Capogrosso, M., Minassian, K., Wagner, F.B. (2022). Spinal Cord Stimulation to Enable Leg Motor Control and Walking; pp 369–400 in: People with Spinal Cord Injury. In: Reinkensmeyer, D.J., Marchal-Crespo, L., Dietz, V. (eds) Neurorehabilitation Technology. Springer, Cham. https://doi.org/10.1007/978-3-031-08995-4_18

Acknowledgements:

Learning Objectives: 1. Share observations
2. Get remarks-suggestions
3. Suggest reproduction to further study the results

Financial Disclosures: no significant relationships

Disclosure: No significant relationships.

327

Poster on Board
POSTER ON BOARD: AS05D. SPINAL CORD: FUNCTIONAL RESTORATION
13-05-2024 08:00 - 19:00

FUNCTIONAL RECOVERY OUTCOMES IN A SPINAL CORD INJURED ANIMAL MODEL USING BRAIN AND SPINAL CORD PAIRED STIMULATION

Chih-Wei Peng, PhD[1], Muhammad Adeel, PhD[2], Kenneth Gustafson, PhD[3]
[1]Taipei Medical University, School Of Biomedical Engineering, Taipei, Taiwan, [2]National Taipei University, Smart Healthcare Management, New Taipei City, Taiwan, [3]Case Western Reserve University, Department Of Biomedical Engineering, Ohio, United States of America

Introduction: Paired stimulation in the form of simultaneous brain and spinal cord stimulation is the latest non-invasive neuromodulation technique with very less side effects in the SCI population. It utilizes repetitive transcranial magnetic stimulation (rTMS) and trans-spinal direct current stimulation (ts-DCS). The long-term functional recovery after spinal cord injury (SCI) can be predicted using paired stimulations. We aimed to predict functional recovery using motor evoked potential (MEP) and Basso, Beattie, and Bresnahan (BBB) locomotor rating scale in the SCI animal model after brain and spinal cord paired stimulations.

Materials / Methods: A total of thirty Sprague Dawley rats were used in this study. The rats were divided into five groups of different stimulations for up to four weeks. There were two kinds of paired stimulations employed including 3 min iTBS/tsDCS and iTBS/ts-iTBS and 20 min rTMS/tsDCS and rTMS/ts-iTBS. The MEP was recorded two times before stimulation intervention and six times after stimulation. While the BBB score was measured after every week for up to four weeks.

Results: The multi-linear regression models were predicted into four categories including (1) the models of week 2 for iTBS/tsDCS, week 3 for iTBS/tsDCS, and week 4 for rTMS/ts-iTBS) groups ($R2=0.86\sim0.95$, $p<0.05$). (2) iTBS/ts-iTBS for week 2 and rTMS/ts-iTBS for week 3 ($R2=0.85\sim0.95$, $p<0.05$). (3) the week 2 model for iTBS/ts-iTBS and week 3 model for rTMS/ts-iTBS ($R2=0.85\sim0.87$, $p<0.05$). (4) the week 2 for iTBS/ts-iTBS and rTMS/ts-iTBS, and week 3 and week 4 ($R2=0.79\sim0.95$, $p<0.05$*) for rTMS/ts-iTBS groups, respectively have predicted significant models.

Discussion: We have obtained a significant correlation between MEP and BBB score for SCI animal model and predicted recovery models. Therefore, these results may help neuroscientists to predict long-term motor recovery after SCI to implicate into the clinical population. This will also help clinicians and physical therapists to design exercise program and evaluate outcome measures based on the level of motor recovery in SCI survivors.

Conclusions: The 3 min iTBS/tsDCS and iTBS/ts-iTBS, and 20 min rTMS/ts-iTBS have predicted significant linear regression models during week 2, week 3, and week 4 for the MEP and BBB scores.

Supplemental Data:

References: None

Acknowledgements: The present study was generously funded by the National Science and Technology Council (112-2221-E-038-004-MY3, 112-2811-E-038-002, 110-2811-E-038-500-MY3, and 109-2221-E-038-005-MY3) and the Higher Education Sprout Project (DP2-TMU-112-N-02) of the Ministry of Education (MOE) in Taiwan, and by the TMU/CWRU (CTSC) Pilot Program [112-3805-003-400].

Learning Objectives: 1.To obtain the correlation between MEP and BBB score for SCI animal model. 2.To predict long-term motor recovery in animals with SCI. 3.To help clinicians and physical therapists to design exercise program and evaluate outcome measures based on the level of motor recovery in SCI survivors.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

328

Poster on Board
POSTER ON BOARD: AS05D. SPINAL CORD: FUNCTIONAL RESTORATION
13-05-2024 08:00 - 19:00

EXPLORING THE EFFECTS OF SPINAL CORD STIMULATION ON AUTONOMIC DYSFUNCTION FOLLOWING SPINAL CORD INJURY: A SCOPING REVIEW

Rahul Sachdeva, PhD[1], Marco Law, BSc (Hons)[1], Tom Nightingale, PhD[2], Parag Gad, PhD[3], Andrei Krassioukov, MD, PhD[1]
[1]818 W10th Ave, Vancouver, Canada, [2]University of Birmingham, Birmingham, United Kingdom, [3]SpineX Inc., los angeles, United States of America

Introduction: Spinal cord injury (SCI) disrupts autonomic pathways, causing cardiovascular, urinary, bowel, and sexual dysfunction. Spinal cord stimulation (SCS), initially used for pain, has gained attention for improving autonomic functions. However, a comprehensive review of SCS effects on SCI-related autonomic dysfunction is needed to inform clinical practice and future research.

Materials / Methods: We analyzed the impact of SCS on autonomic functions following SCI covering cardiovascular, lower urinary tract (LUT), bowel, and sexual functions. Searches included PubMed, EMBASE, and Web of Science from January 1950 to August 2023, and manual reference checks. Three authors independently screened and reviewed studies. Data collection comprised study specifics and autonomic outcomes.

Results: A total of 47 studies, comprising 13 animal and 36 human studies, were included. In the realm of cardiovascular effects, 22 studies were identified with positive alterations to cerebral blood flow, increased resting blood pressure and in response to orthostatic challenge, decreased blood pressure rise during an episode of autonomic dysreflexia, and improved cardiac structural changes and function. Bowel function results from 22 studies reported improvements in terms of reduced time needed for bowel movements or improved bowel function, although minor variations were reported. In 30 studies, LUT function benefited from SCS with improved urine storage, voiding, or reduced lower urinary tract symptoms. In the domain of sexual function, SCS yielded positive results for some participants from 3 studies, including improved arousal and libido.

Discussion: Our review found positive neuromodulatory effects of SCS on cardiovascular, bowel, LUT, and sexual function in individuals with SCI. However, several limitations should be considered. The level of evidence in the reviewed studies varied, with a predominance of observational designs, warranting a need for higher-quality studies to provide stronger evidence of the effects of SCS.

Conclusions: In conclusion, this scoping review sheds light on the multifaceted effects of SCS in individuals with SCI and supports ongoing research into the use of SCS for neuromodulation of autonomic dysfunctions in those with SCI. Notably, there is a need for more rigorously designed research to better understand the sustained impacts of SCS.

Supplemental Data:

References: none

Acknowledgements: Krassioukov laboratory is supported by funds from the Canadian Institute for Health Research, Rick Hansen Foundation, and Canadian Foundation for Innovation, US Department of Defense, and BC Knowledge Development Fund. Rahul Sachdeva is supported by Wings for Life Spinal Cord Research Foundation and US Department of Defense. Marco Law acknowledges support and guidance from the UBC Faculty of Medicine FLEX program.

Learning Objectives: 1. To review the effects of spinal cord stimulation on autonomic function after spinal cord injury. 2. To review the level of evidence in the published literature. 3. to identify the limitations of present evidence and inform future research.

Financial Disclosures: Rahul Sachdeva Name of Company: SpineX Inc. Role: Consultant Level of compensation: $501 - $5,000 USD Parag Gad Name of Company: SpineX Inc. Role: Stockholder Stock Value >5% Level of compensation: $501 - $5,000 USD

Disclosure: No significant relationships.

329

Poster on Board
POSTER ON BOARD: AS05D. SPINAL CORD: FUNCTIONAL RESTORATION
13-05-2024 08:00 - 19:00

CLOSING THE LOOP ON ECAPS IN SCI

Eric Stockwell, MD, Patrick McIntyre, MD, Henry Vucetic, MD
Oklahoma State University, Pain Medicine, Tulsa, United States of America

Introduction: The prevailing consensus is that spinal cord injury (SCI) recovery predominantly occurs during the first year after injury. There is also evidence that recovery is possible after one year, and that epidural dorsal column spinal cord stimulation (SCS) may facilitate recovery. To date, there are few publications on the role of evoked compound action potentials (ECAPs) and closed-loop SCS for SCI.

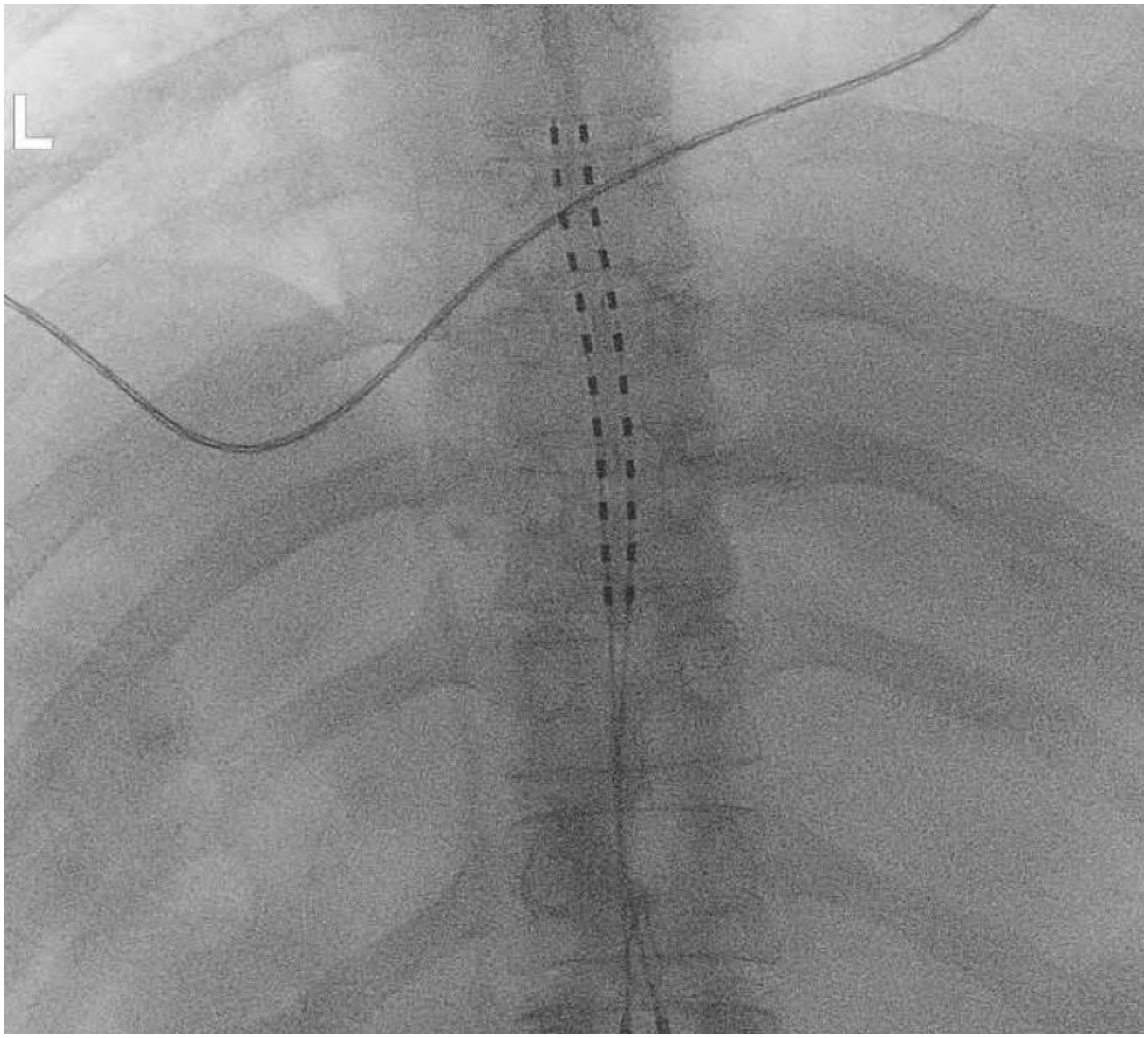
Materials / Methods: The eighth and tenth thoracic vertebrae had closed-loop electrodes percutaneously implanted for back and leg pain in a patient with incomplete C6 SCI. For more than five years, incomplete tetraplegia had limited ambulation and required total assistance. Altered sensation was located distal to the seventh cervical dermatomes bilaterally. The patient also had lower extremity spasticity, edema, and cyanosis. The patient's closed-loop SCS consisted of a forty hertz frequency, 210 microsecond pulse width, and amplitude based upon ECAPs.

Results: Three months after SCS, the patient has taken their first steps in five years. Lower extremity spasticity, cyanosis, and edema improved. There was also increased sensation in the lower extremities and improvement in pain. Balance during sitting, standing, and ambulation gradually developed.

Discussion: Research investigating SCI sensorimotor recovery has placed electrodes at the eleventh thoracic and distal vertebra to improve function[2,3]. Among many theorized mechanisms, SCS may modulate synaptic remodeling[4], distal proprioception, and awaken inhibited neurons to improve gait. Prior to closed-loop SCS, optimal neural dose for SCS could not be measured. With the advent of ECAPs, not only can optimal dose be measured, but it may also help reveal the optimal timeline, location, and mechanism for SCS.

Conclusions: Proprioception, sexual, autonomic, spasticity, bladder, and bowel function are potential modulation target systems that can improve SCI quality of life. A potential disadvantage of closed-loop SCS may be decreased control of the micturition reflex[5]. Potential adverse effects of SCS for insensate patients is also not completely understood. Further research is needed to elucidate the correct location, a model for timing of closed-loop SCS, and which proposed mechanisms influence SCI recovery.

Supplemental Data:



References: Hoglund, B. K., Zurn, C. A., Madden, L. R., Hoover, C., Slopsema, J. P., Balser, D., Parr, A., Samadani, U., Johnson, M. D., Netoff, T. I., & Darrow, D. P. (2023). Mapping spinal cord stimulation-evoked muscle responses in patients with Chronic Spinal Cord Injury. Neuromodulation: Technology at the Neural Interface 26(7), 1371–1380. Jilge, B., Minassian, K., Rattay, F., Pinter, M. M., Gerstenbrand, F., Binder, H., & Dimitrijevic, M. R. (2004). Initiating extension of the lower limbs in subjects with complete spinal cord injury by epidural lumbar cord stimulation. Experimental Brain Research, 154(3), 308–326. Wagner, F. B., Mignardot, J.-B., Le Goff-Mignardot, C. G., Demesmaeker, R., Komi, S., Capogrosso, M., Rowald, A., Seáñez, I., Caban, M., Pirondini, E., Vat, M., McCracken, L. A., Heimgartner, R., Fodor, I., Watrin, A., Seguin, P., Paoles, E., Van Den Keybus, K., Eberle, G., Courtine, G. (2018). Targeted neurotechnology restores walking in humans with Spinal Cord Injury. , (7729), 65–71. Angeli, C. A., Boakye, M., Morton, R. A., Vogt, J., Benton, K., Chen, Y., Ferreira, C. K., & Harkema, S. J. (2018). Recovery of over-ground walking after chronic motor complete Spinal Cord Injury. New England Journal of Medicine, 379(13), 1244–1250. Herrity, A. N., Williams, C. S., Angeli, C. A., Harkema, S. J., & Hubscher, C. H. (2018). Lumbosacral spinal cord epidural stimulation improves voiding function after human spinal cord injury. Scientific Reports, 8(1).

Acknowledgements:

Learning Objectives: 1. Understand the function of closed-loop ECAPs in SCS for SCI 2. Document a SCI patient with significant improvement across multiple systems 3. Describe the systems in SCI that may benefit from closed-loop SCS

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

330

Poster on Board
POSTER ON BOARD: AS05E. SPINAL CORD: CARDIOVASCULAR
13-05-2024 08:00 - 19:00

SPINAL CORD STIMULATION IN POLYVASCULAR PATIENTS

José Manuel Trinidad Martin-Arroyo, MD, Jorge Martín-Cañuelo, MD, Gema Gómez-Benítez, MD, Diego Benítez-Pareja, MD, Manuel Rodríguez-Piñero, MD, Javier Morales-Romero, MD, Antonio Pernia-Romero, MD
Puerta del Mar University Hospital, Cádiz, Spain

Introduction: Peripheral Arterial Disease (PAD) is often accompanied by a widespread atherosclerosis affecting other vascular territories, such as the heart (i.e., coronary arterial disease - CAD). The use of Spinal Cord Stimulation (SCS) to treat PAD pain and mitigate amputation risk is known for decades. However, some results are contradicting, likely due to misaligned patient conditions. Further, not much is known about the SCS effects on central cardiovascular health (e.g., on CAD). In this work, we plan to advance our knowledge on some fundamental questions: 1) which PAD patients are suitable to SCS?; 2) is there any superior SCS modality? and 3) does SCS impact cardiovascular health beyond the periphery?

Materials / Methods: This is a single-center, observational case series with up to 10 PAD patients at Fontaine stage III with a detailed lesion characterization (TASC). Patients will be implanted with SCS and percutaneous leads targeting lower limbs (T10-12). Up to three stimulation modalities will be provided (i.e., conventional, sub-paresthetic, combined). Patients will be characterized before and after SCS (3-,6- and 12-months) with the following assessments: i) clinical questionnaires: pain (NRS), Fontaine, quality of life and functioning (SF36); ii) walking tolerance; iii) echocardiography: left ventricular ejection fraction (LVEF), etc; and iv) blood panel examining key risk factors (e.g. dyslipidemia, inflammation).

Results: To follow later. We aim to present results of our initial cases at the conference.

Discussion: We aim to better define the profile of PAD candidate to SCS by an improved lesion characterization workflow, the SCS therapeutic approach, and to investigate the potential of SCS to improve the overall cardiovascular health of these pluripathological patients.

Conclusions: Specific strategies to spinal cord stimulation could provide pain relief and improve overall cardiovascular health, including heart function.

Acknowledgements:

Learning Objectives: 1) which PAD patients are suitable to SCS? 2) is there any superior SCS modality? 3) does SCS impact cardiovascular health beyond the periphery?

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

331

Poster on Board
POSTER ON BOARD: AS06A. PERIPHERAL NERVE: HEADACHE
13-05-2024 08:00 - 19:00

OCCIPITAL NERVE STIMULATION: DOES THE DISTANCE TO NERVES MAKE ANY DIFFERENCE?

Daniel Benzecry Almeida, MD, Joel Duarte, MD
INSTITUTO DE NEUROLOGIA DE CURITIBA, Neurosurgery, CURITIBA, Brazil

Introduction: Occipital nerve stimulation (ONS) is an established therapeutic option for patients suffering from various debilitating headache disorders. It that precise electrode positioning during the implantation procedure may be essential for optimal outcomes. In this study, we present our case series introducing a novel technique employing intraoperative radiofrequency (RF) guidance to locate the occipital nerves and enhance electrode placement accuracy.

Materials / Methods: We conducted a retrospective analysis of eight patients who underwent this procedure and report the clinical improvement at long-term follow-up. In this technique, a RF electrode is introduced laterally from midline towards the mastoid process, before introducing the electrodes. Stimulation is done to allocate greater and lesser occipital nerves (50 Hz and threshold lower than 0,5 mA). After, RF cannula is cut and left as guide while the 14-gauge Tuohy needle is introduced. Lastly, electrodes are placed under fluoroscopic view to remain in the desired anatomic location.

Results: Eight patients (62,5% male, mean age 47,6±17,8 years) who underwent occipital nerve electrode implantation guided by intraoperative radiofrequency where analyzed. The primary preoperative diagnoses included mainly cluster headache and occipital neuralgia (38% each), but also other etiologies such as paroxysmal hemicrania (13%), and post-operative facial pain (13%). The time from diagnosis to the electrode implantation ranged from 18 to 322 months, with a mean duration of 105 months. Previous interventions included C2-C3 pulsed radiofrequency (47%), sphenopalatine ganglion radiofrequency (19%), and trigeminal balloon compression (19%). The mean improvement in headache severity, as reported by patients, was 67% (median 80%). The mean follow-up period was 73.6 months, during which time no major complications related to the procedure were noted.

Discussion: Occipital nerve field stimulation has been proposed as a potential treatment intervention for some types of refractory headaches. The optimal efficacy of radiofrequency for localizing peripheral nerves is well described in RF ablation reviews. Our results suggest that intraoperative radiofrequency guidance facilitates precise electrode positioning and this may contribute to improved clinical outcomes and less battery use.

Conclusions: The findings of this study indicate that intraoperative radiofrequency guidance for occipital nerve electrode implantation is a promising approach for patients with refractory headache disorders. The technique ensures accurate electrode placement, potentially leading to enhanced pain relief with a favorable safety profile. The long-term follow-up results are encouraging and suggest that this approach may be a valuable addition to the armamentarium of treatment options for patients with medically refractory headache disorders.

Supplemental Data:

References: 1. Michaud, K., Cooper, P., Abd-Elsayed, A., & Kohan, L. (2021). Review of Radiofrequency Ablation for Peripheral Nerves. In Current Pain and Headache Reports (Vol. 25, Issue 10). Springer Science and Business Media LLC. https://doi.org/10.1007/s11916-021-00981-0 2. Yang, Y., Song, M., Fan, Y., & Ma, K. (2015). Occipital Nerve Stimulation for Migraine: A Systematic Review. In Pain Practice (Vol. 16, Issue 4, pp. 509–517). Wiley. https://doi.org/10.1111/papr.12303

Acknowledgements:

Learning Objectives: 1. Gain knowledge about the importance of accurate electrode placement in ONS procedures and its impact on clinical improvement and long-term results. 2. Acquire a comprehensive understanding of the step-by-step procedure involving RF guidance, from RF electrode introduction to the placement of ONS electrodes, and how it contributes to improved clinical outcomes. 3. Recognize the study's implications for clinical practice and the potential of this technique to provide enhanced pain relief and improved safety profiles in the treatment of medically refractory headache disorders.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

332

Poster on Board
POSTER ON BOARD: AS06A. PERIPHERAL NERVE: HEADACHE
13-05-2024 08:00 - 19:00

TREATMENT OF OCCIPITAL AND SUPRAORBITAL NEURALGIA WITH CERVICAL SCS

Ann-Katrin Fritz, MD, Katherine Dyer, RN, Benjamin Morrison, RN, Bethany Roughsedge, DPsych
Norfolk & Norwich University Hospital, Anaesthesia & Pain Management, Norwich, United Kingdom

Introduction: A 48-year-old male victim of a knife assault presented with chronic post-traumatic right occipital and supraorbital neuralgia, along with injury-related depression and PTSD. After failure to several medications, temporary complete relief was achieved through ultrasound guided nerve blocks, and pulse radiofrequency treatments, but durable pain management was unattainable with ongoing numeric rating scores (NRS) 9/10 and 6/10, respectively for occipital and supraorbital neuralgia. High cervical spinal cord stimulation (SCS) with burst stimulation was explored as a targeted treatment strategy, supported by increasing literature detailing its efficacy for treating occipital and supraorbital neuralgia. [1, 2]

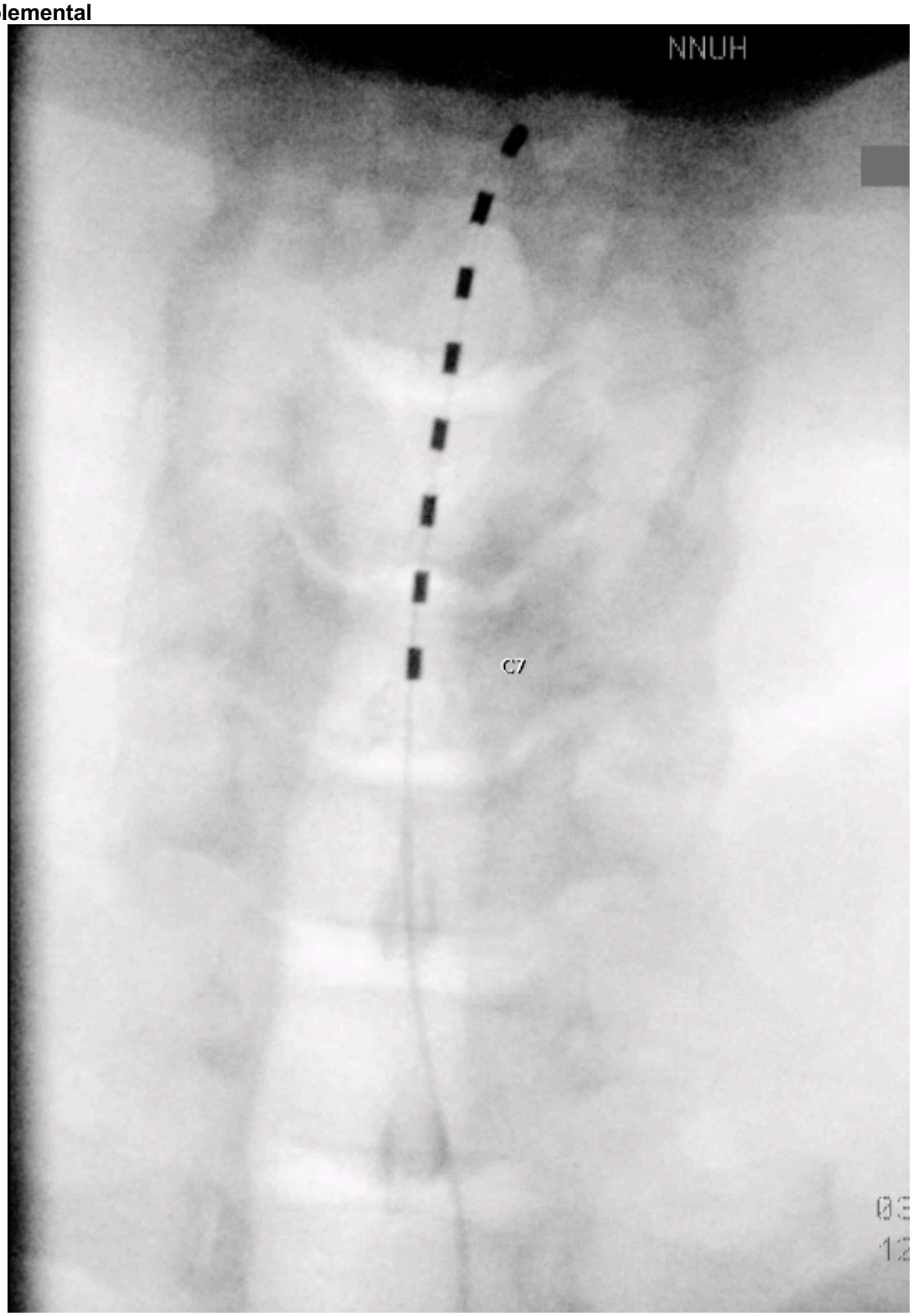
Materials / Methods: The patient was evaluated by a multidisciplinary pain management team via a thorough assessment in the local neuromodulation pathway. A trial with high cervical SCS was initiated, involving percutaneous implantation via the T2/3 vertebrae with tip of a single Octrode lead to C2, using low frequency on table stimulation, which gave coverage of the right neck and cranium including the affected occipital nerve distribution area but not the supraorbital on direct low frequency stimulation. Trial programming was then initiated with microdosed BurstDR stimulation over contacts 2-,3+, 30sec on & 60secs off. Pre- and post-implant pain scores, sleep quality, and medication dependency were monitored as primary outcomes. After a successful seven day temporary trial, the trial lead was removed in clinic and the patient received a full implant a few weeks later.

Results: Three months full post-implant, the patient reported an 80-85% reduction in occipital and supraorbital pain. Additionally, sleep quality improved significantly, and the patient commenced weaning off opioids, gabapentin, and carbamazepine.

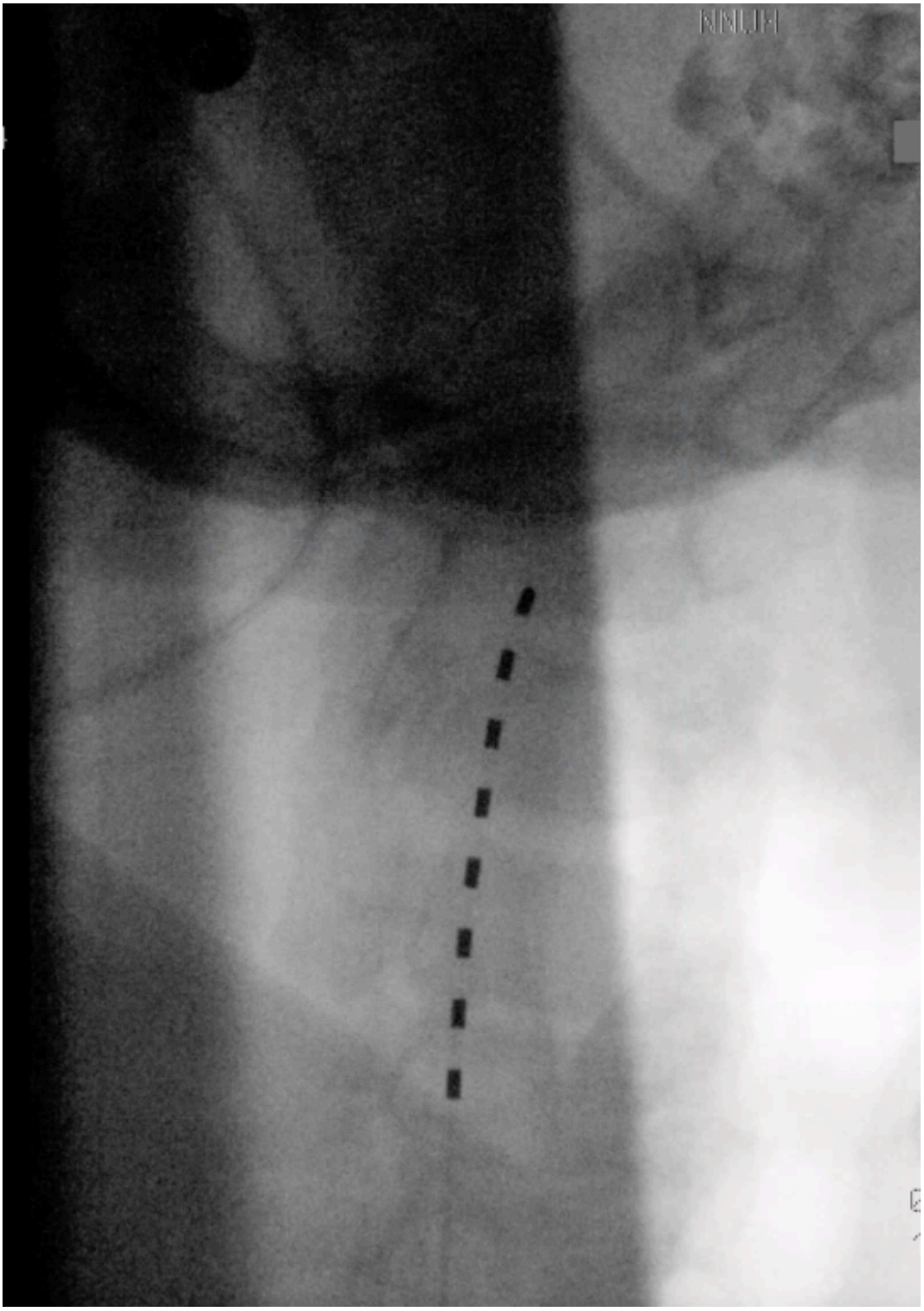
Discussion: While other modalities have previously used peripheral nerve stimulation [3, 4], this case further demonstrates the therapeutic potential of high cervical SCS for neuralgic headaches like post-traumatic occipital and supraorbital neuralgia. [5, 6, 7] The substantial pain reduction aligns with previous reports and adds a new dimension by potentially implicating the cervico-trigeminal complex in the observed clinical outcomes. [1, 8, 9]

Conclusions: High cervical SCS can offer significant relief for complex neuralgic headache cases. This case contributes to the growing body of evidence supporting SCS as a long-term effective treatment option for patients unresponsive to conventional methods.

Supplemental



Data:



1

References: 1 Castien, R., & De Hertogh, W. (2019). A neuroscience perspective of physical treatment of headache and neck pain. Frontiers in Neurology, 2019 Mar 26. 2 Texakalidis, P., et al. (2019). High Cervical spinal cord stimulation for occipital neuralgia: a case series and literature review. J Pain Res, 12, 2547-2553. 3 Slavin, K. V., Nersesyan, H., & Wess, C. (2006). Peripheral neurostimulation for treatment of intractable occipital neuralgia. Neurosurgery, 58(1), 112-119; discussion 112-119. 4 Yakovlev, A. E., & Resch, B. E. (2011). Treatment of chronic intractable atypical facial pain using peripheral subcutaneous field stimulation. Neuromodulation: Technology at the Neural Interface, 14(1), 53-56; discussion 57. 5 Rekatsina, M., & Thomson, S. (2022). High cervical stimulation for facial pain and cervicogenic headaches: case series. Regional Anaesthesia

and Pain Medicine, 2022. 6 Kandel, M., et al. (2022). Percutaneous, high cervical, HD SCS for intractable neck and arm pain, and occipital neuralgia. Neuromodulation, June 2022. 7 Baksh, J. (2021). Effective treatment of facial and headache pain with high cervical burst spinal cord stimulation: two case reports. Pain Medicine Case Reports, 2021, volume 5, number 3, pp 103-107. 8 Smith, J., Doe, R., & Wilson, L. (2015). Neuroanatomy and the cervico-trigeminal complex. Journal of Neurosciences, 20(3), 125-134 9 Johnson, P., & Wilson, G. (2018). Sensory Perception and the Cervico-Trigeminal Complex. Annals of Neurology, 22(1), 56-70.

Acknowledgements:

Learning Objectives: 1. Understanding the cervico-trigeminal complex as an anatomical target for headache treatment 2. Use of high cervical SCS as an alternative to peripheral nerve stimulators 3. Ability of BurstDR stimulation to treat refractory occipital and supraorbital neuralgia via high cervical SCS

Financial Disclosures: Paid speaker and proctor for Abbott, Boston Scientific and Nevro Corp.

Disclosure: No significant relationships.

333

Poster on Board
POSTER ON BOARD: AS06A. PERIPHERAL NERVE: HEADACHE
13-05-2024 08:00 - 19:00

THE IMPACT OF ANCHORED ELECTRODELEADS FOR OCCIPTIAL NERVE STIMULATION IN MEDICALLY INTRACTABLE CHRONIC CLUSTER HEADACHE

Casper Lansbergen, MD[1], Cecile De Vos, PhD[1], Rolf Fronczek, MD, PhD[2], Frank Huygen, MD, PhD[1]
[1]Erasmus Medical Centre, Center For Pain Medicine, Department Of Anesthesiology, Rotterdam, Netherlands, [2]Leiden University Medical Center, Department Of Neurology, Leiden, Netherlands

Introduction: Occipital nerve stimulation (ONS) has gained recognition as a valuable therapeutic approach for addressing medically intractable chronic headache (MICCH).(1) Initially, the off-label use of leads designed for spinal cord stimulation led to a high complication rates, primarily due to lead migration.(2-5) Unfortunately, this led to reservations about recommending this effective and safe treatment.(6) In response, specialized leads with anchor points at both the tip and base of the electrode were developed to address this issue. The objective of this retrospective study is to evaluate whether the use of these specialized leads has reduced the risk of complications while maintaining therapeutic efficacy.

Materials / Methods: Electronic medical records of patients who underwent ONS procedures in Erasmus Medical Center (Rotterdam, the Netherlands) between October 2012 and December 2020 were reviewed. Patients were categorized into two groups based on the lead type implanted: unanchored leads and anchored leads (Ankerstim®, Medtronic, USA). Demographic data, surgical details, pain scores, adverse events, and follow-up information were collected and analyzed.

Results: Nearly 80 patients were included in this retrospective study, with equal numbers in unanchored and anchored group. The two groups were comparable in terms of age, gender, and primary headache diagnosis. Analysis of pain relief and attack frequency reduction revealed no significant differences between the two lead types. The incidence of lead migration was higher in the unanchored group. The need for lead repositioning or revision surgery was higher in the unanchored group. Anchored leads demonstrated significant improvements in complication rate.

Discussion: Due to the retrospective nature of our study, it is important to acknowledge the presence of missing data in both groups. These missing data present a challenge in our analysis and interpretations, but was adjusted for.

Conclusions: Our retrospective study suggests that anchored leads offers a tangible advantage in preventing lead migration and reducing the need for revision surgery without loss of efficacy of Occipital Nerve Stimulation. These findings underscore the clinical significance of utilizing specialized leads with anchor points.

Supplemental Data:

References: 1. Wilbrink LA, de Coo IF, Doesborg PGG, Mulleners WM, Teernstra OPM, Bartels EC, et al. Safety and efficacy of occipital nerve stimulation for attack prevention in medically intractable chronic cluster headache (ICON): a randomised, double-blind, multicentre, phase 3, electrical dose-controlled trial. Lancet Neurol. 2021;20(7):515-25. 2. Burns B, Watkins L, Goadsby PJ. Treatment of medically intractable cluster headache by occipital nerve stimulation: long-term follow-up of eight patients. Lancet. 2007;369(9567):1099-106. 3. Magis D, Allena M, Bolla M, De Pasqua V, Remacle JM, Schoenen J. Occipital nerve stimulation for drug-resistant chronic cluster headache: a prospective pilot study. Lancet Neurol. 2007;6(4):314-21. 4. Burns B, Watkins L, Goadsby PJ. Treatment of intractable chronic cluster headache by occipital nerve stimulation in 14 patients. Neurology. 2009;72(4):341-5. 5. Mueller OM, Gaul C, Katsarava Z, Diener HC, Sure U, Gasser T. Occipital nerve stimulation for the treatment of chronic cluster headache - lessons learned from 18 months experience. Cent Eur Neurosurg. 2011;72(2):84-9. 6. May A, Evers S, Goadsby PJ, Leone M,

Manzoni GC, Pascual J, et al. European Academy of Neurology guidelines on the treatment of cluster headache. Eur J Neurol. 2023;30(10):2955-79.

Acknowledgements:

Learning Objectives: 1. Therapeutic efficacy is maintained with specialized anchored leads. 2. Specialized anchored leads prevent lead migration. 3. Specialized anchored leads reduce the need for revision surgery.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

334

Poster on Board
POSTER ON BOARD: AS06A. PERIPHERAL NERVE: HEADACHE
13-05-2024 08:00 - 19:00

TREATMENT WITH PERIPHERAL NEUROSTIMULATION IN THIRD BRANCH OF THE TRIGEMINAL NERVE AND OCCIPITAL NERVE FOR PATIENTS WITH REFRACTORY TRIGEMINAL NEURALGIA

Raquel Sepulcre, MD, Victor Fajardo, MD, Cristina Abad, MD, David Abejón, MD, Alberto Rios, MD, Astrid Catalán, MD, Carolina Elvira, MD, Eva Monzón, MD
University Hospital Quirónsalud, Pain Management, Madrid, Spain

Introduction: Neurostimulation is an established therapeutic alternative for refractory chronic neuropathic pain (1,2). Peripheral nerve neurostimulation was approved by the Food and Drug Administration FDA) in 1967, and its use has been increasing in recent years (1). For refractory craniofacial pain, peripheral nerve stimulation of the occipital nerve (3) and field stimulation of the terminal branches of the trigeminal nerve (4,5) have been described.

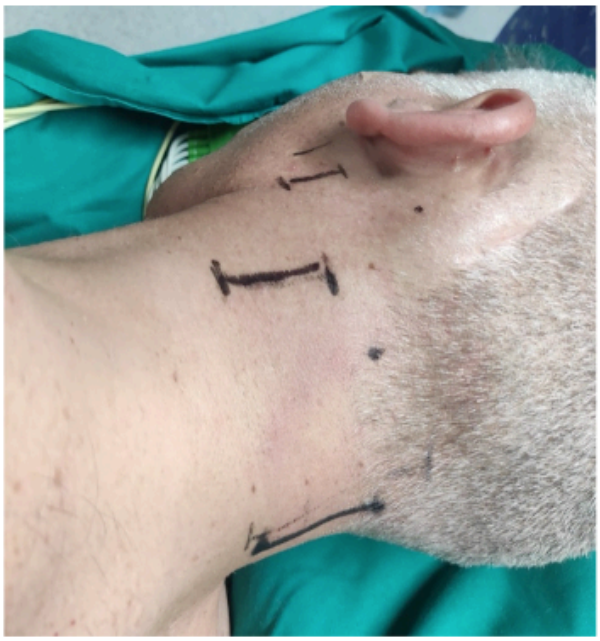
Materials / Methods: CASE 1
A 52-year-old male diagnosed with trigeminal neuralgia in the second (V2) and third (V3) branches on the left side in 2008. Pain exacerbated by touch, speech, and chewing. Pain intensity was assessed using a simple numerical pain scale (NPS) ranging from 0 (no pain) to 10 (unbearable pain), with a baseline NPS of 5/10 and 10/10 during attacks. Cranial magnetic resonance imaging (MRI) and computed tomography (CT) ruled out vascular conflicts.
Various oral medications, trigger point injections, pulsed radiofrequency (PRF) of V2V3, Gamma Knife surgery, and decompressive microsurgery were used for pain management.
Due to the lack of efficacy, it was decided to implant a tetrapolar electrode in the occipital nerve and the left V3 branch of the trigeminal nerve with an Intelis®generator (Medtronic, Inc., Minneapolis, US)
CASE 2
A 71-year-old male diagnosed with bilateral trigeminal neuralgia in V2 and predominantly left V3 in 2002. Aggravated by speech and chewing. NPS 10/10
Refractory to intravenous lidocaine, pulsed radiofrequency of V2V3, Gamma-Knife surgeries and bilateral Janetta decompressive microsurgery.
After long-term pain control with oral treatment, a new, intractable crisis that was resistant to treatment emerged. No significant findings were observed on cranial MRI.
Given the lack of response, it was decided to implant a tetrapolar electrode in the occipital nerve and the left V3 branch of the trigeminal nerve with an Intelis generator (Medtronic, Inc., Minneapolis, US)

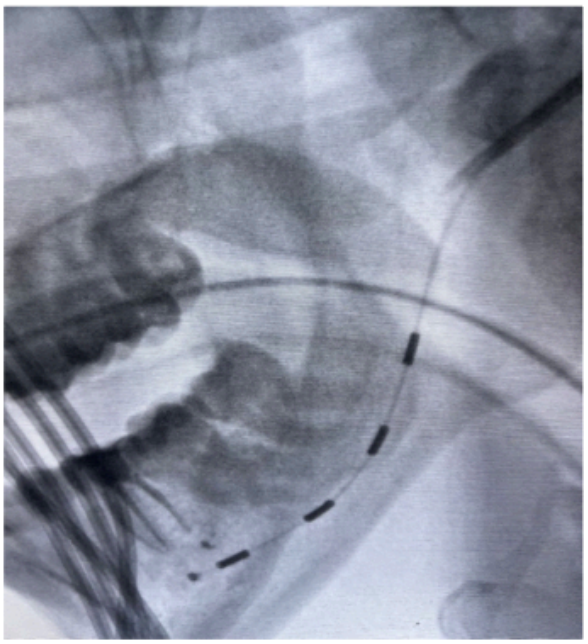
Results: Currently, both patients have good pain control, reducing the intensity, frequency, and duration of their attacks. The oral medication dose has been reduced, and they report a decrease in NPS of 1 point at baseline and 3 during crises. They report less limitations in their daily activities.

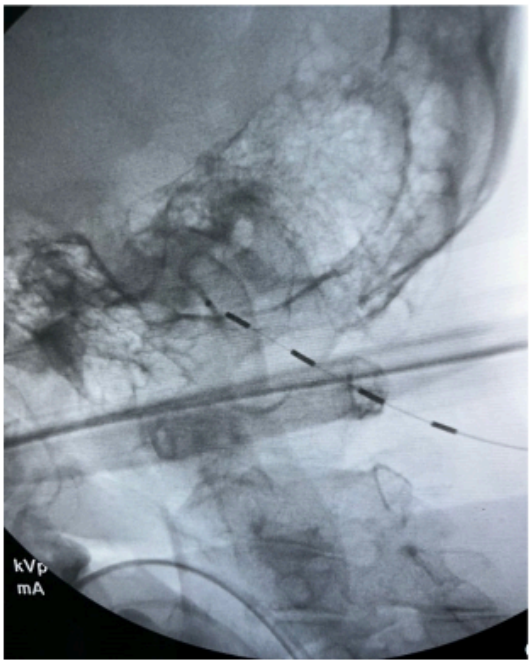
Discussion: Based on the results, an optimal response to neurostimulation implantation is observed, supporting previous studies. Patients who do not respond effectively to conventional treatments are candidates for peripheral nerve neurostimulation.

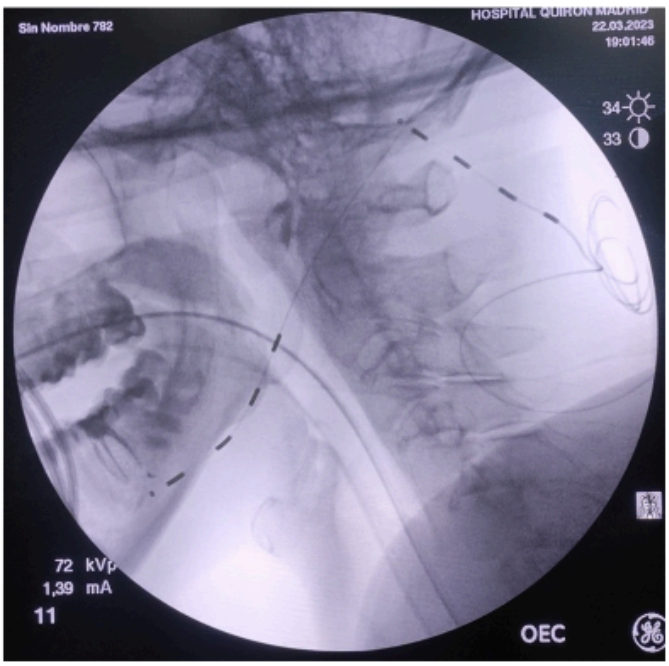
Conclusions: Neurostimulation of trigeminal nerve branches along with the occipital nerve is proposed as a promising alternative for trigeminal neuralgia refractory to other types of treatments.

Supplemental Data:









References: 1.Weiner RL, Reed KL. Peripheral neurostimulation for control of intractable occipital neuralgia. Neuromodulation. 1999;2(3):217–21. Disponible en: http://dx.doi.org/10.1046/j.1525-1403.1999.00217.x 2.Deer TR, Esposito MF, McRoberts WP, Grider JS, Sayed D, Verrills P, et al. A systematic literature review of peripheral nerve stimulation therapies for the treatment of pain. Pain Med. 2020;21(8):1590–603. Disponible en: http://dx.doi.org/10.1093/pm/pnaa030 3.Verrills P, Rose R, Mitchell B, Vivian D, Barnard A. Peripheral nerve field stimulation for chronic headache: 60 cases and long-term follow-up. Neuromodulation. 2014;17(1):54–9. Disponible en: http://dx.doi.org/10.1111/ner.12130 4.Ellis JA, Mejia Munne JC, Winfree CJ. Trigeminal branch stimulation for the treatment of intractable craniofacial pain. J Neurosurg. 2015;123(1):283–8. Disponible en: http://dx.doi.org/10.3171/2014.12.jns14645 5.Slavin KV, Wess C. Trigeminal branch stimulation for intractable neuropathic pain: Technical note. Neuromodulation. 2005;8(1):7–13. Disponible en: http://dx.doi.org/10.1111/j.1094-7159.2005.05215.x

Acknowledgements: To Dr. Abejon's team.

Learning Objectives: 1- Refractory trigeminal neuralgia is a pathology that seriously affects the patient's quality of life and is very difficult to manage. 2- Neurostimulation is an established therapeutic alternative for refractory chronic neuropathic pain. 3- Neurostimulation is a therapeutic alternative for patients in whom medical, interventional, radiotherapy and surgical treatment have failed.

Financial Disclosures: David Abejón is speaker and consultant for Medtronic

Disclosure: No significant relationships.

335

Poster on Board
POSTER ON BOARD: AS06B. PERIPHERAL NERVE: PAIN
13-05-2024 08:00 - 19:00

PERIPHERAL NERVE STIMULATION WITH A HIGH-FREQUENCY ELECTROMAGNETIC COUPLED (HF-EMC) POWERED IMPLANTED RECEIVER REDUCES PAIN IN SUBJECTS WITH CHRONIC KNEE PAIN – A RETROSPECTIVE STUDY

Niek Vanquathem, BA[1], Simon Bayerl, MD[2]
[1]Curonix LLC, Clinical Affairs, Pompano Beach, Belgium, [2]Charité Universitätsmedizin Berlin, Neurosurgery, Berlin, Germany

Introduction: The average age of our population is increasing, resulting in a high incidence of chronic degenerative knee pathologies. Several treatment options, including surgical procedures are available to help mitigate these pathologies. However, the percentage of subjects with chronic post-surgical knee pain is still estimated at 16-20%. Neuromodulation techniques such as spinal cord stimulation (SCS) and dorsal root ganglion stimulation (DRG) are well-documented treatment options for subjects with chronic knee pain. The evidence involving peripheral nerve stimulation (PNS) is minimal due to a limited number of neuromodulation systems capable of targeting the distal part of the lower limbs.

Materials / Methods: Subjects suffering from chronic intractable post-surgical knee pain received landmark-guided peripheral nerve stimulation of the branches of the saphenous nerve. All implants were performed with an externally powered PNS system to avoid lead migration as a result of cross-joint lead positions tunneling towards an IPG to the abdomen. Data was collected retrospectively. Subject-reported outcome was measured via numerical rating scale values on a 10-point scale measuring pain intensity at rest and in motion. Additional data was collected for the subjects treated at the Charité location, including quality of life with the SF-36 form, quality of sleep with the Pittsburgh Sleep Quality Index and mood states with the short form of the General Depression Scale

Results: Thirty-three subjects received direct to permanent implant, landmark-guided peripheral nerve stimulation of the saphenous nerve branches. Six (18.2 %) subjects reported non-sufficient initial benefit from the therapy and were explanted. Two subjects were explanted due to wound infections. The total study population reported included 25 subjects. These subjects reported significant improvements related to pain, quality of life, mood quality, and quality of sleep. Additionally, subjects were able to reduce their opioid medication significantly after PNS therapy

Discussion: In recent years, PNS has gained prominence as a therapeutic option for the treatment of chronic pain. This study specifically addressed the use of landmark-guided PNS implant techniques, which are less invasive than conventional neuromodulation techniques such as Spinal Cord or DRG-stimulation systems. Improvement of pain is in line with other studies that investigated the effects of PNS.

Conclusions: Externally powered peripheral nerve stimulation at the saphenous nerve branches is a minimally invasive and safe technique to treat chronic post-surgical knee pain. Our results are promising and show a considerable reduction in chronic pain, an opioid usage and improved in quality of life.

Supplemental Data:

References: 1. Rupp A, Char S, Hagedorn JM. Dorsal Root Ganglion Stimulation for Chronic Pain After Total Knee Arthroplasty: A Narrative Review. Pain Med. 2022;23(2):421-3. 2. Martin SC, Macey AR, Raghu A, Edwards T, Watson C, Bojanić S, et al. Dorsal Root Ganglion Stimulation for the Treatment of Chronic Neuropathic Knee Pain. World Neurosurg. 2020;143:e303-e8. 3. Hunter CW, Sayed D, Lubenow T, Davis T, Carlson J, Rowe J, et al. DRG FOCUS: A Multicenter Study Evaluating Dorsal Root Ganglion Stimulation and Predictors for Trial Success. Neuromodulation. 2019;22(1):61-79. 4. Deer TR, Mekhail N, Provenzano D, Pope J, Krames E, Leong M, et al. The appropriate use of

neurostimulation of the spinal cord and peripheral nervous system for the treatment of chronic pain and ischemic diseases: the Neuromodulation Appropriateness Consensus Committee. Neuromodulation. 2014;17(6):515-50; discussion 50. 5. Rauck RL, Cohen SP, Gilmore CA, North JM, Kapural L, Zang RH, et al. Treatment of post-amputation pain with peripheral nerve stimulation. Neuromodulation. 2014;17(2):188-97.

Acknowledgements: NA

Learning Objectives: 1. Pain reduction 2. Quality of life 3. Satisfaction

Financial Disclosures: Submitter Niek Vanquathem: Employee of Curonix LLC Presenter Simon Bayerl: Nothing to report

Disclosure: Employee of Curonix LLC

336

Poster on Board
POSTER ON BOARD: AS06B. PERIPHERAL NERVE: PAIN
13-05-2024 08:00 - 19:00

TREATMENT OF SACROILIAC JOINT PAIN WITH PERIPHERAL NERVE STIMULATION – A CASE SERIES FOLLOWED BY A STUDY PROTOCOL OF A RANDOMIZED MULTICENTER STUDY.

Tarik Alp Sargut, MD[1], J Tüttenberg, MD[2], A Heckert, MD[3], S Fleck, MD[4], Simon Bayerl, MD[5]
[1]Charité - Universitätsmedizin Berlin, Neurosurgery, Berlin, Germany, [2]Klinikum Idar-Oberstein, Idar-Oberstein, Germany, [3]Universitätsklinikum für Neurochirurgie Evangelisches Krankenhaus Oldenburg, Neurosurgery, Oldenburg, Germany, [4]Neurochirurgische Gemeinschaftspraxis Greifswald, Greifswald, Germany, Greifswald, Germany, [5]Charité Universitätsmedizin Berlin, Neurosurgery, Berlin, Germany

Introduction: The Prevalence of sacroiliac joint pain (SIJP) is estimated to be 10 % and 30 % in patients with chronic low back pain. Numerous conservative and surgical treatment modalities for SIJP have been described with limited evidence regarding long-term pain relief.
Spinal cord stimulation (SCS) is a well established technique to treat patients with chronic low back pain. However, the effect on patients with SIJP is not consistent. Therefore, peripheral nerve stimulation for chronic SIJP was implemented in experimental trials. Clinical data on PNS for SIJP is still lacking. The authors present a case series and a protocol for a prospective, multicenter study to determine the effect of PNS in patients with chronic intractable SIJP.

Materials / Methods: The authors investigated the prospectively collected patient reported outcome measurements of six patients with chronic SIJP, who received a peripheral nerve stimulation of the lateral branches of S1-S3. To deliver prospective data with a high evidence a multicenter, prospective randomized controlled trial was designed.

Results: All patients benefited from PNS trial and received a permanent device. The mean NRS was reduced after three months follow-up by 40%. After 12 months mean NRS reduction was 60%. Further long-term follow-up results are pending. The RCT was designed to investigate the effect of PNS on chronic SIJP. After 4:3 randomization patients are assigned into two groups. One group receives best medical treatment (BMT group) and one group receives best medical with peripheral nerve stimulation (PNS group). Patients of the PNS group undergo a trial period of 3 to 14 days, followed by a permanent implantation, if 50% pain relief can be achieved. After 6 month patients from the BMT group have the chance to receive PNS treatment as well. Outcome scores and pain medication are followed in visits scheduled 0, 3, 6, and 12 months after inclusion.

Discussion: PNS of the lateral branches of S1 to S3 is a simple, selective and elegant technique to treat patients with chronic SIJP. In this case series no complications occured, durations of surgeries were short and pain relief after three and 12 months was very promising. However, only the recently started multicenter RCT is estimated to generate relevant evidence concerning the effect of PNS on patients with chronic intractable SIJP.

Conclusions: Peripheral nerve stimulation for chronic SIJP is a safe technique. Short-term results are promising and show considerable pain reduction. A recently started multicenter RCT is designed to deliver high level evidence.

Supplemental Data:

References: none

Acknowledgements:

Learning Objectives: 1. PNS of the lateral branches of S1 to S3 is a simple, selective and elegant technique to treat patients with chronic sacroiliac joint pain. 2. A recently started multicenter RCT is designed to deliver high level evidence. 3. Technical aspects of peripheral nerve stimulation for chronic sacroiliac joint pain

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

337

Poster on Board
POSTER ON BOARD: AS06B. PERIPHERAL NERVE: PAIN
13-05-2024 08:00 - 19:00

PRECISION REHABILITATION FOLLOWING RESTORATIVE NEUROSTIMULATION IMPLANTATION FOR MULTIFIDUS DYSFUNCTION

Alexios Carayannopoulos, DO, MPH, DABPMR, Kavita Poply, FRCA, FCARCSI, FFPMRCA, Vivek Mehta, MBBS, MD, FRCA, FFPMRCA
Brown University Warren Alpert Medical School, Neurosurgery, Neurology, Providence, United States of America

Introduction: Quality medical management strategies predicate abilities to distinguish chronic neuropathic lumbar and radicular leg pain from chronic nociceptive mechanical lumbar pain. The latter typically generates underlying multifidus dysfunction and altered neuromuscular control, which biomechanically drive dysfunctional painful movements.[2,3] Patients with mechanical chronic low back pain (CLBP) who have failed conservative management and who do not have surgically addressable conditions often are left to palliative care. Restorative neurostimulation targets multifidus dysfunction and delivers durable benefits in reducing pain, limiting loss of function, and helping reduce downstream healthcare costs.[4–6] Providing precision patient-centric medical management with a robust rehabilitation presence allows the patient and neurostimulation device to gain quality synergy. This paper aims to enhance medical decision-making around rehabilitation referrals and provide general guidelines for rehabilitation specialists to manage patients with CLBP undergoing restorative neurostimulation

Materials / Methods: Pre-implantation decision-making is informed through patient selection utilizing patient-reported outcomes, clinical testing, imaging, and patient history. Following patient identification, implantation of the restorative neurostimulation device ensues. The resulting general guidelines were developed through a consensus from physicians with significant neurostimulation experience and rehabilitation specialists commonly treating CLBP

Results: For two weeks following restorative neurostimulation implantation, activities of daily living (ADLs) and activity intensity are reduced for proper wound healing and scar development. Two weeks postop, the device is programmed to produce strong but comfortable therapeutically dosed contractions to the multifidi. Formal physical therapy (PT) is prescribed about 3-6 weeks post-op to provide a solid foundation of neuromuscular and core muscle re-education in parallel to onboarding neurostimulation therapy. Post-implant patient-centric management should continue for 6-8 weeks to include education in holistic precision health approaches for pharmacological management, retraining movement deficits, and monitoring behavioral health, sleep, and nutrition patterns. Rehabilitation plans should always be individualized to each patient's baseline medical and rehabilitation status

Discussion: With key patient selection, systematic post-implantation recovery, and quality multidisciplinary management, evidence reveals patients with restorative neurostimulation are provided a pathway toward improved patient-reported outcomes, reduction, or discontinuation of opioid consumption, as well as improved functional capabilities. Addition of a comprehensive rehabilitation and precision patient-centered program, developed alongside expert medical and rehabilitation professionals familiar with restorative neurostimulation, aims to streamline recovery and outcomes following restorative neurostimulation implantation

Conclusions: Targeted rehabilitation following restorative neurostimulation implantation is a cornerstone for precision, patient-centered, post-implant recovery. Quality post-implant guidance will not only result in improved individualized outcomes for patients with mechanical CLBP but will also facilitate further reduction in healthcare burdens long-term

Supplemental Data:

References: 1. Wu A, March L, Zheng X, et al. Global low back pain prevalence and years lived with disability from 1990 to 2017: estimates from the Global Burden of Disease Study 2017. *Ann Transl Med* 2020;8:299. 2. Quirk DA, Johnson ME, Anderson DE, et al. Biomechanical Phenotyping of Chronic Low Back Pain: Protocol for BACPAC. *Pain Med* 2022;24:S48–60. 3. Russo M, Deckers K, Eldabe S, et al. Muscle Control and Non-specific Chronic Low Back Pain. *Neuromodulation* 2018;21:1–9. 4. Shaffrey C, Gilligan C. Effect of Restorative Neurostimulation on Major Drivers of Chronic Low Back Pain Economic Impact. *Neurosurgery* 2023;92:716–24. 5. Gilligan C, Volschenk W, Russo M, et al. An implantable restorative-neurostimulator for refractory mechanical chronic low back pain: a randomized sham-controlled clinical trial. *Pain* 2021;162:2486–98. 6. Gilligan C, Volschenk W, Russo M, et al. Three-Year Durability of Restorative Neurostimulation Effectiveness in Patients With Chronic Low Back Pain and Multifidus Muscle Dysfunction. *Neuromodulation* 2023;26:98–108.

Acknowledgements:

Learning Objectives: 1. Understand pre-implantation decision-making through patient selection utilizing patient-reported outcomes, clinical testing, imaging, and patient history. 2. Understand how chronic nociceptive mechanical lumbar pain may be the result of underlying multifidus dysfunction and altered neuromuscular control, which biomechanically drives dysfunctional painful movements. 3. Understand how the addition of a comprehensive rehabilitation and precision patient-centered program streamlines recovery and outcomes following restorative neurostimulation implantation

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

338

Poster on Board
POSTER ON BOARD: AS06B. PERIPHERAL NERVE: PAIN
13-05-2024 08:00 - 19:00

BOTULINUM TOXIN TYPE A INJECTION FOR THE MANAGEMENT OF LOCAL THERMAL DISCOMFORT REACTION AND PROSTHESIS INDUCED HYPERHYDROSIS IN AMPUTEES

Seung Cheol (Paul) Kim, MB ChB, Tacson Fernandez, MD
Royal National Orthopaedic Hospital, Pain Medicine, Stanmore, United Kingdom

Introduction: In England, the prevalence of amputation stands at 26.3 per 100,000, with arterial disease accounting for over 90% of the 5000 major leg amputations per year.[1] A significant number of lower limb amputees fitted with prostheses experience excess sweating and thermal discomfort. One study indicated that up to 70% of amputees report high perspiration, while another estimated that between 32% and 74% suffer at least one skin complication.[2] Despite the advancement in prosthetic biomechanics, management of Local Thermal Discomfort Reaction (LTDR) remains a challenge. Botulinum toxin type A (BoNT), a potent acetylcholine inhibitor at neuromuscular junctions, has recently emerged as a potential treatment option for chronic pain. Here we present our early data on the efficacy of BoNT in managing LTDR.

Materials / Methods: Over the last four years, we analysed the effectiveness of BoNT injections in the management of LTDR within our small patient cohort (n=8). We focused on five key metrics: perspiration, frequency of prosthesis removal, functional rehabilitation, local irritation, and incidences of infection. Patients' Global Impression of Change (PGIC) scale was used to gauge overall patient response.

Results: Between 2019 and 2023, a cohort of 8 amputees experiencing LTDR received BoNT injections; two received injections every six months, four had annual injections, and two received a single injection. Disruptions from the COVID-19 pandemic unfortunately led to delays and potential missed opportunities. Of the cohort, 6 patients reported a 70% or greater reduction in overall pain over residual limb, and all 8 patients experienced clinically significant reduction in hyperhidrosis and pain following injection of BoNT.

Discussion: The potential of BoNT to reduce secondary hyperhidrosis and thermal discomfort on the residual limb is evident from our study. This also addresses challenges associated with donning and doffing prostheses, making it easier for amputees wear and adjust their prosthetic devices, thereby not only improving prosthetic fit but also overall function and quality of life. Questions remain, however, concerning the appropriate BoNT dosage, duration of effect, and its overall impact on chronic pain such as stump and neuropathic pain. Recent studies led by Davletov'sgroup suggest a new botulinum neurotoxin construct, el-iBoNT, as a potential treatment option for chronic neuropathic pain.[3]

Conclusions: The primary goal in the rehabilitation of amputees is to achieve optimal function where prosthetic fitting is a key component. However, with prosthesis satisfaction rates only at 43% among lower limb amputees, it's evident that persistent issues such as LTDR, hyperhydrosis and pain still plague patients, detrimentally affecting their rehabilitation and quality of life.[4] Our study highlights the potential of BoNT as a viable solution.

Supplemental Data:

References: 1. Ahmad N, Thomas GN, Gill P, Chan C, Torella F. Lower limb amputation in England: prevalence, regional variation and relationship with revascularisation, deprivation and risk factors. A retrospective review of hospital data. *J R Soc Med*. 2014;107(12):483-489. doi:10.1177/0141076814557301 2. Ghoseiri K, Safari MR. Prevalence of heat and perspiration discomfort inside prostheses: literature review. *J Rehabil Res Dev*. 2014;51(6):855-868. doi:10.1682/JRRD.2013.06.0133 3. Williams RJ, Takashima A, Ogata T, Holloway C. A pilot study

towards long-term thermal comfort research for lower-limb prosthesis wearers. *Prosthet Orthot Int*. 2019;43(1):47-54. doi:10.1177/0309364618791604 4. Rocha Melo J, Rodrigues MA, Caetano M, Cantista P. Botulinum toxin in the treatment of residual limb hyperhidrosis: A systematic review. *Rehabilitacion (Madr)*. 2023;57(3):100754. doi:10.1016/j.rh.2022.07.003

Acknowledgements: The support of the chronic pain team at the Royal National Orthopaedic Hospital for this project is gratefully appreciated.

Learning Objectives: 1. **Objective**: Understand the pathophysiology of Local Thermal Discomfort Reaction (LTDR) and prosthesis induced hyperhydrosis in amputees and its impact on their quality of life **Desired Result**: Identify the primary symptoms of LTDR, understand its implications for amputees, and recognise its significance in the context of rehabilitation and patient well-being 2. **Objective**: Explore Botulinum toxin A as a treatment modality for LTDR and prosthesis induced hyperhydrosis, discussing its efficacy, safety profile, and mechanism of action **Desired Result**: Understand of proposed mechanism of Botulinum toxin in alleviating LTDR and prosthesis induced hyperhydrosis related symptoms. Discuss the benefits and potential risks associated with this treatment 3. **Objective**: Understand implications for the synthesis of non-paralyzing botulinum molecules for treating chronic neuropathic pain **Desired Result**: Explore the potential of new botulinum neurotoxin construct in targeting specific nerve fibres and rendering pain relief

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

339

Poster on Board
POSTER ON BOARD: AS06B. PERIPHERAL NERVE: PAIN
13-05-2024 08:00 - 19:00

A SINGLE-CENTER, RETROSPECTIVE ASSESSMENT OF A NOVEL EXTRAFORAMINAL APPROACH FOR NERVE ROOT STIMULATION FOR NEUROPATHIC PAIN

Danielle Kohr, MD, MSc, PhD, Michael Kugler, MD
Fachklinik Löwenstein - SLK Kliniken, Pain Medicine, Löwenstein, Germany

Introduction: This retrospective study is designed to evaluate patient data collected at our facility, with a specific focus on individuals who have undergone nerve root stimulation (NRS) using an alternative extraforaminal approach for managing neuropathic pain since 2019. The primary objective is to gain insights into the indications, implantation success rate, long-term outcomes, safety and effectiveness of this particular approach.

Materials / Methods: Data was comprehensively collected from 48 patients with neuropathic pain who underwent NRS using a novel extraforaminal approach since 2019. The collected data included patient-reported outcomes during the trial, clinical assessment, prior therapies and follow-up records. Additionally, we reviewed any adverse events, complications, or procedure-related issues that occurred.

Results: The results revealed that 74% of patients who underwent trial implantation subsequently underwent full implantation. NRS was primarily employed in CRPS (91%) and knee pain (80%). In 2023 23 patients showed a sustained improvement in pain symptoms. Patient satisfaction rates were 59% in 2019, 57% in 2020, 66% in 2021 and reached 100% in 2022. When adjusting the satisfaction rate through exclusion of patients lost to dropout or explantation, the rate rose to 82% in 2019 and 80% in 2020 in patients who are currently implanted. In the years 2019 and 2020, NRS was primarily considered for patients with a history of failed DRG stimulation. In 2019, 93% and in 2020 all patients with NRS implantation had experienced previous DRG failures. There were no intraoperative complications. The most common postoperative complication observed was electrode migration (30%). Within the first two years there were also instances of device malfunction. Additionally, the system was explanted in four cases due to the absence of MRI compatibility.

Discussion: This retrospective study provides a comprehensive understanding of the safety profile and assesses the impact of NRS using a novel approach of extraforaminal lead placement in patients with neuropathic pain. The spinal nerve root presents a promising target for stimulation. Our analysis suggests its viability as an option for patients who are ineligible or have experienced poor results with other stimulation techniques. Issues of lead migration still remain a challenge.

Conclusions: In conclusion, this study offers valuable insight into the safety and effectiveness of NRS for neuropathic pain. The long-term effects and focus in patients with failed prior treatments make this approach a promising alternative. However, the need for continuous refinement, particularly in addressing complications such as lead migration and enhancing MRI compatibility are underscored. The potential target of the spinal nerve root and the call for prospective studies open up exciting avenues for future research and advancement in pain management techniques.

Supplemental Data: Table 1. Overview of Indications and Implantation Rate of extraforaminal Nerve Root Stimulation.

Indications		Number of trials*	Number of implants	Implantation Rate (Implants/Trial)
CRPS		11	10	91%
CRPS 1		8	7	88%
CRPS 2		3	3	100%
Knee pain		15	12	80%
PSPS		9	6	67%
PSPS 1		1	0	0%
PSPS 2		8	6	75%
Groin pain		9	6	67%
Nerve lesion lower limb		3	3	100%
Pelvic pain		2	0	0%
Postherpetic neuropathy		1	0	0%
Total		50	37	74%

*48 Patients: 2 Patients with 2 indications (CRPS 2+ Groin pain and PSPS 2 + Knee pain)

References:

Acknowledgements:

Learning Objectives: 1. Understanding extraforaminal Nerve Root Stimulation: To comprehend the technique of extraforaminal nerve root stimulation as an innovative approach for managing neuropathic pain. 2. Evaluating outcomes: To learn how to assess the implantation success rate, long-term outcomes, complication and safety profile of the procedures. 3. Identifying patient eligibility and target populations: To recognize the indications for extraforaminal nerve root stimulation and to explore the potential benefits and limitations of this approach for patients who have not responded to or are ineligible for other neuromodulation techniques.

Financial Disclosures: Authors have no financial interests or compensation to declare related to the subject matter discussed in this context.

Disclosure: No significant relationships.

340

Poster on Board
POSTER ON BOARD: AS06B. PERIPHERAL NERVE: PAIN
13-05-2024 08:00 - 19:00

SPINAL CORD STIMULATION: AN UNDISCOVERED FIELD TO BE EXPLORED

Linda Kollenburg, BSc (Hons)[1], Robert Van Dongen, MD[2], Inge Arnts, PhD[2], Heinrich Moser, MD[2], Frank Van Haren, MD[2], Mark Van Ooijen, MD[2], Christopher Robinson, MD, PhD[3], Erkan Kurt, MD[1]
[1]Radboud University Medical Center, Department Of Neurosurgery, Nijmegen, Netherlands, [2]Radboud University Medical Center, Department Of Anesthesiology, Pain And Palliative Medicine, Nijmegen, Netherlands, [3]Beth Israel Deaconess Medical Center, Department Of Anesthesia, Critical Care, And Pain Medicine, Boston, United States of America

Introduction: Peripheral neuropathy (PN) affects 7-10% of the general population and is characterized by burning, tingling and/or stabbing sensations[1,2]. PN refers to damage of the peripheral nerves and is often caused by various conditions e.g. persistent spinal pain syndrome (PSPS), diabetes mellitus and complex regional pain syndromes. Spinal cord stimulation (SCS) is an effective therapy for chronic pain caused by these etiologies, with an overall response rate of 47-83%[3,4]. Despite this success, limited research has been performed on SCS for PN caused by physical peripheral nerve injury[2]. As patients with chronic pain from peripheral nerve injury are often refractory to conventional pain strategies, face poor nerve generation and incomplete functional recovery, SCS should also be considered for these patients[5,6]. Hence, this study aims to evaluate the efficacy of SCS in patients with chronic pain caused by peripheral nerve injury.

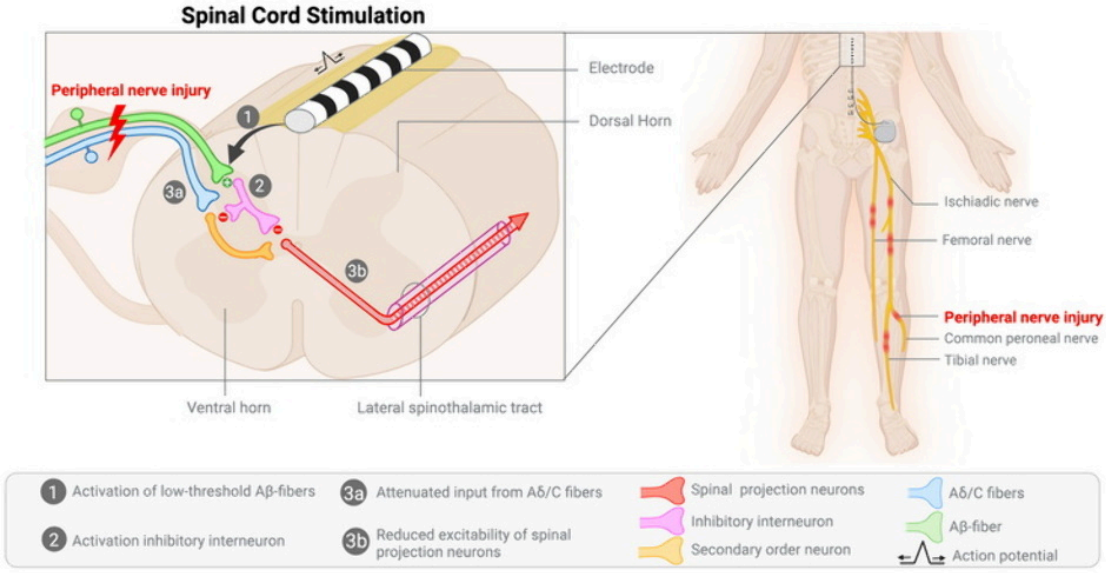
Materials / Methods: A cohort study was performed including patients with peripheral neuropathy pain caused by peripheral nerve injury (traumatic or iatrogenic factors) in the lower extremities. All patients underwent SCS implantation with the top of the lead between level T8 and Th11. Outcomes on patient satisfaction, pain intensity and pain medication use were retrieved retrospectively from our patient database.

Results: Fifteen patients (M= 8; 49 ± 12 years) were included, with a follow up period of ≥ 2 yrs (2-18). Five patients suffered a traumatic nerve injury due to a fracture of bones and ten patients developed pain after a surgical intervention in the lower limb. At last follow-up, the VAS score decreased with 64% (8.1 ± 0.8 to 3.1 ± 1.9) and the pain medication use with >50%. During the last follow up, all patients reported to be satisfied with their implant. Two patients asked to remove their SCS system since their original pain had disappeared after years of stimulation.

Discussion: The restriction on data regarding SCS for PN from physical peripheral nerve injury is likely caused by the limitation of clinical experience, the absence of reimbursement for this indication, and the restricted area that requires coverage by stimulation. Hence most physicians perform peripheral nerve stimulation (PNS) instead. Results of PNS in these patients can be ineffective as trauma and/or iatrogenic etiologies often affect multiple nerves leading to the occurrence of the pain.

Conclusions: SCS appears to be an effective treatment for patients with physical peripheral nerve lesion in the lower extremities and should be further researched as potential strategy to optimize management in these patients.

Supplemental Data:



References: 1. Baskozos G, Hébert HL, Pascal MM, Themistocleous AC, Macfarlane GJ, Wynick D, et al. Epidemiology of neuropathic pain: an analysis of prevalence and associated factors in UK Biobank. Pain reports. 2023;8(2):e1066. 2. Castelli G, Desai KM, Cantone RE. Peripheral Neuropathy: Evaluation and Differential Diagnosis. Am Fam Physician. 2020;102(12):732-9. 3. Fontaine D. Spinal cord stimulation for neuropathic pain. Rev Neurol (Paris). 2021;177(7):838-42. 4. Hoikkanen T, Nissen M, Ikäheimo T-M, Jyrkkänen H-K, Huttunen J, von und zu Fraunberg M. Long-term outcome of Spinal cord stimulation in complex regional pain syndrome. Neurosurgery. 2021;89(4):597–609. 5. Houschyar KS, Momeni A, Pyles MN, Cha JY, Maan ZN, Duscher D, et al. The Role of Current Techniques and Concepts in Peripheral Nerve Repair. Plast Surg Int. 2016;2016:4175293. 6. Wojtkiewicz DM, Saunders J, Domeshek L, Novak CB, Kaskutas V, Mackinnon SE. Social impact of peripheral nerve injuries. Hand (N Y). 2015;10(2):161-7.

Acknowledgements: No acknowledgements to declare.

Learning Objectives: 1. The field of SCS for peripheral nerve injury pain is an undiscovered field that needs to be explored 2. Physical peripheral nerve injury leads to damage of the peripheral nerve, causing peripheral neuropathic pain 3. Pain from physical injury in the peripheral nerve system can be reduced by neurostimulation of the spinal cord

Financial Disclosures: Nothing to disclose.

Disclosure: No significant relationships.

341

Poster on Board
POSTER ON BOARD: AS06B. PERIPHERAL NERVE: PAIN
13-05-2024 08:00 - 19:00

PERIPHERAL BURST STIMULATION FOR THE TREATMENT OF NEURALGIA ASSOCIATED WITH ALLODYNIA: A REPORT ON TWO CASES

Beatriz Mansilla, MD[1], María Román De Aragón, MD[2], Jose Paz Solis, MD[2]
[1]University Hospital La Paz, Neurosurgery, MADRID, Spain, [2]University Hospital La Paz, Neurosurgery, Madrid, Spain

Introduction: Peripheral nerve injuries can be associated with allodynia. This painful syndrome, with both central and peripherical origins, significantly impacts the quality of life of affected patients. When medical treatment becomes insufficient, neuromodulation therapies can be key in pain relief. Less invasive techniques (peripheral stimulation) combined with paresthesia-free stimulation modalities (bursts) may be a good option for certain patients with limited area, high comorbidity, or those who reject spinal cord stimulation. We present two examples of using this stimulation modality in an elderly patient with postherpetic occipital neuralgia and an adolescent with intreatable meralgia paresthesia. We aim to assess burst stimulation as a therapeutic option in peripheral stimulation for the treatment of allodynia-associated neuralgia.

Materials / Methods: Case 1: An 83-year-old male with high comorbidity presented with right postherpetic neuralgia in the C2-C3 territory, associated with allodynia in that area, persisting for 4 years. The initial pain score (EVA) was 8/10, reaching 10/10 with touch. Despite inadequate pain control with antidepressants and antiepileptics, neuromodulation was proposed. After declining spinal cord stimulation, peripheral stimulation was offered occipitally using a paresthesia-free burst mode. Two eight-contact electrodes were placed (3-4 separation, 4 mm between poles) from the midline with the tips at the mastoid and retroauricular areas (toward the helix). Case 2: A 16-year-old female presented with left meralgia paresthetica associated with hyperalgesia and allodynia following a traumatic femoral nerve injury. The baseline pain score was 9/10, reaching 10/10 with touch. Inadequate control with antidepressants and antiepileptics and limited response to local infiltration were noted. Peripheral burst stimulation was proposed at the inguinal and left thigh levels using two eight-contact electrodes (same configuration as in the previous case).

Results: Burst stimulation was performed in both cases using the following parameters (400us-40Hz in microbursts of 5 pulses) with maximum electrode coverage. Both patients reported improvement in the initial pain score, reducing it to 3/10 and 2/10, with approximately 90% territory coverage, significantly reducing allodynia. Moreover, their quality of life in daily activities improved while maintaining their usual treatment.

Discussion: Burst stimulation can relief intractable neurophatic allodynia.

Conclusions: The mechanisms of pain relief in paresthesia-free stimulation modalities remain unknown. Peripheral nerve stimulation, known for its advantage of being the least invasive technique, has traditionally been associated with tonic and low-efficiency stimulation in relieving neuralgia associated with allodynia. The use of paresthesia-free modalities may be a therapeutic option for patients with a limited area, high comorbidity, or those who reject spinal cord stimulation.

Supplemental Data:

References: 1. Sweet JA, Mitchell LS, Narouze S, Sharan AD, Falowski SM, Schwalb JM, Machado A, Rosenow JM, Petersen EA, Hayek SM, Arle JE, Pilitsis JG. Occipital Nerve Stimulation for the Treatment of Patients With Medically Refractory Occipital Neuralgia: Congress of Neurological Surgeons Systematic Review and Evidence-Based Guideline. Neurosurgery 2015;77(3):332-41. 2. Petersen EA. Improved ONS Efficacy and Increased Pain Relief in Occipital Neuralgia with Burst Stimulation: Two Cases. 3. Manning A., Fitzgerald J., Green A., Aziz T., Bojanic S., Garcia R.O., Moir

L., Edwards T. 2019. Burst or Conven- tional Peripheral Nerve Field Stimulation for Treatment of Neuropathic Facial Pain. Neuromodulation 2019; E-pub ahead of print. DOI:10.1111/ner.12922.

Acknowledgements:

Learning Objectives: To assess burst stimulation as a therapeutic option in peripheral stimulation for the treatment of allodynia-associated neuralgia.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

342

Poster on Board
POSTER ON BOARD: AS06B. PERIPHERAL NERVE: PAIN
13-05-2024 08:00 - 19:00

NOVEL NEEDLE INFILTRATION ASSISTED TECHNIQUE FOR PERIPHERAL NERVE STIMULATOR LEAD EXPLANTATION: A CASE SERIES

Sam Nia, MD[1], Alexandra Adler, MD[2], Pascal Scemama, MD[3]
[1]Nassau University Medical Center, Neurosciences, East Meadow, United States of America, [2]Tufts University School of Medicine Partner, Lowell General Hospital Pain Management Center, Anesthesiology, Lowell, United States of America, [3]University of Massachusetts, Anesthesiology, Worcester, United States of America

Introduction: PNS Manufacturers use prongs or tines on leads to anchor them in place. Tines leverage the body's fibrotic tissue generation to enmesh and secure leads, making explantation difficult. This case series discusses a novel needle infiltration-assisted PNS lead explantation technique.

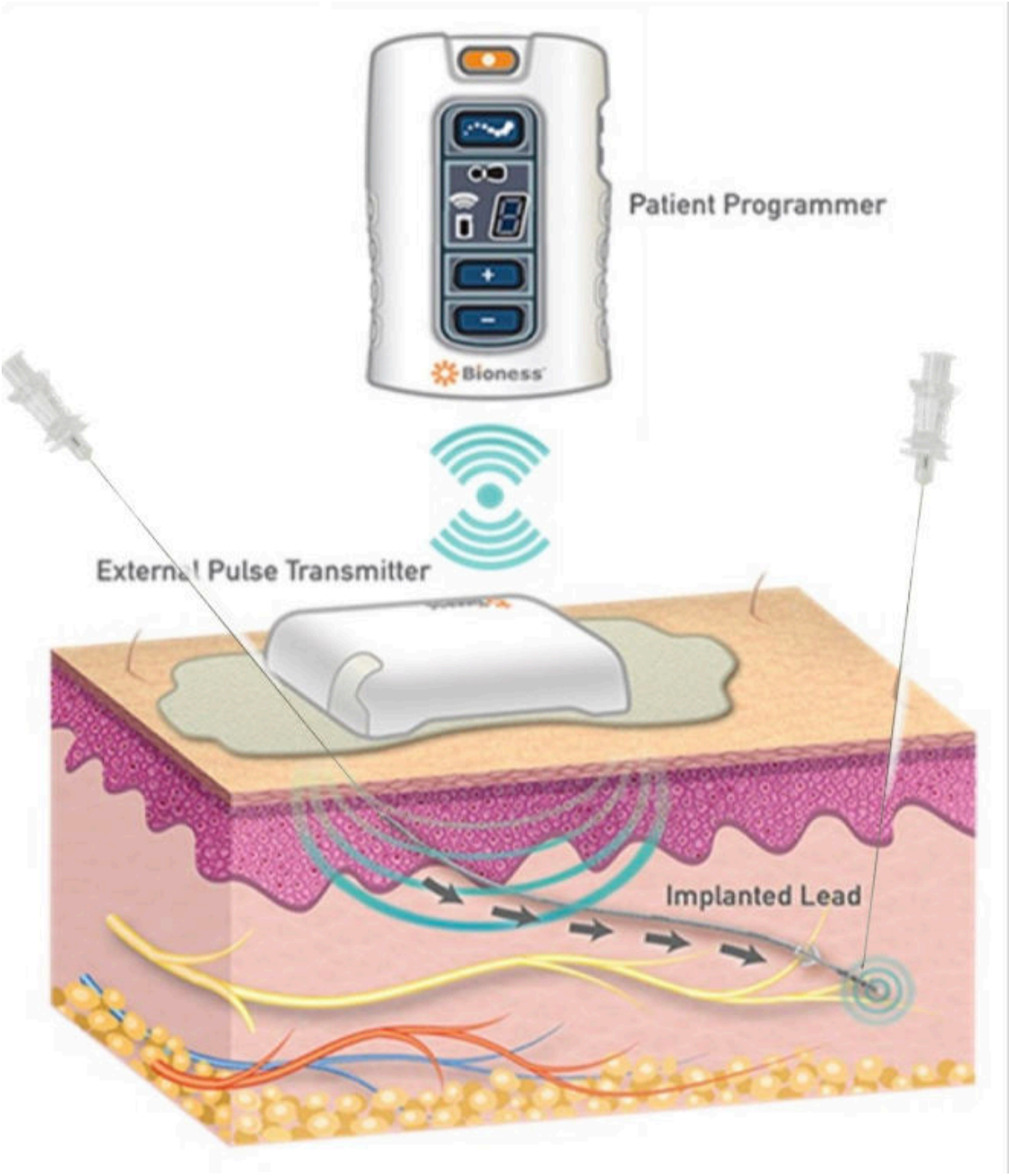
Materials / Methods: Case 1: A 68 F with a saphenous nerve Bioventus StimRouterÒ (Durham, NC, USA) implant for small fiber neuropathy needing a leg MRI, prompting lead explant. Under general anesthesia, fluoroscopic guidance marked both the receiver and tined end of each lead in AP and lateral views. A linear ultrasound probe visualized the length of the lead with an in-line view. An echogenic PajunkÒ (Geisingen, Germany) needle was introduced and guided along the lead. It was difficult to visualize the tined end under US, so another Pajunk (Geisingen, Germany) needle was fluoroscopically guided to the tines. Hydrodissection with saline disrupted the fibrotic tissue around the tines, releasing the lead. The intact lead was extracted smoothly through a small skin incision. **Case 2:** A 41 F with a peroneal nerve Bioventus StimRouter (Durham, NC, USA) for foot/ ankle CRPS 6 months prior. Under sedation, the receiver end of the lead was visualized with fluoroscopy and traced with ultrasound to the skin insertion site, enabling dissection with a small incision. Under ultrasound (in and out of plane views) of the lead, hydrodissection was performed with sterile NS using a 25 gauge 2" needle. Ultrasonographically, the lead was slightly displaced with saline infiltration. The lead was gently pulled and removed intact. **Case 3:** A 77 M with brachial plexopathy and a lateral cord Bioventus Stimrouter (Durham, NC, USA) lead required explantation. Under MAC anesthesia, the lead was identified using fluoroscopy and ultrasound. A 15 blade in conjunction with gentle blunt dissection was used to identify the receiver end of the lead. It was gripped with gentle traction, then an echogenic nerve block needle was used with in and out of plane views to hydrodissect saline along the length of the lead focusing most on the tines to disrupt the fibrous tissue, freeing the lead. The lead was explanted intact with gentle traction.

Results: All leads were explanted intact using this novel needle infiltration assisted technique.

Discussion: Tines are used to secure PNS leads which causes difficult explantation. We describe an image guided needle infiltration assisted technique for PNS lead explantation using hydrodissection primarily at the tines, disrupting the fibrous tissue, freeing the lead.

Conclusions: We introduce a novel needle infiltration-assisted technique for explantation. Further attempts should refine this technique in the future.

Supplemental Data:



References: Strand, N., D'Souza, R.S., Hagedorn, J.M., Pritzlaff, S., Sayed, D., Azeem, N., Abd-Elsayed, A., Escobar, A., Huntoon, M.A., Lam, C.M. and Deer, T.R., 2022. Evidence-based clinical guidelines from the American Society of Pain and Neuroscience for the use of implantable peripheral nerve stimulation in the treatment of chronic pain. *Journal of Pain Research*, pp.2483-2504.

Acknowledgements:

Learning Objectives: 1.) To describe why it may be challenging to explant PNS leads. 2.) To discuss the role of tines in securing PNS leads. 3.) To explain a novel needle infiltrasion assisted technique for PNS lead explantation.

Financial Disclosures: Sam Nia, MD A) Name of companies: Bioventus, Nalu B) What role: Educational Consultant C) Level of compensation: $5,001 - $20,000 USD Aexandra Adler, MD A) Name of companies: Metronic, Bioventus B) What role: Speaker Program C) Level of compensation: $5,001 - $20,000 USD Pascal Scemama, MD A) Name of company: Bioventus, Vertex Pharmaceuticals B) What role: Educational Consultant C) Level of compensation: $5,001 - $20,000 USD

Disclosure: Sam Nia, MD is an educational consultant with Bioventus and Nalu.

343

Poster on Board
POSTER ON BOARD: AS06B. PERIPHERAL NERVE: PAIN
13-05-2024 08:00 - 19:00

USE OF RADIOFREQUENCY LESIONING FOR CHRONIC PAIN MANAGEMENT IN PATIENTS WITH IMPLANTED CARDIAC PACEMAKERS AND DEFIBRILLATORS

Dimitrios Peios, MD[1], Athanasia Tsaroucha, MD[2], Georgios Matis, MD[3], Christina Ble, MD[1], Ilias Kopatzidis, MD[1], Aikaterini Polyzoi, MD[1], Aikaterini Kyriakidou, MD[1], Athanasios Koulousakis, MD[4]
[1]St Luce's Hospital, Panorama Thessaloniki, Functional Neurosurgery, Thessaloniki, Greece, [2]Aretaieio University Hospital, Pain Unit, Athens, Greece, [3]University Hospital Cologne, Neurosurgery, Cologne, Germany, [4]Kunibertsklinik, Cologne, Germany

Introduction: Radiofrequency ablation (RFA) and pulsed radiofrequency (PRF) are used extensively in treating various pain syndromes, both cancer and benign, such as facet, knee and sacroiliac joint pain, trigeminal and occipital neuralgia and many more. There are only a few studies that have tested the safety of these procedures in patients with implanted pacemakers or defibrillators. We present our data on radiofrequency procedures in such patients under specific conditions and operating room settings.

Materials / Methods: We monitored the performance of both heart pacemakers and defribrilators during radiofrequency invasive procedures for pain management. All procedures were performed in the angiography suite of our hospital, with the presence of a cardio-anaesthesiologist and a trained lab technician. All patients were reevaluated postprocedural after one month.

Results: We treated 17 patients with implanted cardiac devices, 12 men and 5 women, with an average of 70.7 years old. 14 had pacemakers and 3 defibrillators. 5 underwent PRF and the rest 12 classic RFA. 2 patients were treated for occipital neuralgia and migraine, 5 for trigeminal neuralgia and 10 for facet, sacroiliac or knee joint pain or combination of them. No technical or functional disturbance at the implanted device was observed throughout the procedures. Additionally, no incident was observed at 1 month followup.

Discussion: Older studies raised concern over the use of radiofrequency in patients with implanted cardiac devices. Same restrictions are still described in the manuals of such devices. Newer studies have demonstrated the safety for specific interventional procedures. We showed that in a controlled setting, with the assistance of specialized personnel, such a cardio-anaesthesiologist and a trained device technician, these procedures can be performed with safety for various indications, regardless of the uni- or bipolar fashion.

Conclusions: Our results showed that RFA and PRF are safe procedures for patients with implanted pacemakers or defribrilators, when performed by and with the assistance of specialized and trained personnel. An intraoperative monitoring of the device can ensure the safe completion of these procedures, regardless of the pain etiology or the site of intervention.

Supplemental Data:

References: 1.Wray JK, Dixon B, Przkora R. Radiofrequency Ablation. [Updated 2023 Jun 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482387/ 2.Jordan Sam et al. Pulsed Radiofrequency in Interventional Pain Management: Cellular and Molecular Mechanisms of Action – An Update and Review. Pain Physician 2021; 24:525-532 3.Smith et al. Radiofrequency Neurotomy for Facet Joint Pain in Patients with Permanent Pacemakers and Defibrillators. Pain Medicine, 2019; 20(2): 411–412 4. Friedrich J et al. Management of Cardiac Implantable Electrical Devices in Patients Undergoing Radiofrequency Ablation for Spine Pain: Physician Survey and Review of Guidelines. Pain Physician 2020; 23:E335-E342

Acknowledgements:

Learning Objectives: 1. share data and experience 2. note remarks and comments 3. promote further investigation

Financial Disclosures: Proctoring services about radiofrequency techniques in Greece and Cyprus for Medtronic Hellas and 77 Medical Ware distributors

Disclosure: No significant relationships.

344

Poster on Board
POSTER ON BOARD: AS06E. PERIPHERAL NERVE: SYSTEMIC DISEASE
13-05-2024 08:00 - 19:00

ELECTRONEUROMYOGRAPHY IN THE EARLY STAGES OF DIABETIC POLYNEUROPATHY IN PATIENTS WITH COVID-19

Rustambek Matmurodov, BSN, Surayyo Umirova, BPT
Tashkent medical academy, Tashkent, Uzbekistan

Introduction: Currently, there is a large increase in the number of cases of coronavirus infection caused by COVID-19. The outbreak of the new coronavirus infection SARS-CoV-2 has spread to most countries of the world.

Materials / Methods: The study included 75 patients, they were divided into 3 groups: group 1 included 30 patients with type 2 diabetes who had coronavirus infection, the 2nd control group included 35 patients with type 2 diabetes who did not have coronavirus infection, and also 10 healthy volunteers. Persons included in the CG did not have a history of carbohydrate metabolism disorders, the fasting venous plasma glucose level was less than 7.0 mmol/l, glycated hemoglobin (HbA1c) was less than 6.5%. All examined had no symptoms and clinical signs of distal polyneuropathy (DPN). Participants were assessed for symptoms of neuropathy using the Neuropathy Symptom Score (NSS), assessed for signs of DPN using the Neuropathic Dysfunctional Score NDS

Results: In a group According to ENMG data, type 2 diabetes mellitus was detected in 87% of people who had coronavirus infection. Sensory variant of DDPN was detected in 12 patients (34.8%), sensorimotor neuropathy was detected in 14 (40.6%) patients, motor DDPN was detected in 4 patients (11.6%) from the control group with DM 2. The additionally examined medial and lateral plantar nerves were most often affected (p=0.017 and p=0.003, respectively). In the control group of 20 individuals, 13 (32.5%) showed signs of DPN in combination with radiculopathy. ENMG parameters indicative of DDPN: latency and amplitude and speed of propagation of excitation for 3 sensory (n. plantaris lateralis, n. plantaris medialis, n. suralis) and 2 motor nerves (n. peroneus, n. tibialis) were significantly worse in people with type 2 diabetes who have had a coronavirus infection, than in the CG who did not tolerate coronavirus infection, both in those examined with and without radiculopathy. Persons with type 2 diabetes who had coronavirus infection and sensorimotor DDPN had a longer duration of diabetes (p=0.503), higher HbA1c (p=0.087) and BMI (p=0.060) in comparison with those examined with type 2 diabetes and sensory neuropathy, without reaching statistical significance.

Discussion: How does coronavirus affect the course of diabetic prolineuropathy?

Conclusions: The data obtained indicate that COVID-19 exacerbates the manifestations of diabetic polyneuropathy in patients with type 2 diabetes. The results of the study confirmed the effectiveness and suitability of ENMG in the early diagnosis of DPN, and also made it possible to select the optimal ENMG indicators necessary for this.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. Covid-19 2. Diabetic polyneuropathy 3. Early diagnostic

Financial Disclosures: No financial disclosures

Disclosure: No significant relationships.

345

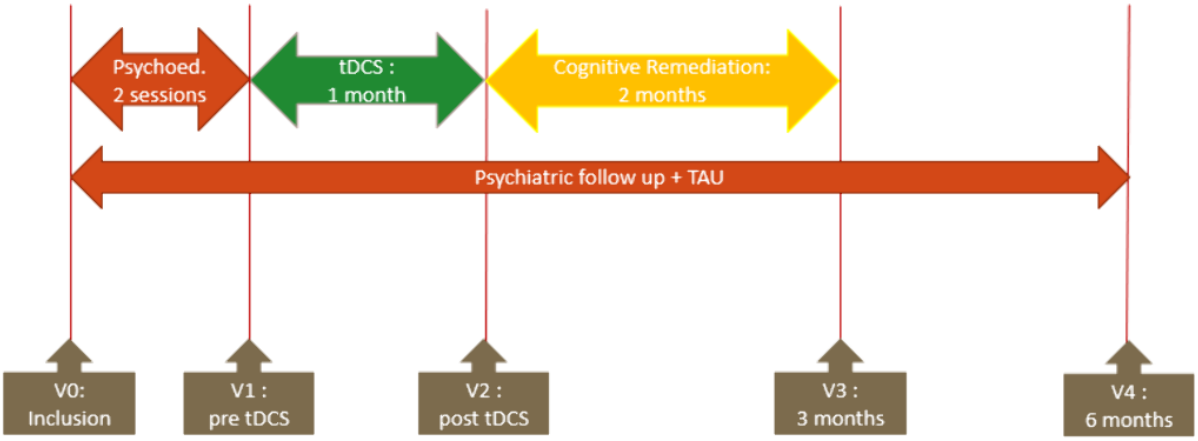
Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

THE FEASIBILITY OF A COMBINED APPROACH INCLUDING NEUROMODULATION BY TDCS AND COGNITIVE REMEDIATION FOR PEOPLE WITH BORDERLINE PERSONALITY DISORDER (BPD)

Mariam Ahmed, BSc (Hons)[1], Lionel Cailhol, MD[2], Frédérique Delisle, BSc (Hons)[1]
[1]Institut of mental health of Montreal, Cloutier Wing, Montreal, Canada, [2]Integrated university center for health and social services of the east of the island of montreal (CIUSSS-EMTL), Psychiatry, Montreal, Canada

Introduction: Longitudinal studies related to BPD show a reduction of symptoms related to the disorder but very little improvement in functionality. The betterment of executive functions of people with BPD after psychotherapy is very limited. The efficacy of those treatments on functionality appears to be mild with a small effect size. This study explores the feasibility of a combined approach by neuromodulation and cognitive remediation as the first line of treatment for people with BPD by evaluating their impact on impulsivity and executive functions. Based on previous studies, transcranial direct current stimulation (tDCS) can be used to improve impulsivity and emotional instability in patients with BPD. Moreover, cognitive remediation focuses on reducing neuropsychological alterations by re-educating patients and applying specific strategies to aid them long term in certain daily functions like developing healthy habits, executive functions, problem solving, attention, working memory and cognition.

Materials / Methods:



The protocol includes 10 daily sessions of tDCS for 2 weeks and 8 weekly group meetings for the cognitive remediation. Based on studies conducted on people with BPD, the settings for the tDCS are as follows; 20 minutes of continuous current at the intensity of 2mA and the electrodes are placed on specific stimulation sites related to impulsivity. To verify the effectiveness of the combination regarding the symptoms and to evaluate the cognition and executive functions of the patients; questionnaires and neuropsychological tests are conducted at the beginning of the study, after the tDCS, after the cognitive remediation and 3 months after the end of the study.

Results: The expected results of this study are that the combination of the two treatments will reduce the symptoms of BPD, such as impulsivity, and improve executive functions compared to the treatment as usual or tDCS alone.

Discussion: In fact, neuropsychological anomalies are correlated with the symptomatic severity of BPD. Also, a study on the correlation of symptom severity and neuropsychological deficits demonstrates that cognitive reinforcement can help improve clinical symptoms. Additionally, cognitive

training of neuropsychological skills in other disorders, like eating disorders and schizophrenia, show improvements in psychotherapeutic effectiveness.

Conclusions: The execution of this treatment will allow a reduction in costs and time dedicated to treatments, thus making it easily implementable in communities furthest from urban centers. It will explore a new therapeutic pathway based on the combination of biological and non-biological interventions. The study will collect pilot data to test the effectiveness of the design which will permit further studies such as a randomized controlled study.

Supplemental Data:

References: References 1. Zanarini MC, Temes CM, Frankenburg FR, Reich DB, Fitzmaurice GM. Description and prediction of time-to-attainment of excellent recovery for borderline patients followed prospectively for 20 years. Psychiatry Res. 2018;262:40-5. 2. Chakhssi F, Zoet JM, Oostendorp JM, Noordzij ML, Sommers-Spijkerman M. Effect of Psychotherapy for Borderline Personality Disorder on Quality of Life: A Systematic Review and Meta-Analysis. J Pers Disord. 2021;35(2):255-69. 3. Cristea IA, Gentili C, Cotet CD, Palomba D, Barbui C, Cuijpers P. Efficacy of Psychotherapies for Borderline Personality Disorder: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2017;74(4):319-28. 4. Jørgensen MS, Storebø OJ, Stoffers-Winterling JM, Faltinsen E, Todorovac A, Simonsen E. Psychological therapies for adolescents with borderline personality disorder (BPD) or BPD features-A systematic review of randomized clinical trials with meta-analysis and Trial Sequential Analysis. PLoS One. 2021;16(1):e0245331. 5. Cambridge OR, Knight MJ, Mills N, Baune BT. The clinical relationship between cognitive impairment and psychosocial functioning in major depressive disorder: A systematic review. Psychiatry Res. 2018;269:157-71. 6. Vita A, Deste G, Barlati S, Poli R, Cacciani P, De Peri L, et al. Feasibility and effectiveness of cognitive remediation in the treatment of borderline personality disorder. Neuropsychol Rehabil. 2018;28(3):416-28. 7. Lisoni J, Miotto P, Barlati S, Calza S, Crescini A, Deste G, et al. Change in core symptoms of borderline personality disorder by tDCS: A pilot study. Psychiatry Res. 2020;291:113261. 8. Lisoni J, Barlati S, Deste G, Ceraso A, Nibbio G, Baldacci G, et al. Efficacy and tolerability of Brain Stimulation interventions in Borderline Personality Disorder: state of the art and future perspectives - A systematic review. Prog Neuropsychopharmacol Biol Psychiatry. 2022;116:110537. 9. Schulze L, Grove M, Tamm S, Renneberg B, Roepke S. Effects of transcranial direct current stimulation on the cognitive control of negative stimuli in borderline personality disorder. Sci Rep. 2019;9(1):332. 10. Molavi P, Aziziaram S, Basharpoor S, Atadokht A, Nitsche MA, Salehinejad MA. Repeated transcranial direct current stimulation of dorsolateral-prefrontal cortex improves executive functions, cognitive reappraisal emotion regulation, and control over emotional processing in borderline personality disorder: A randomized, sham-controlled, parallel-group study. J Affect Disord. 2020;274:93-102. 11. Wolkenstein L, Rombold-Bruehl F, Bingmann T, Sommer A, Kanske P, Plewnia C. Challenging control over emotions in borderline personality disorder - a tDCS study. Neuropsychologia. 2021;156:107850. 12. Vai B, Cazzetta S, Scalisi R, Donati A, Bechi M, Poletti S, et al. Neuropsychological deficits correlate with symptoms severity and cortical thickness in Borderline Personality Disorder. J Affect Disord. 2021;278:181-8. 13. Dingemans AE, Danner UN, Donker JM, Aardoom JJ, van Meer F, Tobias K, et al. The effectiveness of cognitive remediation therapy in patients with a severe or enduring eating disorder: a randomized controlled trial. Psychother Psychosom. 2014;83(1):29-36. 14. Drake RJ, Day CJ, Picucci R, Warburton J, Larkin W, Husain N, et al. A naturalistic, randomized, controlled trial combining cognitive remediation with cognitive-behavioural therapy after first-episode non-affective psychosis. Psychol Med. 2014;44(9):1889-99. 15. Peña J, Ibarretxe-Bilbao N, Sánchez P, Iriarte MB, Elizagarate E, Garay MA, et al. Combining social cognitive treatment, cognitive remediation, and functional skills training in schizophrenia: a randomized controlled trial. NPJ Schizophr. 2016;2:16037. 16. Herpertz SC, Schneider I, Schmahl C, Bertsch K. Neurobiological Mechanisms Mediating Emotion Dysregulation as Targets of Change in Borderline Personality Disorder. Psychopathology. 2018;51(2):96-104.

Acknowledgements: The support and financial ressources of the University Mental Health Institute of Montreal and the Quebec network on suicide, mood disorders and associated disorders for this project is gratefully acknowledged.

Learning Objectives: 1) Evaluate the feasibility and efficacy of a combined approach by analyzing the recruitment, retention, and participation rates, and the symptomatic efficacy and the cognitive progression of a combined approach by reviewing the results of questionnaires and

neuropsychological tests. 2) Assess the long-term functionality of the patients by examining the outcomes of functional assessment tools like the WHODAS 2.0 and the *Functional Assessment of Borderline personality disorder* (FAB). 3) Discuss the impact of a combined approach on the reduction of symptoms (ex: impulsivity) and the improvement of executive functions.

Financial Disclosures: no significant relationships

Disclosure: No significant relationships.

346

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

REAL-LIFE OUTCOMES OF SCS FOR CHRONIC PELVIC PAIN: DATA FROM A TERTIARY ACADEMIC CENTER

Sireedhorn Assavanop, MD, Anuj Bhatia, MD, Victoria Bains, RN, Danielle Alvares, PhD, Pranab Kumar, MD
University Health Network, Department Of Anesthesia, Toronto Western Hospital, Toronto, Canada

Introduction: Chronic pelvic pain (CPP) is a complex and debilitating condition that affects a number of individuals in many aspects. A variety of factors, ranging from gynecological to gastrointestinal, urological, or musculoskeletal issues could contribute to this condition and often result in challenges to treat with pharmacotherapy and injections. Spinal cord stimulation (SCS) has been used to relieve pain in patients with CPP with variable success rates. We present here data from our center to evaluate SCS outcomes in CPP patients.

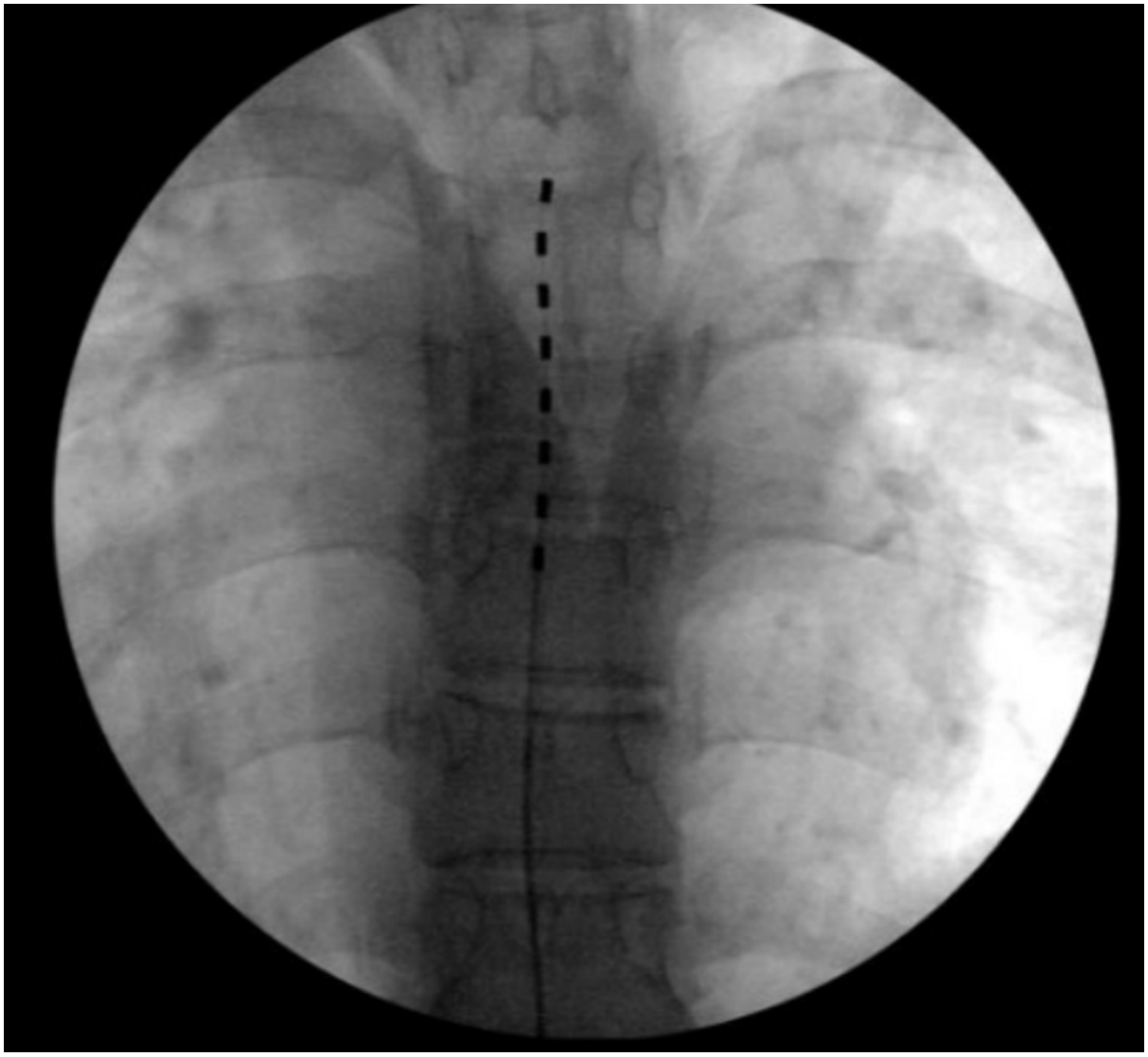
Materials / Methods: We conducted a retrospective review of the medical records of three patients (Patients A, B, and C) who underwent SCS trials and implants to treat CPP at our center. We collected data at baseline, three times during the trial phase, and at 6 weeks, 6 months, 1 year, and annually post-implantation. We monitored several outcomes, such as pain intensity, use of breakthrough analgesics, physical function, quality of sleep, mental health, quality of life, adverse effects, and details of programming and patients' use of SCS modes.

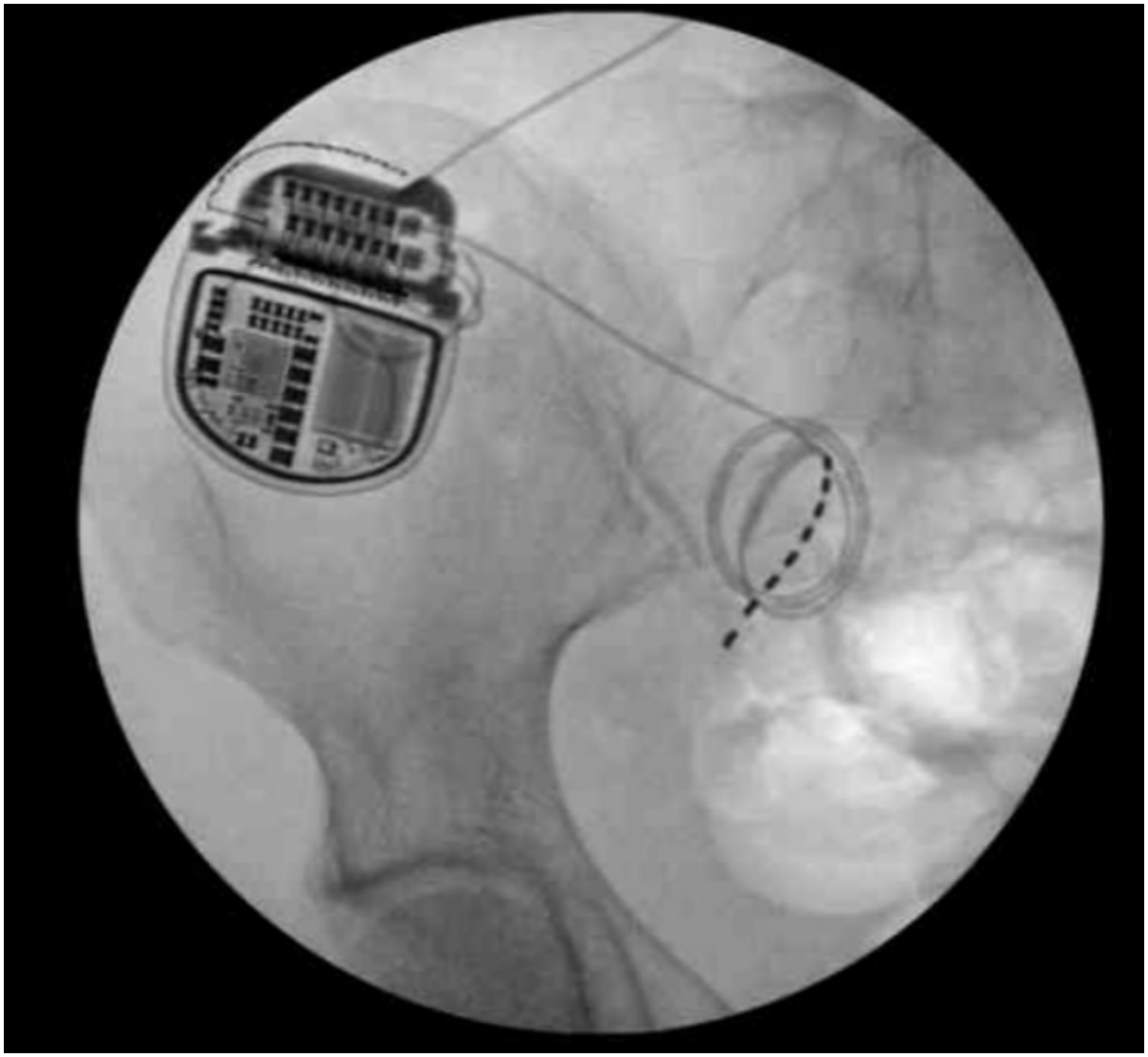
Results: SCS trials were successful for all three patients, and they proceeded to have implants. All patients received dual leads system, with the majority receiving one in the dorsal thoracic epidural space and one in the sacral foramen. The rest has both leads sitting at the S3 level bilaterally. Each patient reported a reduction in pain on the Visual Analog Scale score (VAS) and an improvement in overall condition, as witnessed by the Patient’s Global Impression of Change scale (PGIC). Two patients reported improvement in their psychological condition, as shown by the reduction of General Anxiety Disorder-7 (GAD-7) and Patient Health Questionnaire-9 item for depression (PHQ-9). Based on records, paresthesia-based mode is the most frequently utilized mode by patients. None of the subjects displayed any neurological deficits or severe adverse effects.

Discussion: With successful SCS implants, the majority of patients with CPP experienced an improvement in physical and mental function, as well as a reduction in pain interference in daily life. One patient who received an SCS implant in less than two months will undergo long-term monitoring to assess its effectiveness. Available data demonstrated promising results of paresthesia-based stimulation for the treatment of CPP without any unexpected adverse events.

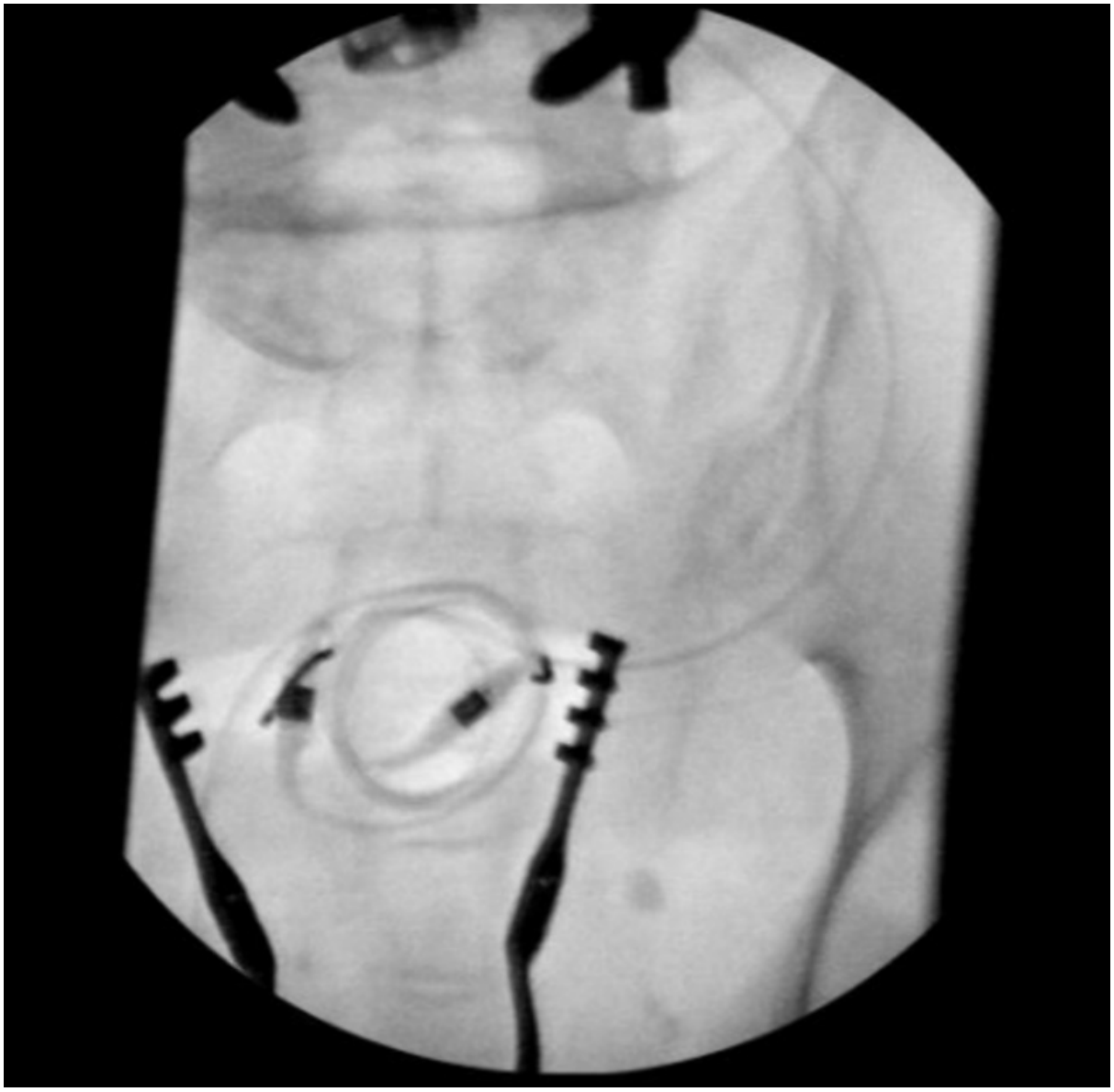
Conclusions: Although there are indications that neuromodulation could be beneficial in alleviating CPP and enhancing quality of life, the confirmation of SCS effectiveness awaits larger, well-controlled studies.

Supplemental Data: Picture 1 and 2: Single S3 and Thoracic leads





Picture 3 and 4: S3 double electrodes



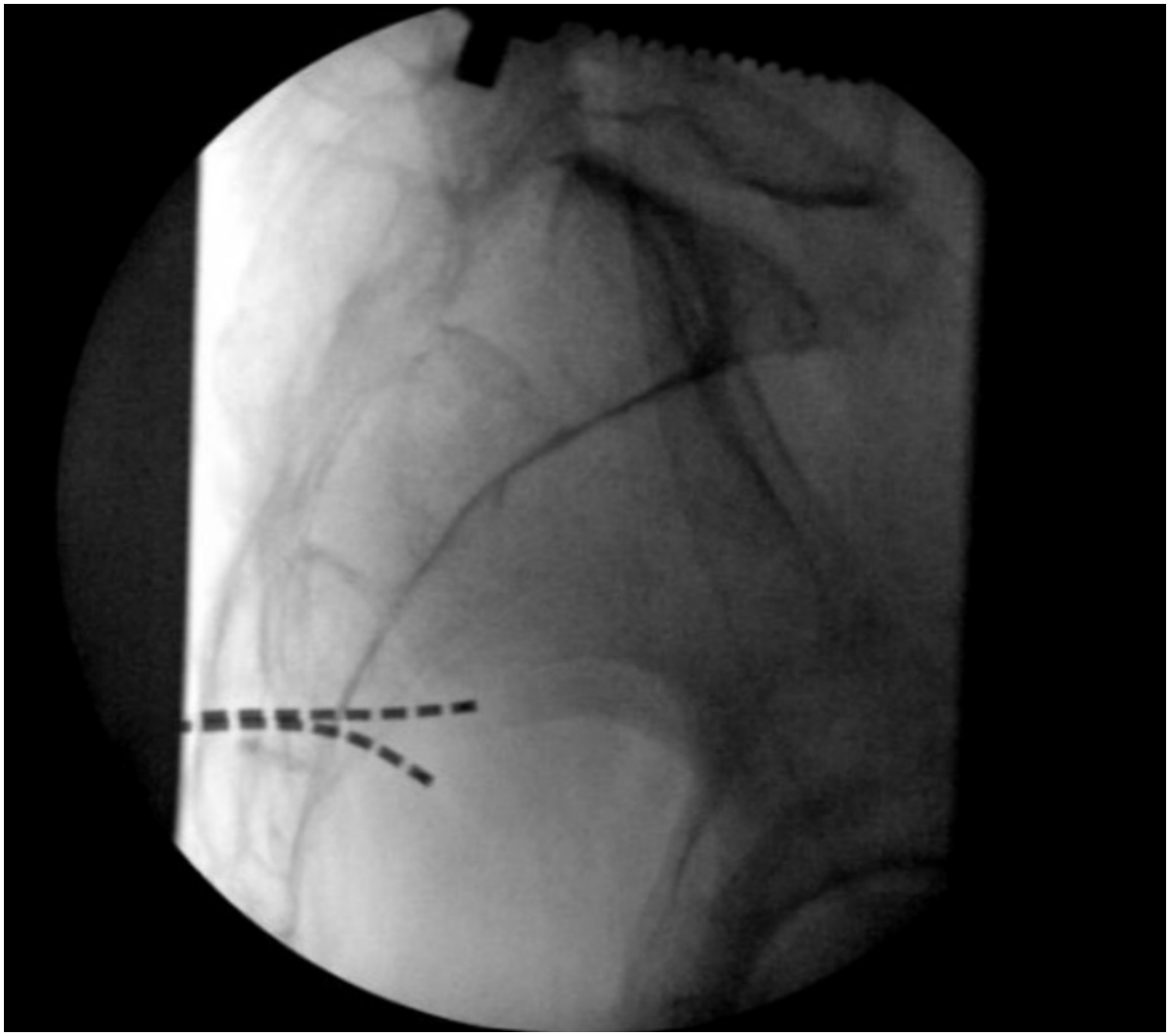


Table 1. Baseline characteristics and Post-SCS implant data for Patient A *Pain location: Pubis and buttocks *Etiology: Post low anterior resection, posterior vaginectomy and end colostomy for rectal cancer *Duration of pain prior to implants: 2.5 years *SCS Leads location: 2 leads; dorsal thoracic epidural space (T8 level) and left Sacral Nerve 3 (S3) foramen *Setting predominantly used: Paresthesia	**Outcomes measured**	Baseline	6 weeks post-implant	1 year post-implant	2 years post-implant
	Average Pain VAS score (0-10)	6	5	N/A	N/A
	BPI-Interference (0-70)	68	34	N/A	N/A
	NPSI (0-100)	60	59	N/A	N/A
	GAD-7 score (0-21)	13	3	N/A	N/A
	PHQ-9 (0-27)	18	3	N/A	N/A
	EQ-5D (0-100)	25	40	N/A	N/A
	PGIC (worse/no change/improved)	N/A	improved	N/A	N/A

Table 2. Baseline characteristics and Post-SCS implant data for Patient B *Pain location: Pelvic and left abdominal wall *Etiology: Endometriosis with multiple	**Outcomes measured**	Baseline	6 weeks post-implant	1 year post-implant	2 years post-implant
	Average Pain VAS score (0-10)	8	5	3	3

laparoscopies as well as a hysterectomy. *Duration of pain prior to implants: 8 years *SCS Leads location: 2 leads; dorsal thoracic epidural space (T5 level) and left Sacral Nerve 3 (S3) foramen *Setting predominantly used: Paresthesia	BPI-Interference (0-70)	57	42	12	15
	NPSI (0-100)	68	36	49	50
	GAD-7 score (0-21)	9	7	3	5
	PHQ-9 (0-27)	21	9	2	3
	EQ-5D (0-100)	20	65	85	90
	PGIC (worse/no change/improved)	N/A	improved	improved	improved

	Outcomes measured	Baseline	6 weeks post-implant	1 year post-implant	2 years post-implant
Table 3. Baseline characteristics and Post-SCS implant data for Patient C *Pain location: Perineal and peri-rectal *Etiology: Post-spinal decompression and fusion *Duration of pain prior to implants: 8 years *SCS Leads location: 2 leads at S3 level bilaterally *Setting predominantly used: Paresthesia	Average Pain VAS score (0-10)	6	6	4	4
	BPI-Interference (0-70)	45	33	27	57
	NPSI (0-100)	27	13	14	32
	GAD-7 score (0-21)	18	5	16	18
	PHQ-9 (0-27)	22	6	18	26
	EQ-5D (0-100)	50	90	90	100
	PGIC (worse/no change/improved)	N/A	No change	improved	improved

VAS: Visual Analog Scale score; BPI-interference: Brief Pain Inventory Score: For interference scale, the higher the score, the greater interference the patient experiences in their daily lives due to pain; NPSI: Neuropathic Pain Symptom Inventory: The higher the score, the higher likelihood that the patient experiences characteristics of neuropathic pain; GAD-7: General Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9 item for depression; EQ-5D VAS: EuroQol group 5-dimension Visual Analogue Scale (0 means the worst health the patient can imagine, 100 means the best health the patient can imagine); PGIC: Patient's Global Impression of Change scale

References: 1. Tate JL, Stauss T, Li S, Rotte A, Subbaroyan J. A prospective, multi-center, clinical trial of a 10-kHz spinal cord stimulation system in the treatment of chronic pelvic pain. Pain Practice. 2021 Jan;21(1):45-53. 2. Kapural L, Narouze SN, Janicki TI, Mekhail N. Spinal cord stimulation is an effective treatment for the chronic intractable visceral pelvic pain. Pain Medicine. 2006 Sep 1;7(5):440-3. 3. Hunter CW, Yang A. Dorsal root ganglion stimulation for chronic pelvic pain: a case series and technical report on a novel lead configuration. Neuromodulation: Technology at the Neural Interface. 2019 Jan 1;22(1):87-95. 4. Patel CB, Patel AA, Diwan S. The Role of Neuromodulation in Chronic Pelvic Pain: A Review Article. Pain Physician. 2022;25(4):E531. 5. Cottrell AM, Schneider MP, Goonewardene S, Yuan Y, Baranowski AP, Engeler DS, Borovicka J, Dinis-Oliveira P, Elneil S, Hughes J, Messelink BJ. Benefits and harms of electrical neuromodulation for chronic pelvic pain: a systematic review. European urology focus. 2020 May 15;6(3):559-71. 6. Mahran A, Baaklini G, Hassani D, Abolella HA, Safwat AS, Neudecker M, Hijaz AK, Mahajan ST, Siegel SW, El-Nashar SA. Sacral neuromodulation treating chronic pelvic pain: a meta-analysis and systematic review of the literature. International Urogynecology Journal. 2019 Jul 1;30:1023-35.

Acknowledgements: -

Learning Objectives: 1. Determine the effectiveness of SCS in managing chronic pelvic pain by evaluating patients' clinical presentations and questionnaires. 2. Examine the safety and tolerability of SCS as a treatment for chronic pelvic pain. 3. Improve the efficacy and outcomes of SCS procedures

by refining technical aspects such as electrode placement, stimulation parameters, and patient-specific settings.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

347

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

TRIGEMINAL NERVE ROOT ENTRY ZONE INTRAOPERATIVE TOPOGRAPHY MAPPING

Daniel Benzecry Almeida, MD[1], Joel Duarte, MD[2]
[1]INSTITUTO DE NEUROLOGIA DE CURITIBA, Functional Neurosurgery, CURITIBA, Brazil, [2]INSTITUTO DE NEUROLOGIA DE CURITIBA, Functional Neurosurgery, Curitiba, Brazil

Introduction: The trigeminal nerve root entry zone (REZ) is a place of particular significance, it's where the trigeminal nerve interfaces closely with blood vessels, often implicated in trigeminal neuralgia. In refractory cases, microvascular decompression is the primary surgical option, demonstrating efficacy in 62-89% of cases. Intraoperative electrophysiological mapping aids in microvascular decompression, helping identify trigeminal branches. However, the precise localization of trigeminal nerve territories at the REZ varies across studies, making it essential for individualized surgical approaches. This study is the first to investigate neurophysiological mapping at the neurovascular compression site and its correlation with clinical outcomes.

Materials / Methods: This series included 23 cases of electrophysiological mapping of the trigeminal nerve during microvascular decompression for classic trigeminal neuralgia treatment. We designated 3 distinct zones at the trigeminal nerve REZ for the purposes of antidromic stimulation and compound nerve action potential (CNAP) recording: Zone 1 (superior/rostral), Zone 2 (intermediate), and Zone 3 (inferior/caudal).

Results: On average, patients were 55 years old, predominantly female (60.8%), and had experienced symptoms for 94 months before treatment. The most affected nerve division was V2+V3 (29%), followed by V1+V2 (25%) and V3 (21%). Patients had pre-operative BNIs of IV (54%) or V (46%). The distribution of pain by compression site was significantly different ($p = 0.008$). The mapping technique revealed a somatotopic organization within the trigeminal nerve, wherein stimulation of Zone 1 predominantly evoked upper facial activity, Zone 2 yielded responses in the middle face, and Zone 3 elicited lower facial responses, with favorable outcomes for total correlation cases. Follow-up averaged 34.95 months, with most patients achieving BNI I (57%) or II (30%).

Discussion: The results of this study imply the possible benefits of using intraoperative monitoring to inform surgical choices during trigeminal nerve decompression. This implication is reinforced by the discovery of differing pain distribution patterns in trigeminal neuralgia, dependent on the site of the neurovascular conflict, which aligns with prior research descriptions. Moreover, the study establishes a link between the location of the neurovascular conflict and neurophysiological stimulation, indicating that the compression site significantly affects the pain territory experienced by patients.

Conclusions: This research highlights the promising clinical utility of intraoperative mapping in trigeminal neuralgia, which assists in accurately pinpointing and isolating the causative vessel behind neurovascular compression, thereby improving the effectiveness of microvascular decompression.

Supplemental Data:

References: 1. Sindou M, Brinzeu A (2020) Topography of the pain in classical trigeminal neuralgia: Insights into somatotopic organization. Brain 143:531–540. doi: 10.1093/brain/awz407 2. Stechison MT, MØller A, Lovely TJ (1996) Intraoperative Mapping of the Trigeminal Nerve Root: Technique and Application in the Surgical Management of Facial Pain. Neurosurgery 38:76–82. doi: 10.1097/00006123-199601000-00018 3. Hatayama T (2004) Intraoperative mapping of the trigeminal nerve root during MVD. Int Congr Ser 1259:347–352. doi: 10.1016/S0531-5131(03)01407-9

Acknowledgements:

Learning Objectives: 1. Gain insight into the pathophysiology of TN, particularly the role of neurovascular compression at the trigeminal nerve root entry zone (REZ) in causing excruciating facial pain. 2. Comprehend the utility of intraoperative neurophysiological mapping in the context of microvascular decompression surgeries for TN. This includes understanding how this technique aids in precise identification and isolation of the offending vessel responsible for neurovascular compression. 3. Learn how clinical parameters, pain distribution, and topographical anatomy are meticulously correlated in trigeminal neuralgia surgery.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

348

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

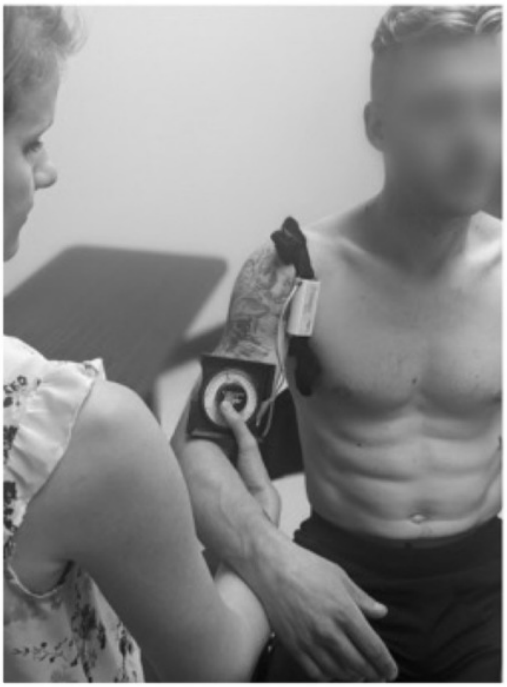
TESTING SENSORIMOTOR PROCESSING WITH TENDON VIBRATION AND TRANSCRANIAL MAGNETIC STIMULATION IN SUBACROMIAL IMPINGEMENT SYNDROME

Émilie Bouchard, MSc[1], Lydiane Lauzier, MSc[1], Mathieu Boudier-Revéret, MD[2], Stéphane Sobczak, PhD[3], Laurence Munger, BSc (Hons)[1], Kossi Épiphane Ketounou, BSc (Hons)[1], Marie-Pier Perron, BSc (Hons)[1], Suzy Ngomo, PhD[1], Louis-David Beaulieu, PhD[1]
[1]UQAC, Science De La Santé, Chicoutimi, Canada, [2]CHUM, Physiatrie, montréal, Canada, [3]UQTR, Anatomie, Trois-Rivière, Canada

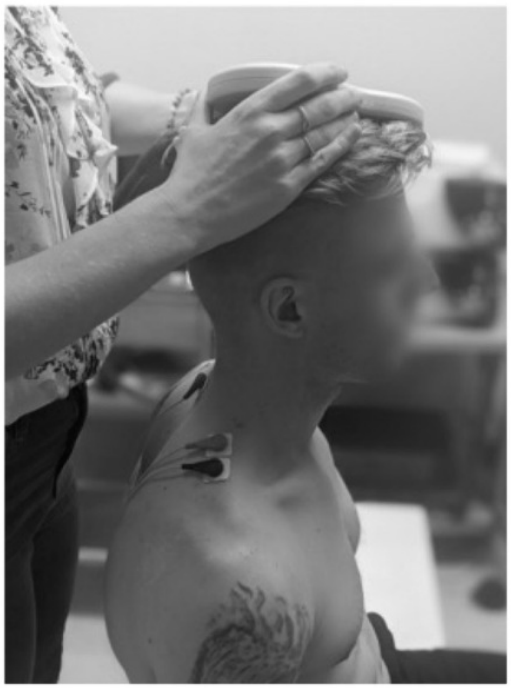
Introduction: More than 2/3 of the population will suffer from shoulder pain, for instance caused by an shoulder impingement syndrome (SIS), that persist more than 3 years in up to 50% of cases. We do know with researches that SIS often presents with an altered proprioception and control over the upper trapezius (UT) and scapular muscles during shoulder elevation. However, neural mechanisms involved in these sensorimotor alterations remain understudied. We decided to use transcranial magnetic stimulation (TMS) and vibration-induced kinesthetic illusions (VIB-KI) so we could improve our knowledge around SIS and hopefully open up new sensory-based therapeutics approaches. Therefore, the primary objective of this study was to assess and compare VIB- and TMS-related measures of sensorimotor functions between healthy and SIS populations, as well as between sides. The hypothesis was that illusions would be less clear and of lower speed/amplitude, along with lower corticospinal excitability in the painful shoulder vs. the non-painful one and vs. healthy counterparts.

Materials / Methods: Fifteen participants with SIS and fifteen controls took part of one session including SIS tests, questionnaires, and ultrasound imagery. Then, proprioceptive processing was tested by VIB-KI and TMS measures of corticospinal excitability of the UT muscles were obtained.

A

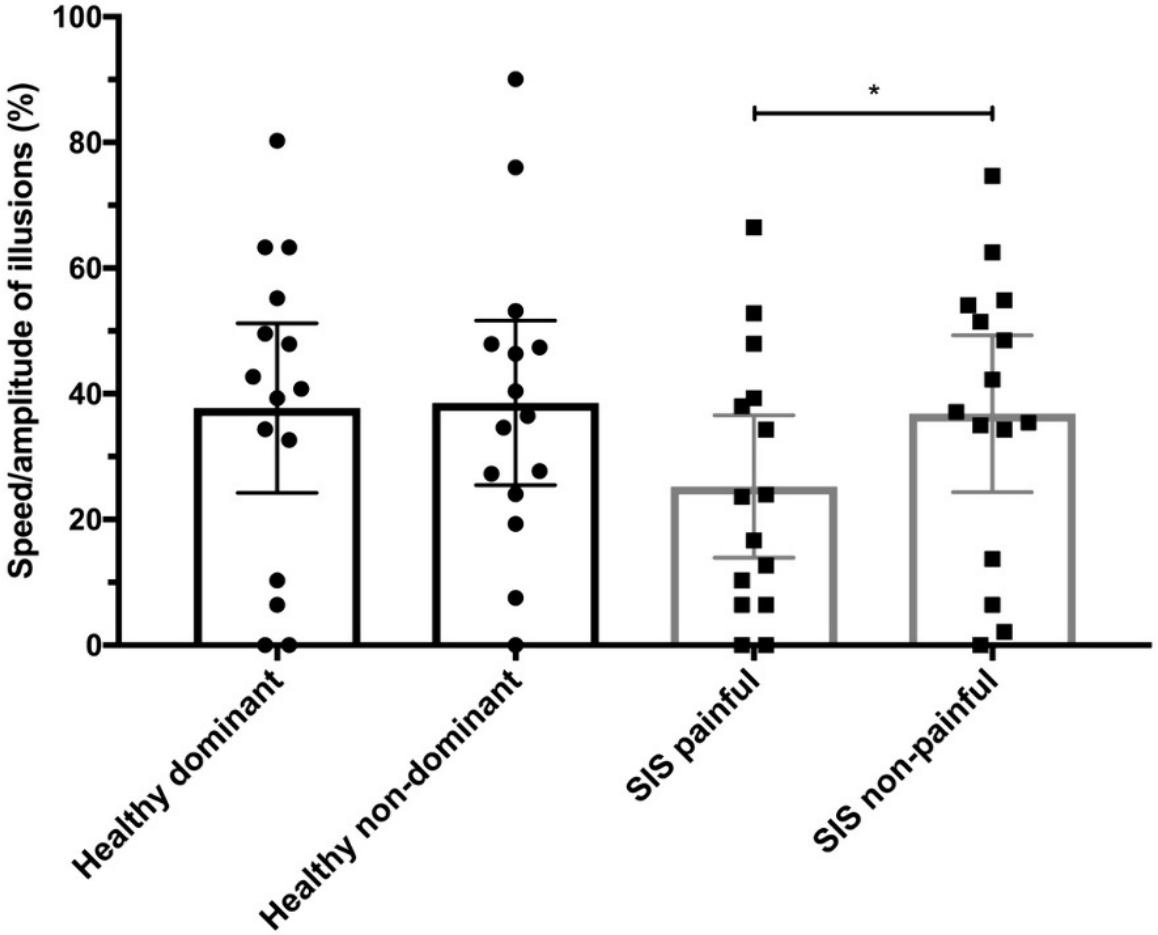


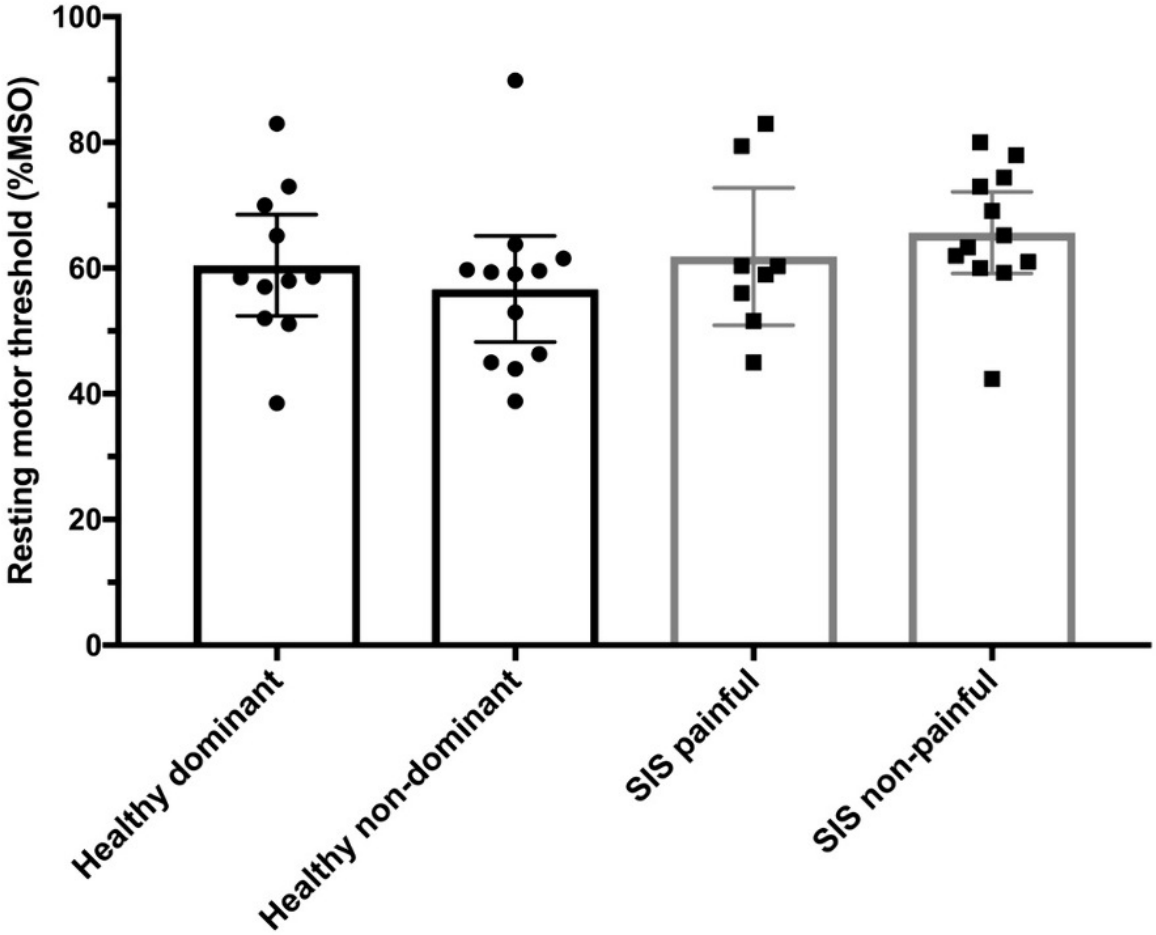
B



Results: Participants with SIS and controls reported similar VIB-induced illusions in terms of clearness, direction and success rate. However, they showed significantly lower speed/amplitude on the painful versus non-painful side in participants with SIS ($p = 0.035$). No difference was found for

TMS data, but procedures were challenged by high motor thresholds, discomfort and fear of pain, especially in participants with
SIS.


Speed/amplitude of illusions (%)
100
80
60
40
20
0
*
Healthy dominant
Healthy non-dominant
SIS painful
SIS non-painful



Discussion: The lower speed/amplitude of illusions obtained on the painful side in our study might be implying a less effective, but still functional processing of muscle spindles afferents. Pain and non-use of affected limbs can have a profound impact on distributed neural networks involved in perceptual, cognitive/emotional and motor functions. A lower corticospinal function of key muscles involved in shoulder control could be linked to pain-induced maladaptive plasticity, fear-avoidance mechanisms and limb non-use. The pairing of VIB and TMS technologies thus appear complementary for a specific investigation of mechanisms underlying sensory (VIB) and motor (TMS) impairments.

Conclusions: Our study provides novel evidence on the integrity of proprioceptive and corticospinal functions in persons living with SIS. Neurostimulation tools like VIB and TMS show promise to better understand mechanisms underlying sensorimotor dysfunctions in those populations, and even propose novel therapeutic methods that could specifically target these mechanisms.

Supplemental Data:

References: 1) Beaulieu, L.-D., Schneider, C., Massé-Alarie, H., & Ribot-Ciscar, E. (2020). A new method to elicit and measure movement illusions in stroke by means of muscle tendon vibration: the Standardized Kinesthetic Illusion Procedure (SKIP). *Somatosensory & motor research*, *37*(1), 28-36. doi: 10.1080/08990220.2020.1713739 2) Chung, Y. C., Chen, C. Y., Chang, C. M., Lin, Y. L., Liao, K. K., Lin, H. C., ... Shih, Y. F. (2022). Altered corticospinal excitability of scapular muscles in individuals with shoulder impingement syndrome. *PloS one*, *17*(5), e0268533. doi: 10.1371/journal.pone.0268533 3) de Oliveira, F. C. L., Bouyer, L. J., Ager, A. L., & Roy, J. S. (2017). Electromyographic analysis of rotator cuff muscles in patients with rotator cuff tendinopathy: A systematic review. *Journal of electromyography and kinesiology : official journal of the International Society of Electrophysiological Kinesiology*, *35*, 100-114. doi: 10.1016/j.jelekin.2017.06.002 4) Dubé, M.-O., Desmeules, F., Lewis, J., & Roy, J.-S. (2020). Rotator cuff-related shoulder pain: does the type of exercise influence the

outcomes? Protocol of a randomised controlled trial. *BMJ open*, *10*(11), e039976. doi: 10.1136/bmjopen-2020-039976 5) Dubé, M.-O., Desmeules, F., Lewis, J. S., & Roy, J.-S. (2023). Does the addition of motor control or strengthening exercises to education result in better outcomes for rotator cuff-related shoulder pain? A multiarm randomised controlled trial. *British Journal of Sports Medicine*. 6) Ager, A. L., Borms, D., Deschepper, L., Dhooghe, R., Dijkhuis, J., Roy, J. S., & Cools, A. (2020b). Proprioception: How is it affected by shoulder pain? A systematic review. *Journal of hand therapy : official journal of the American Society of Hand Therapists*, *33*(4), 507-516. doi: 10.1016/j.jht.2019.06.002 7) Lewis, J. S., Wright, C., & Green, A. (2005). Subacromial impingement syndrome: the effect of changing posture on shoulder range of movement. *The Journal of orthopaedic and sports physical therapy*, *35*(2), 72-87. doi: 10.2519/jospt.2005.35.2.72 8) Ribot-Ciscar, E., Milhe-De Bovis, V., Aimonetti, J.-M., Lapeyssonnie, B., Campana-Salort, E., Pouget, J., & Attarian, S. (2015). Functional impact of vibratory proprioceptive assistance in patients with facioscapulohumeral muscular dystrophy. *Muscle & nerve*, *52*(5), 780-787. doi: 10.1002/mus.24605 9) Ribot-Ciscar, E., Tréfouret, S., Aimonetti, J.-M., Attarian, S., Pouget, J., & Roll, J.-P. (2004). Is muscle spindle proprioceptive function spared in muscular dystrophies? A muscle tendon vibration study. *Muscle & Nerve*, *29*(6), 861-866. doi: 10.1002/mus.20044 10) Umer, M., Qadir, I., & Azam, M. (2012). Subacromial impingement syndrome. *Orthopedic reviews*, *4*(2), e18. doi: 10.4081/or.2012.e18 11) Roll, J. P., Vedel, J. P., & Ribot, E. (1989). Alteration of proprioceptive messages induced by tendon vibration in man: a microneurographic study. *Experimental brain research*, *76*(1), 213-222. 12) Michener, L. A., Walsworth, M. K., Doukas, W. C., & Murphy, K. P. (2009). Reliability and diagnostic accuracy of 5 physical examination tests and combination of tests for subacromial impingement. *Archives of physical medicine and rehabilitation*, *90*(11), 1898-1903. doi: 10.1016/j.apmr.2009.05.015

Acknowledgements: The authors would like to thank all the participants who took part in our study. This work was supported by the *Quebec Pain Research Network* [Stimulus grant 2020-21]. LDB research program is supported by the *Fonds de Recherche du Québec – Santé* (Research Scholar Junior 1; #297854, https://frq.gouv.qc.ca).

Learning Objectives: 1) VIB-induced illusions had lower speed/amplitude on the painful vs. non-painful side; testing proprioception exercices in research and in clinic should be made. 2) Since VIB-induced illusions without pain, using this sensory-based evaluative and treatment tool with SIS should be investigated and tested; 3) TMS was challenged by high thresholds and fear of pain, especially in SIS group, further work to determine the best methodological procedures for increasing the relevance and success-rate of TMS when testing populations suffering from musculoskeletal pain and disabilities

Financial Disclosures: 'No significant relationships'.

Disclosure: No significant relationships.

349

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

PERCUTANEOUS LEFT STELLATE GANGLION BLOCK FOR THE ACUTE MANAGEMENT OF SUPRAVENTRICULAR ARRHYTHMIAS

Arianna Morena, MD[1], Simone Frea, MD[1], Filippo Angelini, MD[1], Carol Gravinese, MD[1], Pier Paolo Bocchino, MD[1], Paolo Boretto, MD[1], Francesco Bruno, MD[1], Andrea Saglietto, MD[1], Guglielmo Gallone, MD[1,2], Giulia De Lio, MD[1], Antonio Toscano, MD[3], Jacopo Forni, MD[2], Mario Giordano, MD[2], Gianluca Lomartire, MD[2], Giuseppe Giannino, MD[2], Federico Ferraris, MD[1,2], Matteo Anselmino, MD[1,2], Gaetano Maria De Ferrari, MD[1,2], Veronica Dusi, MD, PhD[1,2]
[1]Città della Salute e della Scienza, Division Of Cardiology, Cardiovascular And Thoracic Department, turin, Italy, [2]University of Turin, Cardiology, Department Of Medical Sciences, Turin, Italy, [3]Città della salute e della scienza, Department Of Anesthesia, Critical Care And Emergency, turin, Italy

Introduction: Percutaneous left stellate ganglion block (PLSGB) has recently gained a role for the acute treatment of refractory ventricular arrhythmias (VAs). Its beneficial effect on supraventricular arrhythmias (SVAs) is well characterized in animal models, less in humans.

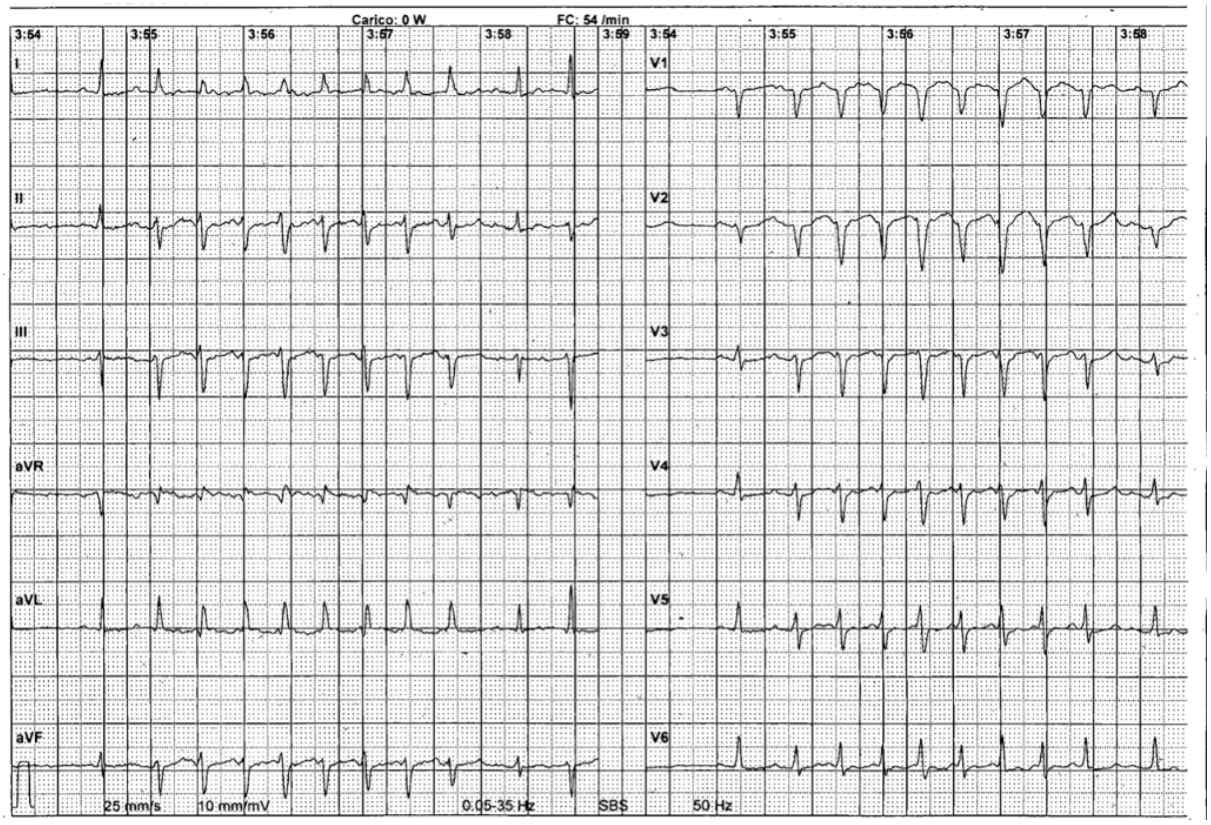
Materials / Methods: We present two paradigmatic cases of PLSGB used for the acute management of SVAs: a drug-refractory focal atrial tachycardia (AT) and an atrial fibrillation (AF) with rapid ventricular response in the setting of acute decompensated heart failure (ADHF).

Results: Patient 1 was a 68-year-old man with hypokinetic ischemic cardiomyopathy (ICM) who presented to the emergency department (ED) for palpitations and worsening dyspnea due to an ectopic AT with a 1:1 atrioventricular (AV) conduction with heart rate (HR) up to 160 bpm and runs of non-sustained VAs (maximum 8 beats). Amiodarone, lidocaine, and intravenous (iv) unloading therapy were tried, without benefits on heart rhythm, so, awaiting catheter ablation, PLSGB with an ultrasound-guided lateral approach (lidocaine 100 mg + ropivacaine 20 mg) was performed. Over the next 15 hours a progressive reduction of the AT burden, of the mean hourly HR (from 84 to 50 bpm, -40%) and of the mean HR during AT (from 158 to 84 bpm, -47%) were observed. Also non-sustained VAs disappeared. Patient 2 was a 72-years-old man with severe hypokinetic ICM, persistent AF and multiple previous hospitalizations for biventricular HF. He presented to the ED with rapid response AF and ADHF with a septic component. Intravenous treatment with diuretic, antibiotics and vasodilators was started, combined to inotropic support with dobutamine and milrinone, which worsened the ventricular penetrance of AF despite Amiodarone iv; PLSGB (lidocaine 100 mg + ropivacaine 100 mg) determined a progressive reduction of the mean HR during AF (from 140 to 105 bpm, -25%) in the following 6 hours despite ongoing inotropes, resulting in hemodynamic stabilization.

Discussion: Stellate ganglia do not only modulate ventricular but also supraventricular and nodal electrical activity, with an asymmetrical distribution on the nodal structures (Left stellate ganglion has a larger control on the AV node). Small clinical trials suggest a significant prolongation of atrial refractory period, a reduction of AF inducibility and duration and of intra- and postoperative atrial arrhythmias in cardiothoracic surgery (1, 2, 3); the presented clinical cases highlight these effects in the acute setting.

Conclusions: PLSGB may be effective in the acute treatment of drug refractory SVAs either by suppressing/reducing them, or by reducing AV node conduction. More data needed.

Supplemental Data:



References: (1) Leftheriotis D, Flevari P, Kossyvakis C, Katsaras D, Batistaki C, Arvaniti C, Giannopoulos G, Deftereos S, Kostopanagiotou G, Lekakis J. Acute effects of unilateral temporary stellate ganglion block on human atrial electrophysiological properties and atrial fibrillation inducibility. Heart Rhythm. 2016 Nov;13(11):2111-2117. doi: 10.1016/j.hrthm.2016.06.025. Epub 2016 Jun 21. PMID: 27353237. (2) Connors CW, Craig WY, Buchanan SA, Poltak JM, Gagnon JB, Curry CS. Efficacy and Efficiency of Perioperative Stellate Ganglion Blocks in Cardiac Surgery: A Pilot Study. J Cardiothorac Vasc Anesth. 2018 Feb;32(1):e28-e30. doi: 10.1053/j.jvca.2017.10.025. Epub 2017 Oct 20. PMID: 29162313. (3) Wu CN, Wu XH, Yu DN, Ma WH, Shen CH, Cao Y. A single-dose of stellate ganglion block for the prevention of postoperative dysrhythmias in patients undergoing thoracoscopic surgery for cancer: A randomised controlled double-blind trial. Eur J Anaesthesiol. 2020 Apr;37(4):323-331. doi: 10.1097/EJA.0000000000001137. PMID: 31860606.

Acknowledgements:

Learning Objectives: 1. Cardiac sympathetic ganglia modulate electophysiology and arrhythmogenesis not only at the ventricular level but also at the atrial and nodal level with asymmetric distribution particularly on nodal structures. 2. PLSGB may be effective in the acute treatment of supraventricular arrhythmias refractory to medical therapy (either by suppressing them and/or by reducing AV node conduction). 3. Very preliminary data are available in the prevention of intra- and postoperative supraventricular arrhythmias, further studies needed.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

350

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

CONTINUOUS STELLATE GANGLION BLOCK FOR VENTRICULAR ARRHYTHMIAS: SINGLE CENTER EXPERIENCE, SYSTEMATIC REVIEW, AND COMPARISON WITH EPIDURAL ANAESTHESIA

Arianna Morena, MD[1,2], Filippo Angelini, MD[2], Antonio Toscano, MD[3], Carol Gravinese, MD[2], Simone Frea, MD[2], Pier Paolo Bocchino, MD[2], Paolo Boretto, MD[2], Guglielmo Gallone, MD[1,2], Giulia De Lio, MD[2], Andrea Saglietto, MD[1,2], Matteo Giunta, MD[3], Andrea Costamagna, MD[4], Luca Brazzi, MD[4], Mauro Rinaldi, MD[4], Matteo Anselmino, MD[1,2], Gaetano Maria De Ferrari, MD[1,2], Veronica Dusi, MD, PhD[1,2]
[1]University of Turin, Cardiology, Department Of Medical Sciences, Turin, Italy, [2]Città della Salute e della Scienza, Division Of Cardiology, Cardiovascular And Thoracic Department, turin, Italy, [3]Città della salute e della scienza, Department Of Anesthesia, Critical Care And Emergency, turin, Italy, [4]Univerisy of Turin, Department Of Surgical Sciences, Turin, Italy

Introduction: Percutaneous single bolus injection left stellate ganglion block (PLSGB) and thoracic epidural anaesthesia from T1 to T4 (TEA) have been proposed for the acute management of refractory ventricular arrhythmias (VAs). Data on continuous PLSGB (C-PLSGB) are scant.

Materials / Methods: Consecutive patients receiving C-PLSGB at our center were enrolled. Data was collected from medical and ICD records. The study was approved by the local IRB. The systematic literature review was performed following the latest PRISMA criteria; 17 papers were submitted to the systematic review. A complete response was defined as no more episodes of sustained or treated VA, while a partial response was qualitatively defined as VA reduction allowing for patient's acute stabilization.

Results: Our single-center case series (15 pts, 93% male, 59 ±18 years, all with structural heart disease, mean left ventricular ejection fraction 22 ± 8%), supports that C-PLSGB is feasible and safe, even on fully anticoagulated patients (9/15, 60%) and leads to a complete VAs suppression in many of them (60%) and to a clinical benefit (partial response) in all. Most of our patients (73%) presented with monomorphic VT (MMVT), none with incessant VT. Overall, considering previously published data, 52 patients received C-PLSGB (96% with ultrasound guided lateral approach), and 18 TEA for refractoryVAs. Most (11/18, 61%) in the TEA group were intubated and on general anesthesia, as opposed to 17/52 (33%) in the C-PLSGB group ($p=0.05$); 50% of patients were on full anticoagulation at C-PLSGB, none at TEA ($p<0.01$). The prevalence of MMVT was similar between C-PLSGB and TEA (66% vs 56%, $p=0.56$), as opposed to that of incessant VT (0% vs 39%, respectively, $p<0.01$). Finally, C-PLSGB efficacy was significantly higher compared to TEA: 48/52 pts (92%) had a complete or at least partial response after C-PLSGB, compared to 13/18 (72%) after TEA ($p=0.04$). No major complications occurred, yet the discontinuation rate was significantly higher in the TEA compared to C-PLSGB (22% versus 2%, $p=0.03$).

Discussion: The aims of the present study are to report our single center experience with C-PLSGB and to perform a systematic review on C-PLSGB and TEA in order to preliminary compare these 2 techniques. Based on our results C-PLSGB seems feasible, safe and effective for the acute management of refractory VAs (92% of the patients did not require additional urgent antiarrhythmic strategies).

Conclusions: C-PLSGB efficacy seems even higher than TEA and may be accomplished with less concerns of anticoagulation, and lower discontinuation rate.

Supplemental Data:

References: none

Acknowledgements:

Learning Objectives: 1. C-PLSGB seems feasible, safe and effective for the acute management of refractory VAs. 2. C-PLSGB efficacy seems even higher than TEA and may be accomplished with less concerns of anticoagulation, and lower discontinuation rate. 3. More clinical data needed.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

351

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

MULTIFIDUS ATROPHY AND DYSFUNCTION FOLLOWING LUMBAR RADIOFREQUENCY ABLATION: A SYSTEMATIC REVIEW.

Vinny Francio, MD, MS[1], Michael Glicksman, MD[2], Logan Leavitt, MD[3], Benjamin Gill, DO[4], Anuj Shah, DO[5], Benjamin Westerhaus, MD[6], Christopher Lam, MD[1], Ryan D'Souza, MD[7]
[1]University of Kansas, Dept Anesthesiology And Pain Medicine, Kansas City, United States of America, [2]UPMC, Pm&r, Pittsburgh, United States of America, [3]University of Kansas, Pm&r, Kansas City, United States of America, [4]University of Utah, Anesthesiology, Salt Lake City, United States of America, [5]Detroit Medical Center, Pm&r, Detroit, United States of America, [6]Cantor Spine Center at the Paley Institute, Interventional Spine, West Palm Beach, United States of America, [7]Mayo Clinic, Department Of Anesthesiology, Rochester, United States of America

Introduction: Lumbar medial branch radiofrequency ablation/neurotomy (LRFA) is an effective interventional procedure that may be used to treat axial chronic low back pain (CLBP) of lumbar facet joint etiology. Because the lumbar medial branch nerves (LMBN) also innervate the multifidus muscle, LRFA may pose a risk of multifidus atrophy and/or dysfunction, although this association remains unclear. Therefore, a systematic review of the available literature was performed to elucidate this long-standing concern regarding the functional impact of LRFA on the multifidus muscle.

Materials / Methods: A systematic review was performed with an *a priori* registered protocol and compliant with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The primary outcome of this review was to evaluate the presence of multifidus atrophy and/or dysfunction as determined by diagnostic imaging or electromyography (EMG) following LRFA. Evaluation of the study quality adhered to the Newcastle–Ottawa-Quality-Assessment-Scale (NOS), the Grading-Recommendations-Assessment-Development-Evaluation (GRADE) criteria.

Results: Of 1565 studies that were screened for eligibility, only five cohort studies (two retrospective and three prospective) assessed LFRA and multifidus muscle atrophy and/or dysfunction. There was presence of high bias in the comparability domain per the NOS criteria (Table 1). No study has evaluated the significance of repeat LRFA on multifidus function, atrophy or LMBN recovery. Our review found very limited and low-quality GRADE evidence discussing this topic (Table 2). There are three-level 1B and two-level IC studies with a very low level of certainty to support a relationship between LRFA and subsequent multifidus atrophy/dysfunction.

Discussion: Significant reduction in shear modulus in certain postures following LRFA has been documented and is suggestive of multifidus dysfunction. Studies assessing fat-subtracted multifidus cross-sectional areas with MRI and EMG demonstrated varying levels of multifidus atrophy but did not reach statistical significance. Given the destructive nature of LRFA and the subsequent inherent denervation muscle segments, some degree of multifidus atrophy and/or dysfunction is plausible.

Conclusions: This is the first study to systematically review the current literature on multifidus atrophy and/or dysfunction following LRFA. The paucity of literature on this topic is substantial and further restricted by small sample sized, absence of control groups or covariate analyses, and lack of blinding. However, given the confirmed electromyographic and diagnostic imaging findings from these observational studies, some multifidus atrophy and/or dysfunction is plausible. This review emphasizes the lack of standardization in evaluation of multifidus atrophy and/or dysfunction following LRFA and highlights the need for high-quality prospective studies to clarify its relevance in clinical practice.

Supplemental Data:

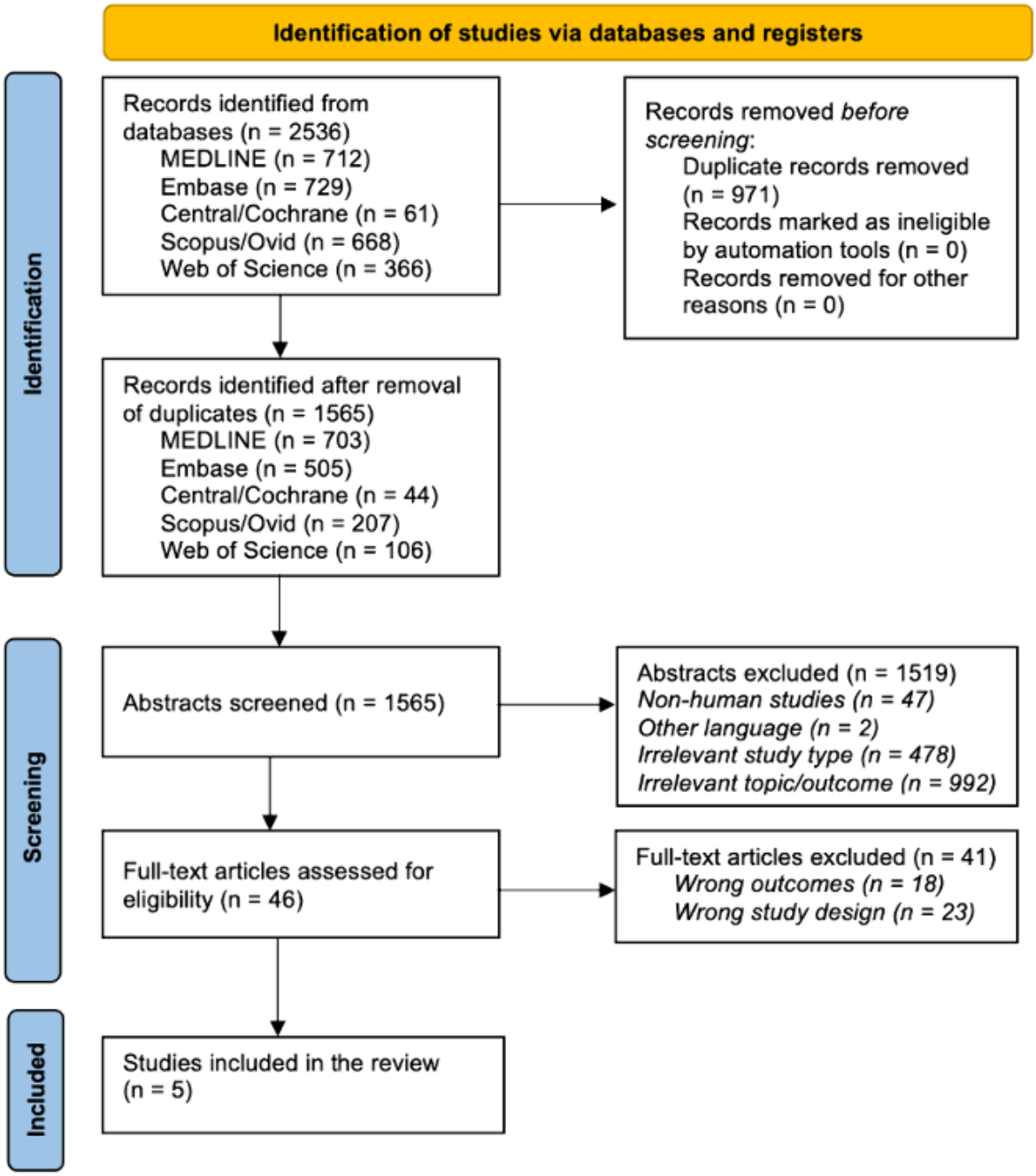


Figure 1: PRISMA diagram. Flow chart for study selection process including identification of studies from multiple databases and sources, screening process, assessment of eligibility and final study inclusion. PRISMA, Preferred Report Items for Systematic Reviews and Meta-Analyses.

Table 1. Cohort Study Quality Rating using the Newcastle-Ottawa scale (NOS), which evaluates three categories: selection (maximum 4 stars), comparability (maximum 2 stars), and outcome (maximum 3 stars).

Author	Year	Selection	Comparability	Exposure/ Outcome
Oswald *et al.*	2023	****	*	**
Böning *et al.*	2021	***	–	**
Sadeghi *et al.*	2020	**	**	**
Smuck *et al.*	2013	****	**	**
Dreyfuss *et al.*	2009	**	–	***

Table 2. Overall Quality of Evidence per the Grading of Recommendations Assessment, Development, and Evaluation (GRADE). The GRADE assessment uses standard criteria to evaluate the certainty of evidence as being of very low, low, moderate, and high utilizing the GRADEpro software (Evidence Prime).[29]

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	lumbar medial branch RFA	control	Relative (95% CI)	Absolute (95% CI)	
Multifidus dysfunction											
5	observational studies	very serious[a]	very serious[b]	very serious[c]	serious[d]	all plausible residual confounding would suggest spurious effect, while no effect was observed	-/115	-/59	not pooled	see comment	⊕◯◯◯ Very low

a. Oswald *et al.*, Sadeghi *et al.*, and Smuck *et al.* included control groups, however Oswald *et al.* only used a control group for those undergoing unilateral RFA (9/20 total participants). Only Dreyfuss *et al.* explicitly mentioned that there was blinding in the study. Smuck *et al.* and Böning *et al.* were retrospective cohort studies and all 5 studies had small sample sizes.
b. None of the studies evaluated multifidus dysfunction in an identical manner. Oswald *et al.* measured intramuscular fat volume of the multifidus muscle via semi-automatic analysis, Böning *et al.* assessed multifidus muscle volume via manual measurements, Sadeghi *et al.* implemented SWE to evaluate multifidus dysfunction at the middle level, Smuck *et al.* measured fat-subtracted multifidus cross-sectional area, and Dreyfuss *et al.* evaluated the ability of neuromuscular radiologists to correctly identify perceived atrophy of segmental multifidus muscle.
c. Only Dreyfuss *et al.* included physiologic evaluation of multifidus dysfunction with EMG. All other studies used indirect surrogates to evaluate multifidus dysfunction.
d. Only Oswald *et al.* provided a confidence interval in describing multifidus dysfunction following LRFA.

References: GBD 2021 Low Back Pain Collaborators. Global, regional, and national burden of low back pain, 1990-2020, its attributable risk factors, and projections to 2050: a systematic analysis of the Global Burden of Disease Study 2021. Lancet Rheumatol. 2023;5(6):e316-e329. Published 2023 May 22. doi:10.1016/S2665-9913(23)00098 Manchikanti L, Manchikanti KN, Cash KA, Singh V, Giordano J. Age-related prevalence of facet-joint involvement in chronic neck and low back pain. Pain Physician. 2008;11(1):67-75. Sayed D, Grider J, Strand N, Hagedorn JM, Falowski S, Lam CM, Tieppo Francio V, Beall DP, Tomycz ND, Davanzo JR, Aiyer R, Lee DW, Kalia H, Sheen S, Malinowski MN, Verdolin M, Vodapally S, Carayannopoulos A, Jain S, Azeem N, Tolba R, Chang Chien GC, Ghosh P, Mazzola AJ, Amirdelfan K, Chakravarthy K, Petersen E, Schatman ME, Deer T. The American Society of Pain and Neuroscience (ASPN) Evidence-Based Clinical Guideline of Interventional Treatments for Low Back Pain. J Pain Res. 2022 Dec 6;15:3729-3832. doi: 10.2147/JPR.S386879. Erratum in: J Pain Res. 2022 Dec 24;15:4075-4076. PMID: 36510616; PMCID: PMC9739111. Binder DS, Nampiaparampil DE. The provocative lumbar facet joint. Curr Rev Musculoskelet Med. 2009;2(1):15-24. doi:10.1007/s12178-008-9039-y Tran J, Peng P, Loh E. Anatomical study of the medial branches of the lumbar dorsal rami: implications for image-guided intervention. Reg Anesth Pain Med. 2022 May 19:rapm-2022-103653. doi: 10.1136/rapm-2022-103653. Epub ahead of print. PMID: 35589133. Lee DW, Pritzlaff S, Jung MJ, et al. Latest Evidence-Based Application for Radiofrequency Neurotomy (LEARN): Best Practice Guidelines from the American Society of Pain and Neuroscience (ASPN). J Pain Res. 2021;14:2807-2831. Published 2021 Sep 8. doi:10.2147/JPR.S325665 Tieppo Francio V, Westerhaus BD, Rupp A, Sayed D. Non-Spinal Neuromodulation of the Lumbar Medial Branch Nerve for Chronic Axial Low Back Pain: A Narrative Review. Front Pain Res (Lausanne). 2022 Feb 25;3:835519. doi: 10.3389/fpain.2022.835519. PMID: 35295793; PMCID: PMC8915554. Perolat R, Kastler A, Nicot B, et al. Facet joint syndrome: from diagnosis to interventional management. Insights Imaging. 2018;9(5):773-789. doi:10.1007/s13244-018-0638-x Shuang F, Hou SX, Zhu JL, et al. Clinical Anatomy and Measurement of the Medial Branch of the Spinal Dorsal Ramus. Medicine (Baltimore). 2015;94(52):e2367. doi:10.1097/MD.0000000000002367 Cohen SP, Bhaskar A, Bhatia A, et al. Consensus practice guidelines on interventions for lumbar facet joint pain from a multispecialty, international working group. Reg Anesth Pain Med. 2020;45(6):424-467. doi:10.1136/rapm-2019-101243 Russo MA, Santarelli DM. Development and Description of a New Multifidus-Sparing Radiofrequency Neurotomy Technique for Facet Joint Pain. Pain Pract. 2021;21(7):747-758. doi:10.1111/papr.13010 Wang K, Deng Z, Chen X, et al. The Role of Multifidus in the Biomechanics of Lumbar Spine: A Musculoskeletal Modeling Study. Bioengineering (Basel). 2023;10(1):67. Published 2023 Jan 4. doi:10.3390/bioengineering10010067 Kim CW, Gottschalk LJ, Eng C, et al. The multifidus muscle is the strongest stabilizer of the lumbar spine. Spine J. 2007;7(5):76S. Freeman MD, Woodham MA, Woodham AW. The role of the lumbar multifidus in chronic low back pain: a review. PM R. 2010;2(2):142-167. doi:10.1016/j.pmrj.2009.11.006 Tieppo Francio V, Westerhaus BD, Carayannopoulos AG, Sayed D. Multifidus Dysfunction and Restorative Neurostimulation: A Scoping Review. Pain Med. 2023 Jul 13:pnad098. doi: 10.1093/pm/pnad098. Epub ahead of print. PMID: 37439698. Seyedhoseinpoor T, Taghipour M, Dadgoo M, et al. Alteration of lumbar muscle morphology and composition in relation to low back pain: a systematic review and meta-analysis. Spine J. 2022;22(4):660-676. doi:10.1016/j.spinee.2021.10.018 Gabel CP, Mokhtarinia HR, Melloh M. The Politics of Chronic LBP: Can We Rely on a Proxy-Vote? Linking Multifidus Intra-Myo-Cellular Lipid (IMCL) Fatty Infiltration With Arthrogenic Muscle Inhibition (AMI)-induced Chronic Nonspecific Low Back Pain. Spine (Phila Pa 1976). 2021 Jan 15;46(2):129-130. doi: 10.1097/BRS.0000000000003758. PMID: 33079906. Hides J, Gilmore C, Stanton W, Bohlscheid E.

Multifidus size and symmetry among chronic LBP and healthy asymptomatic subjects. Man Ther. 2008 Feb;13(1):43-9. doi: 10.1016/j.math.2006.07.017. Epub 2006 Oct 27. PMID: 17070721. Cooley JR, Jensen TS, Kjaer P, Jacques A, Theroux J, Hebert JJ. Spinal degeneration is associated with lumbar multifidus morphology in secondary care patients with low back or leg pain. Sci Rep. 2022 Aug 29;12(1):14676. doi: 10.1038/s41598-022-18984-1. PMID: 36038653; PMCID: PMC9424282. Jun HS, Kim JH, Ahn JH, Chang IB, Song JH, Kim TH, Park MS, Chan Kim Y, Kim SW, Oh JK, Yoon DH. The Effect of Lumbar Spinal Muscle on Spinal Sagittal Alignment: Evaluating Muscle Quantity and Quality. Neurosurgery. 2016 Dec;79(6):847-855. doi: 10.1227/NEU.0000000000001269. PMID: 27244469. Kalichman L, Klindukhov A, Li L, Linov L. Indices of Paraspinal Muscles Degeneration: Reliability and Association With Facet Joint Osteoarthritis: Feasibility Study. Clin Spine Surg. 2016 Nov;29(9):465-470. doi: 10.1097/BSD.0b013e31828be943. PMID: 27137159. Starr JB, Gold L, McCormick Z, Suri P, Friedly J. Trends in lumbar radiofrequency ablation utilization from 2007 to 2016. Spine J. 2019;19(6):1019-1028. doi:10.1016/j.spinee.2019.01.001 Mann SJ, Viswanath O, Singh P. Lumbar Facet Arthropathy. [Updated 2023 Jul 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Dieleman JL, Baral R, Birger M, et al. US Spending on Personal Health Care and Public Health, 1996-2013. JAMA. 2016;316(24):2627-2646. doi:10.1001/jama.2016.16885 Page MJ, Shamseer L, Tricco AC. Registration of systematic reviews in prospero:
30,000 records and counting. Syst Rev 2018;7:32. Page MJ, McKenzie JE, Bossuyt PM, et al. The prisma 2020 statement: an updated
guideline for reporting systematic reviews. BMJ 2021;372:n71. Bramer WM, Giustini D, de Jonge GB, Holland L, Bekhuis T. De-duplication of database search results for systematic reviews in EndNote [published correction appears in J Med Libr Assoc. 2017 Jan;105(1):111]. *J Med Libr Assoc*. 2016;104(3):240-243. doi:10.3163/1536-5050.104.3.014 Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Feb 2009. Kavanagh BP. The grade system for rating clinical guidelines. PLoS Med. 2009;6:e1000094. Oswald KAC, Ekengele V, Hoppe S, Streitberger K, Harnik M, Albers CE. Radiofrequency Neurotomy Does Not Cause Fatty Degeneration of the Lumbar Paraspinal Musculature in Patients with Chronic Lumbar Pain-A Retrospective 3D-Computer-Assisted MRI Analysis Using iSix Software. Pain Med. 2023 Jan 4;24(1):25-31. doi: 10.1093/pm/pnac103. PMID: 35775938. Böning G, Hartwig T, Freyhardt P, de Bucourt M, Teichgräber U, Streitparth F. MR-guided lumbar facet radiofrequency denervation for treatment of patients with chronic low back pain in an open 1.0 Tesla MRI system. Ann Transl Med. 2021 Jul;9(13):1056. doi: 10.21037/atm-21-633. PMID: 34422968; PMCID: PMC8339805. Sadeghi S, Bible JE, Cortes DH. Quantifying Dysfunction of the Lumbar Multifidus Muscle After Radiofrequency Neurotomy and Fusion Surgery: A Preliminary Study. J Eng Sci Med Diagn Ther. 2020 Nov 1;3(4):041001. doi: 10.1115/1.4047651. Epub 2020 Jul 13. PMID: 35832607; PMCID: PMC8597558. Smuck M, Crisostomo RA, Demirjian R, Fitch DS, Kennedy DJ, Geisser ME. Morphologic changes in the lumbar spine after lumbar medial branch radiofrequency neurotomy: a quantitative radiological study. Spine J. 2015 Jun 1;15(6):1415-21. doi: 10.1016/j.spinee.2013.06.096. Epub 2013 Nov 14. PMID: 24239488. Dreyfuss P, Stout A, Aprill C, Pollei S, Johnson B, Bogduk N. The significance of multifidus atrophy after successful radiofrequency neurotomy for low back pain. PM R. 2009 Aug;1(8):719-22. doi: 10.1016/j.pmrj.2009.05.014. PMID: 19695523. Shamsrizi P, Gladstone BP, Carrara E, Luise D, Cona A, Bovo C, Tacconelli E. Variation of effect estimates in the analysis of mortality and length of hospital stay in patients with infections caused by bacteria-producing extended-spectrum beta-lactamases: a systematic review and meta-analysis. BMJ Open. 2020 Jan 20;10(1):e030266. doi: 10.1136/bmjopen-2019-030266. PMID: 31964661; PMCID: PMC7044956. Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, Atkins D, for the Methods Work Group, Third U.S. Preventive Services Task Force. A review of the process. Am J Prev Med 2001;20:21-35. Hansen L, de Zee M, Rasmussen J, et al. Anatomy and biomechanics of the back muscles in the lumbar spine with reference to biomechanical modeling. Spine (Phila Pa 1976). 2006;31(17):1888–1899. Wu PBJ, Date ES, Kingery WS. The lumbar multifidus muscle is polysegmentally innervated. Electromyog Clin Neurophysiol. 2000;40(8):483–485. Hildebrandt M, Fankhauser G, Meichtry A, Luomajoki H. Correlation between lumbar dysfunction and fat infiltration in lumbar multifidus muscle in patients with low back pain. BMC Musculoskelet Disord. 2017;18(1):12. Hodges PW, James G, Blomster L, et al. Multifidus muscle changes after back injury are characterized by structural remodeling of muscle, adipose and connective tissue, but not muscle atrophy: molecular and morphological evidence. Spine. 2015;40(14):1057–1071. Jul 15. Goubert D, Oosterwijck JV, Meeus M, et al. Structural Changes of lumbar muscles in non-specific low back pain: a systematic review. Pain Physician. 2016;19(7):E985–E1000. Goubert D, De Pauw R, Meeus M, et al. Lumbar muscle structure and function in chronic versus recurrent low back pain: a cross-sectional study. Spine J. 2017;17(9):1285–1296. Fortin M, Lazáry À, Varga PP, et al.

Association between paraspinal muscle morphology, clinical symptoms, and functional status in patients with lumbar spinal stenosis. Eur Spine J. 2017;26(10):2543–2551. Hodges PW, Danneels L. Changes in structure and function of the back muscles in low back pain: different time points. Observations and mechanisms. J Ortho Sports Phys Ther. 2019;6:464–473. MacDonald D, Moseley LG, Hodges PW. Why do some patients keep hurting their back? Evidence of ongoing back muscle dysfunction during remission from recurrent back pain. Pain. 2009;142(3):183–188. Macintosh JE, Valencia F, Bogduk N, Munro RR. The morphology of the human lumbar multifidus. Clin Biomech (Bristol, Avon). 1986 Nov;1(4):196-204. doi: 10.1016/0268-0033(86)90146-4. PMID: 23915550. Kalichman L, Carmeli E, Been E. The association between imaging parameters of the paraspinal muscles, spinal degeneration, and low back pain. Biomed Res Int. 2017;2017:2562957. Almalki FA, Cortes DH. Multifidus Denervation After Radiofrequency Ablation of the Medial Nerve Alters the Biomechanics of the Spine-A Computational Study. J Appl Biomech. 2023 Aug 29:1-7. doi: 10.1123/jab.2022-0258. Epub ahead of print. PMID: 37643753. Cooley JR, Jensen TS, Kjaer P, Jacques A, Theroux J, Hebert JJ. Spinal degeneration is associated with lumbar multifidus morphology in secondary care patients with low back or leg pain. Sci Rep. 2022 Aug 29;12(1):14676. doi: 10.1038/s41598-022-18984-1. PMID: 36038653; PMCID: PMC9424282. Cooley JR, Kjaer P, Jensen TS, Jacques A, Theroux J, Hebert JJ. Lumbar multifidus muscle morphology is associated with low back-related pain duration, disability, and leg pain: A cross-sectional study in secondary care. PLoS One. 2023 Jun 2;18(6):e0285993. doi: 10.1371/journal.pone.0285993. PMID: 37267391; PMCID: PMC10237427. Carlson BM. The Biology of Long-Term Denervated Skeletal Muscle. Eur J Transl Myol. 2014;24(1):3293. Published 2014 Mar 27. doi:10.4081/ejtm.2014.3293. McCormick ZL, Marshall B, Walker J, McCarthy R, Walega DR. Long-Term Function, Pain and Medication Use Outcomes of Radiofrequency Ablation for Lumbar Facet Syndrome. Int J Anesth Anesth. 2015;2(2):028. doi: 10.23937/2377-4630/2/2/1028. PMID: 26005713; PMCID: PMC4440581.

Acknowledgements: N/A

Learning Objectives: (1) To review the association between lumbar radiofreuency ablation/neurotomy (LRFA) and multifidus muscle atrophy and/or dysfunction. It has been proposed that denervation of the lumbar medial branch enrve may lead to multifidus atrophy and/or dysfunction, however there is presently no conclusive high-level evidence to support this claim. Therefore, this is the first review to systematically review this topic. (2) To discuss the current state of the literature and the paucity of published research that addresses whether LRFA leads to multifidus atrophy and/or dysfunction. Presently, no currently existing study has evaluated the significance of repeat LRFA on multifidus function, atrophy or lumbar medial branch nerve recovery. (3) To highlight the facts and myths regardign LRFA and multifidus atrophy/dysfunction based on the available literature. To date, there is electromyographic and diagnostic imaging evidence of multifidus atrophy and/or dysfunction at 6 months following LRFA. However statistical and clinical significance, and correlation with EMG findings has not been clearly established. These findings also emphasize the lack of standardization in evaluating multifidus atrophy and/or dysfunction following LRFA, and highlight the need for high-quality prospective studies to further evaluate this concern and its clinical relevance. Given the prevalence of LRFA, it is essential to further explore the relationship between LRFA and multifidus atrophy and/or dysfunction in chronic low back pain.

Financial Disclosures: VTF reports investigator-initiated grant funding from Nevro Corp. RDS reports investigator-initiated grant funding paid to institution from Nevro Corp and Saol Therapeutics. The other authors declare no conflicts of interest. The authors have no sources of funding to declare for this abstract.,

Disclosure: No significant relationships.

352

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

PULSED RADIOFREQUENCY TREATMENT FOR CHRONIC PAIN: REAL-WORLD OUTCOMES IN EUROPE

Fabrizio Cassini, MD[1], Felice Occhigrossi, MD[2], Isaac Peña, MD[3], Cleo Mertz, MSc[4], Lilly Chen, MD[4], Edward Goldberg, MD[4]
[1]Presidio Ospedale Civile Santi Antoni, Pain Unit, Alessandria, Italy, [2]San Giovanni - Addolorata Hospital, Pain Unit, Rome, Italy, [3]Hospital Virgen Del Rocio, Pain Unit, Seville, Spain, [4]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: Collection of real-world data can offer the aggregation of additional evidence and help drive discovery of new therapeuticaspects for evaluation in future clinical studies. In this report, we describe real- world outcomes from a cohort of patients whoreceived pulsed radiofrequency (PRF) as a treatment method for the treatment of chronic pain.

Materials / Methods: This is a real-world, retrospective, observational, case-series study of patients in Europe who used a device capable of pulsedradiofrequency (Boston Scientific, Marlborough, MA, USA) for treatment of chronic pain. Key data and clinical assessmentsinclude demographic characteristics, pain diagnosis, baseline and post-treatment pain scores, and percent pain relief.Institutional Review Board (IRB)-approved waivers of consent were obtained.

Results: To date, 69 patients who received PRF for treatment of chronic pain have been assessed. As measured immediately followingthe PRF procedure, NRS pain score was reduced to 4.1 from 8.1 (as assessed at baseline prior to procedure). At last follow-up(mean = 271.8 days), a significant 3.9-point improvement ($p < 0.0001$) in pain intensity (NRS) scores was documented.Additional data to be presented.

Discussion: While PRF is now a well-established therapeutic modality for chronic pain, periodic assessment of real-world patient data cancontribute to the overall compendium of existing evidence as well as spur the initiation of new clinical studies As such, in thisreport, we describe our assessment of outcomes from a European case series of patients who underwent a PRF procedure forthe treatment of chronic pain.

Conclusions: Preliminary data from this ongoing, European, multicenter, observational case series of 69 chronic pain patients (with no newonset of pain at follow up) who utilized PRF demonstrate significant improvement in pain scores at post procedure at last follow-up.

Supplemental Data:

Learning Objectives: To assess the following in patients utilizing pulsed radiofrequency:
1. mean baseline pain
2. NRS pain score at last follow-up
3. responder rate

Financial Disclosures: Dr. Occhigrossi has a consulting agreement with Boston Scientific. a) Boston Scientific b) consultant c) 1-5k

Disclosure: Study sponsored by Boston Scientific. Cleo Mertz, Lilly Chen, Edward Goldberg are employees of Boston Scientific.

353

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

HEADACHE AS A COMPLICATION OF THORACOLUMBAR HFSCS

Hemkumar Pushparaj, MD[1], Dr Manohar Sharma, FRCA FFPMRCA[2], Ramkumar Kalaiyarasan, MD FRCA[2], Alison Cox, RN[2], Kathryn Wilford, RN[2]
[1]WCFT, Pain Medicine, Liverpool, United Kingdom, [2]The Walton Centre NHS Foundation Trust, Liverpool, United Kingdom, Department Of Pain Medicine, Liverpool, United Kingdom

Introduction: Spinal cord stimulator [SCS] for chronic pain is a rapidly evolving field with proven long term benefit in various pathologies. Interaction of the device with the nervous system is still not fully understood. While newer programmes and service expansion makes SCS available everywhere, uncommon side effects will emerge. We present 2 cases of new onset headache after thoracolumbar High Frequency SCS [HFSCS] implantation which resolved after device deactivation.

Materials / Methods: We retrospectively extracted data of the 2 patients in our neuromodulation service with complaints of new onset headache after HFSCS implant. Patient demographics, pain history, other comorbidities, details on implant and post operative complications were extracted. Follow-up data were extracted. The cases are presented in a narrative format.

Results: A 50 y old computer businessman had HFSCS implant for post laminectomy pain in the right lower limb. There were no other comorbidities nor confounding factors. Post-implant he slowly started to lose analgesic efficacy of the implant. He also noted unpleasant twitching which started in his left eye to later spread to his face. A 55y old undertaker had HFSCS implant for left lower limb neuropathic pain in 2019. He also mentioned a declining benefit followed by new onset twitching and bloodshot in his left eye with associated headache. He switched off the device and found temporal association with these symptoms. In both the cases other causes were ruled out and the device was explanted after MDT discussion. Symptoms resolved completely in due course.

Discussion: In this case report we present treatment limiting but not life threatening complications after HFSCS. The onset was temporally related to activation of SCS. Long-term neuroplastic changes after HFSCS are not fully understood. Disturbance in the dorsal column pathway and vestibular system from the electrica interface may cause symptoms. Activation of PAG and dorsal raphe nucleus might contribute. Immunomodulation, minor allergic reaction might be causative as well.

Conclusions: The bio-electrical interface of SCS programmes is not fully understood yet. Many uncommon side effects are underreported. Headache and other non life-threatening side effects must be robustly reported and studied to find alternate waveforms which may be more acceptable in such patients.

Supplemental Data:

References: Golovlev AV, Hillegass MG. New Onset Tinnitus after High-Frequency Spinal Cord Stimulator Implantation. Case Rep Anesthesiol. 2019 May 2;2019 Christie C, Srivastava S, Richeimer SH. Headaches and neurological symptoms as a complication of spinal cord stimulator placement: a case report. Conference: 54th American Headache Society Annual Meeting. 2012 Jun; Vol 3

Acknowledgements:

Learning Objectives: 1. Interaction of SCS device and programmes with the CNS is not fully understood- more robust research needed 2. Uncommon sideeffcets might emerge as SCS is more widely available now- keen eye to report all side effects in a registry is must 3. Better waveforms might be needed in such population to be more compliant with therapy

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

354

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

SIGNIFICANT IMPROVEMENT IN PAIN OUTCOMES USING A DISPOSABLE ALL-IN-ONE RADIOFREQUENCY INJECTION ELECTRODE IN A MULTICENTER, OBSERVATIONAL EUROPEAN CASE-SERIES

Felice Occhigrossi, MD[1], Georgios Kyriakopoulos, MD[2], Fabrizio Cassini, MD[3], Isaac Peña, MD[4], David Abejón, MD[5], Jan Willem Kallewaard, MD[6], Lilly Chen, MD[7], Cleo Mertz, MSc[7], Edward Goldberg, MD[7]
[1]San Giovanni - Addolorata Hospital, Pain Unit, Rome, Italy, [2]St. Marien Hospital Hamm, Pain Unit, Hamm, Germany, [3]Presidio Ospedale Civile Santi Antoni, Pain Unit, Alessandria, Italy, [4]Hospital Virgen Del Rocio, Pain Unit, Seville, Spain, [5]University Hospital Quirónsalud, Pain Management, Madrid, Spain, [6]Amsterdam university centre, Anesthesiology And Pain Management, Arnhem, Netherlands, [7]Boston Scientific Neuromodulation, Clinical, Valencia, United States of America

Introduction: Radiofrequency (RF) is a commonly undertaken therapeutic approach for chronic pain used extensively in pain management clinics to treat patients worldwide. Developing radiofrequency technology that allows for maximizing practical efficiencies while maintaining clinical efficacy and patient safety is thus of great interest to relevant stakeholders. For example, use of tools that minimize the number of steps of clinical procedures, or eliminate the need for pre-sterilization of equipment, represent modest but key innovations that collectively help to support an improved patient experience when undergoing an RF-based procedure, and in turn may even help foster better outcomes. In this report, we describe our clinical experience using a disposable, all-in- one RF injection electrode (i.e., cannula, electrode, and injection tube) in patients with chronic pain as part of a multicenter European case-series.

Materials / Methods: This is a real-world, retrospective, observational, case-series study of patients in Europe who underwent a radiofrequency- based procedure for chronic pain and were treated using a disposable, "all-in-one" RF injection electrode with combined cannula, electrode, and injection tube (Unified RF, Boston Scientific, Valencia, CA USA). Key data and clinical assessments include demographic characteristics, pain diagnosis, baseline, and post-treatment pain scores (Numeric Rating Scale, NRS), and percent pain relief.

Results: To date, 250 enrolled subjects (mean age = 67.5 ± 23 years) who underwent an RF procedure for chronic pain using a disposable, all-in-one electrode have been assessed. Mean overall NRS pain score at baseline was 7.9. Patient-reported pain locations were the following: joints (11.6%), back (43.2%), hip (4.8%). The mean follow-up duration among all patients assessed was 292 days. Evaluation of overall pain demonstrated a mean NRS pain score improvement of 4.2-points ($p<0.0001$) representing a mean overall NRS pain score of 3.7 at last-follow-up. Additional data is being collected and updated results are to be reported.

Discussion: The use of a disposable all-in-one RF injection electrode allows for reducing procedural steps. Moreover, it also helps with reducing the potential for infection by eliminating pre-sterilization needs. This can lead to a safe and improved experience for patients undergoing RF treatment of chronic pain

Conclusions: Results obtained in this evaluation demonstrate that use of a disposable, "all-inone" RF injection electrode is associated with clinically meaningful pain relief outcomes in patients undergoing radiofrequency procedures for treatment of chronic pain.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1) To assess baseline pain in patients undergoing a radiofrequency procedure. 2) To evaluate NRS pain scores in patients undergoing a radiofrequency procedure and treated using a disposable, “all-in-one”RF injection electrode. 3) To assess the locations of pain in patients undergoing a radiofrequency procedure and treated using a disposable, “all-in-one” RF injection electrode.

Financial Disclosures: Drs. Occhigrossi, Abejon, and Kallewaard have consulting agreements with Boston Scientific. 1) Boston Scientific 2) consultant 3) 5-20k

Disclosure: This study is sponsored by Boston Scientific. Lilly Chen and Edward Goldberg are employees of Boston Scientific.

355

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

PROPOSAL TO CHANGE THE SURGICAL TECHNIQUE OF OPEN CORDOTOMY FOR THE PEDIATRIC POPULATION

Gustavo Lages, MD[1], José Oswaldo Oliveira Júnior, PhD[2], Maria Toledo, BChir[3], Natally Santiago, MD[4], Ramon Barbosa, MD[1], Leandro Batista, MD[5], Thiago Afonso, MD[6]
[1]Medular Clinic, Montes Claros, Brazil, [2]IAMSPE, São Paulo, Brazil, [3]Unifipmoc-AFYA, Montes Claros, Brazil, [4]Beneficiência Portuguesa Hospital, São Paulo, Brazil, [5]Santa Casa Montes Claros, Montes Claros, Brazil, [6]Santa Casa de Montes Claros, Montes Claros, Brazil

Introduction: Cordotomy is an established procedure for controlling cancer pain. Since percutaneous cervical technique requires patient collaboration, open thoracic cordotomy becomes the viable alternative for pediatric patients. In a case of open cordotomy in a child with pain in the lower limb, the size of the lesion and the single characteristics of the procedure in this age group were questioned. In the literature, were found three rare cases of cordotomy in children. However, we didn't find information regarding the technique and variations depending on the age group. We also didn't find anatomical or radiological studies of the transverse diameter of the spinal cord at the thoracic level in children. The final goal of this study was to evaluate spinal cord diameter in the pediatric population of different ages to estimate the size of the lesion necessary for pain control.

Materials / Methods: We selected fifty magnetic resonances of the thoracic spine at levels from T1 to T4 of patients between 0 and 12 years of age. The T2 Fast-Spin Echo sequence was used to millimetrically evaluate the transverse diameter (TD) of the spinal cord at levels most commonly used in open cordotomy.

Results: The results revealed a tendency of progressive spinal cord growth up to seven years of age. From the eighth year onwards, this growth slows down, approaching the values of the adult age group, with 10±1mm of TD.

Discussion: Given the variation in calibers, the lesions range from 3 to 5 mm deep in the anterolateral quadrant of the spinal cord in open cordotomy both by the anterior and posterior approachs, associating cold blade section at a depth of 4 mm and blunt dissection. In children under seven years of age, it was possible to observe a reduction in the value of the medullary diameter of approximately 20%. Therefore, it is understandable that the size of the incision by cold lamina of the spinal cord should be adapted to 3.2 mm to avoid unwanted effects associated with contralateral or posterior cord violation, depending on the approach.

Conclusions: Based on the results found, it states that after eight years of age, the spinal cord diameter becomes equivalent to that of the adult patient, that is, maintaining the surgical technique. However, under seven years, we propose a reduction in the size of the lesion by at least 0.8mm by reducing the final average depth from the surface to 2.4 to 4mm.

Supplemental Data:

References: 1 - SPILLER WG, MARTIN E. The treatment of persistent pain of organic origin in the lower part of the body by division of the anterolateral column of the spinal cord. ***JAMA***. 1912;LVIII(20):1489–1490. 2 - Javed S, Viswanathan A, Abdi S. Cordotomy for Intractable Cancer Pain: A Narrative Review. ***Pain Physician***. 2020;23(3):283-292. 3 - MEHLER WR, FEFERMAN ME, NAUTA WJ. Ascending axon degeneration following anterolateral cordotomy. An experimental study in the monkey. ***Brain***. 1960; 83:718-750. 4 - VORIS HC. Variations in the spinothalamic tract in man. ***J Neurosurg***. 1957;14(1):55-60. 5 - KAHN EA. Anterolateral chordotomy for intractable pain. *J**AMA***. 1933;100(24):1925–1928. doi:10.1001/jama.1933.02740240021007 6 – Foerster, O., Breslau, O.G. Die Vorderseitenstrangdurchschneidung beim Menschen. *Z. f. d. g. Neur.*

u. Psych. 138, 1–92 (1932). 7 - KAHN EA, PEET MM. The technique of anterolateral cordotomy. ***J Neurosurg*.** 1948;5(3):276-283. doi:10.3171/jns.1948.5.3.0276 8 - Steel D, Kirkman MA, Thompson DNP, Aquilina K. Open thoracic anterolateral cordotomy for pain relief in children: report of 2 cases. *J* ***Neurosurg Pediatr*.** 2017;20(3):278-283. 9 - Mooij JJ, Bosch DA, Beks JW. The cause of failure in high cervical percutaneous cordotomy: an analysis. ***Acta Neurochir (Wien)***. 1984;72(1-2):1-14. 10 - QUEINNEC MC, ESTEVE M, VEDRENNE J. Positive effect of regional analgesia (RA) in terminal stage paediatric chondrosarcoma: a case report and the review of the literature. ***Pain*.** 1999;83(2):383-385. 11- Remes VM, Heinänen MT, Kinnunen JS, Marttinen EJ. Reference values for radiological evaluation of cervical vertebral body shape and spinal canal. ***Pediatr Radiol*.** 2000;30(3):190-195. 12 - FROSTELL A, Hakim R, Thelin EP, Mattsson P, Svensson M. A Review of the Segmental Diameter of the Healthy Human Spinal Cord. ***Front Neurol*.** 2016;7:238. Published 2016 Dec. 13 - IŞIK S, SAMANCI MY. ANALYSIS OF MRI MORPHOMETRIC PARAMETERS OF THE PEDIATRIC CERVICAL SPINE AND SPINAL CORD. **J Turk Spinal Surg** 2019;30:157-161 14 - OZBEY, O; ARSLAN F.Z; KIREZ, M.K; Özbey Ö, Arslan FZ PAYASLI, M . Do we know the normal anterior-posterior diameters of the spinal cord and canal in newborns?. **J Health Sci Med** 2023; 6(2): 456-461.

Acknowledgements:

Learning Objectives: 1- Understand if there is a reason for adapting the cordotomy technique in different age groups 2- Evaluate the size of the chorodtomy lesion in children 3 - Evaluate whether there is a need to adapt the cordotomy technique for pediatric patients

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

356

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

LONG-TERM OUTCOMES OF SPINAL CORD STIMULATION IN PATIENTS WITH CHRONIC PERSISTENT SPINAL PAIN

Mette Nissen, MD, PhD[1], Henna-Kaisa Jyrkkänen, MD, PhD[1], Antti Luikku, MD[1], Mikael Von Und Zu Fraunberg, MD, MSc, PhD[2], Tiina-Mari Ikäheimo, RN[1], Jukka Huttunen, MD, PhD[1]
[1]Kuopio University Hospital, Neurocenter - Neurosurgery, Kuopio, Finland, [2]Oulu University Hospital, Neurosurgery At Neurocenter, Oulu, Finland

Introduction: Spinal cord stimulation (SCS) has become a key therapeutic intervention for chronic pain conditions such as persistent spine pain syndrome (PSPS) [1][2]. The long-term efficacy of SCS, particularly with regard to the potential need for device explantation, requires further investigation.

Materials / Methods: A dataset of 139 patients who underwent SCS was analyzed, focusing on two cohorts: permanent SCS (63 patients) and explanted SCS (30 patients) over a minimum period of three years. Trial only group was excluded from analysis (46 patients). Comprehensive statistical analyzes, including Mann-Whitney U tests, were performed to detect significant differences between groups.

Results: The permanent SCS group showed more significant improvement in limb pain at 6 months and greater reduction in disability at 3 months. In contrast, results varied in the explanted SCS group, with some measures indicating improvement while others remained stable or fluctuated. Table 1. The mean change in scores from baseline for various questionnaires across different follow-up periods: 6 months, 12 months, and 3 years. The data is presented for patient groups: Permanent SCS and Explanted
SCS

Variable	Class 1 Mean (Permanent SCS)	Class 1 Range	Class 2 Mean (Explanted SCS)	Class 2 Range	p-value
BAI Δ6m	-1.4	-23.0 - 22.0	3.1	-5.0 - 9.0	0.03
BAI Δ12m	-1.9	-21.0 - 17.0	-1.2	-7.0 - 4.0	0.75
BAI Δ3y	-3.6	-40.0 - 16.0	-0.3	-8.0 - 4.0	0.51
BDI Δ6m	-1.5	-20.0 - 8.0	-1.0	-11.0 - 6.0	0.79
BDI Δ12m	-1.1	-18.0 - 17.0	-0.5	-7.0 - 8.0	0.97
BDI Δ3y	-4.2	-24.0 - 33.0	0.3	-6.0 - 9.0	0.42
OSWESTRY Δ6m	-8.8	-42.0 - 12.0	3.8	-10.0 - 26.0	0.03
OSWESTRY Δ3y	-13.5	-44.0 - 22.0	3.3	-24.0 - 30.0	0.24
PAINDETECT NRS (limb) Δ6m	-2.1	-6.0 - 2.0	-0.5	-3.0 - 1.0	0.02
PAINDETECT NRS (limb) Δ12m	-1.6	-6.0 - 2.0	-0.2	-3.0 - 1.0	0.07
PAINDETECT NRS (limb) Δ3y	-1.6	-6.0 - 2.0	0.7	0.0 - 1.0	0.06
PAINDETECT (limb) Δ6m	-5.6	-16.0 - 9.0	-1.2	-4.0 - 1.0	0.03
PAINDETECT (limb) Δ12m	-4.4	-20.0 - 8.0	-3.0	-7.0 - 1.0	0.71
PAINDETECT (limb) Δ3y	-5.0	-22.0 - 4.0	-1.7	-4.0 - 0.0	0.42
PAINDETECT NRS (back) Δ6m	-1.2	-6.0 - 3.0	-0.3	-2.0 - 2.0	0.34
PAINDETECT NRS (back) Δ12m	-1.0	-6.0 - 5.0	-1.2	-3.0 - 0.0	0.68
PAINDETECT NRS (back) Δ3y	-1.1	-5.0 - 2.0	2.0	1.0 - 3.0	0.01*

Fig. 1 30 day NRS average for limb pain compared between Permanent SCS and Explanted SCS groups

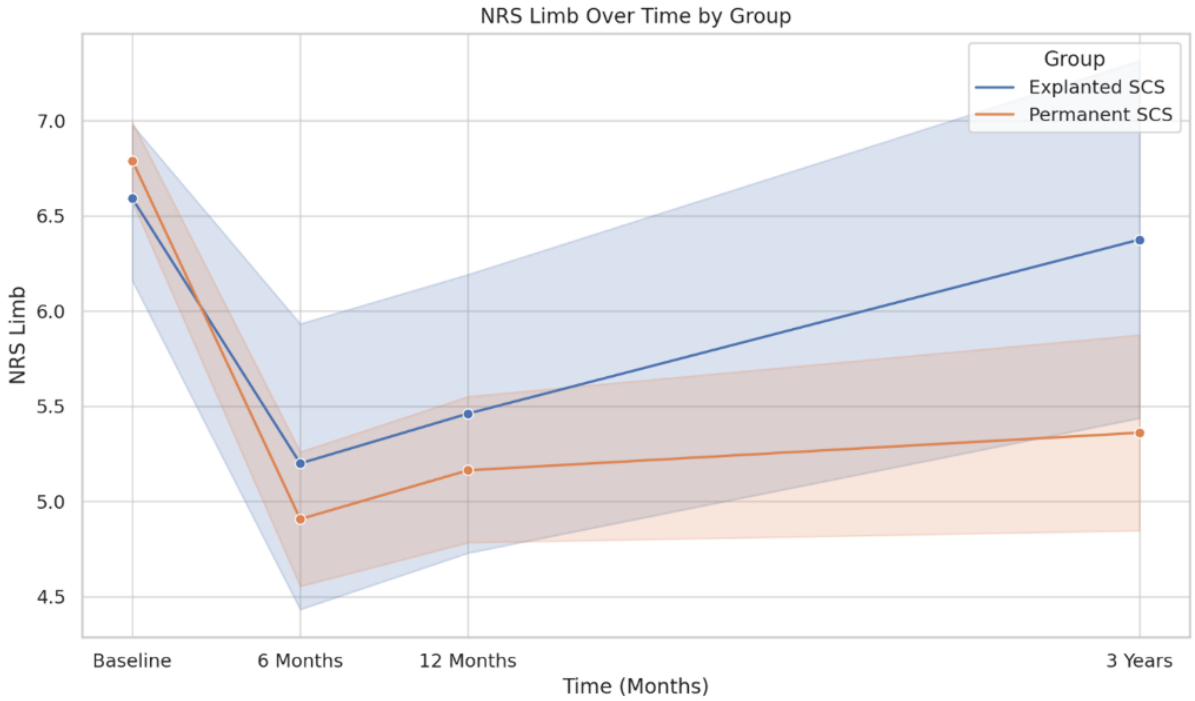
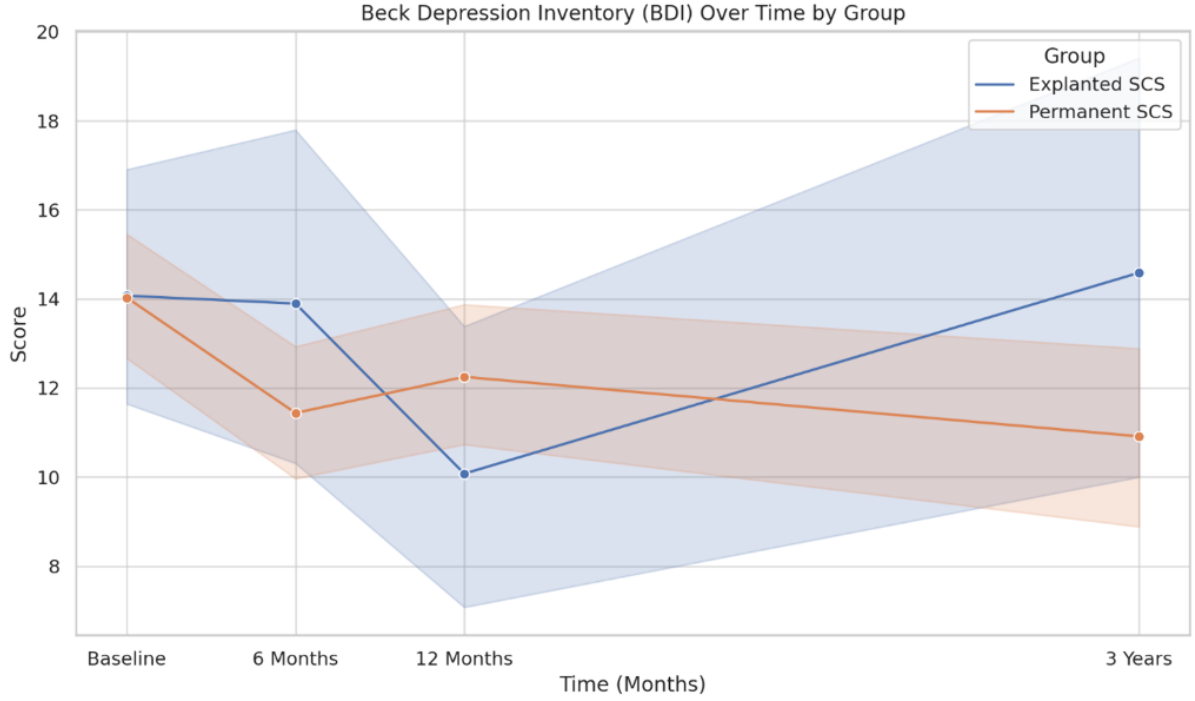


Fig. 2 Beck Depression Inventory (BAI) compared between Permanent SCS and Explanted SCS groups



Discussion: The results highlight the differential impact of permanent and explanted SCS on patient outcomes over time. The sustained improvements in the permanent SCS group are consistent with previous studies demonstrating the potential benefits of SCS in the management of chronic pain. [2] However, the variable outcomes in the explanted SCS group highlight the need for personalized treatment plans and further research on long-term efficacy. [3]

Conclusions: This study sheds light on the long-term outcomes of SCS and confirms the potential benefits of permanent SCS. At the same time, it underscores the need for individualized treatment approaches given the variable outcomes in the group of explanted SCS.

Supplemental Data:

References: [1] Smith, J. A., & Johnson, K. L. (2020). Long-term follow-up in spinal cord stimulation for Failed Back Surgery Syndrome. Journal of Pain Research, 13, 1129-1136. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10188261/ [2] Williams, R. T., & Patel, S. C. (2022). A systematic review and meta-analysis of spinal cord stimulation in management of chronic neuropathic pain secondary to FBSS. Pain Medicine, 21(5), 987-998. https://pubmed.ncbi.nlm.nih.gov/36943763/ [3] Taylor, R., & Harding, G. (2023). Innovative waveforms in spinal cord stimulation technology for Persistent Spine Pain Syndrome. Neuromodulation: Technology at the Neural Interface, 26(2), 156-164. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9334973/

Acknowledgements:

Learning Objectives: Understanding of Spinal Cord Stimulation (SCS) Efficacy Over Time: Participants will gain a comprehensive understanding of the long-term efficacy of SCS in managing chronic pain condition like Persistent Spinal Pain Syndrome (PSPS). They will be able to differentiate between the outcomes associated with Permanent and Explanted SCS, and comprehend the significance of personalized treatment plans based on individual patient conditions. **Interpretation of Statistical Analysis in Clinical Studies:** Participants will develop the ability to interpret statistical analyses, including the use of descriptive statistics and Mann-Whitney U tests, employed in the study to discern significant differences between patient groups. They will understand how these statistical methods contribute to the identification of significant findings and the implications of these findings for clinical practice. **Application of Research Findings in Clinical Decision-Making:** Participants will learn how to apply the findings from this study in clinical decision-making to optimize treatment plans for patients with chronic spinal pain. They will appreciate the necessity for a meticulous evaluation of SCS's long-term efficacy and the potential need for device explantation, thereby making more informed treatment decisions to improve patient outcomes.

Financial Disclosures: Nothing to disclose

Disclosure: No significant relationships.

357

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

WIKISTIM.ORG UPDATE

Richard North, PhD, Jane Shipley, BA
The Neuromodulation Foundation, Inc., Baltimore, United States of America

Introduction: The increasing number of neurostimulation articles published in a variety of journals makes it difficult to keep track of, access, and evaluate reports presenting primary data. Our website, WIKISTIM.org, (1) facilitates and enhances these activities.

Materials / Methods: WIKISTIM.org offers the following: The capacity to search curated lists of neurostimulation papers (updated monthly) reporting primary data and study protocols. The lists are presented in sections (currently DBS, DRG, GES, PNS, SCS, and SNS) and are sortable by author, title, journal, etc. Each section has a customized list of data categories for uploading WIKI-abstracted data from a paper, creation of evidence tables, study design, manuscript creation, and peer review. Multiple (or single) datasheets from the list of papers or a search are downloadable into a CSV spreadsheet that exhibits all data headings and rows to permit comparison.

WIKISTIM has a discussion section that allows unlimited conversation and immediate correction of errors. A monthly email newsletter lists new citations for each stimulation target. Access to WIKISTIM is free after registration

Results: Current status (as of October 2023):
Registrants = 1769.
DBS = 7852 entries; DRG = 257; GES = 523; PNS = 724; SCS = 3198; SNS = 1192. All lists are comprehensive.

WIKISTIM can be viewed on screens of any size.

Discussion: As resources permit, we will add new sections (e.g., ONS, VNS), link data fields to additional information, create search templates on commonly accessed topics, offer the ability to save searches, provide automatic updates of results of saved searches or searches identified as important, and incorporate data visualization techniques that will update as new data are extracted and uploaded.

Conclusions: We encourage the neuromodulation community to explore WIKISTIM and contribute to its development. Eventually WIKISTIM will list all reports containing primary neurostimulation data, with the goal of having all possible data extracted to support comparative analysis. WIKISTIM, thus, points the way to a new method of publishing and evaluating primary data. The ultimate and most important goal of WIKISTIM is to improve patient care.

Supplemental Data:

References: 1. North RB, Shipley J. WIKISTIM.org: an on-line database of published neurostimulation studies. Neuromodulation 2018 Dec;21(8):828-836.

Acknowledgements: WIKISTIM received financial and in-kind support (past and/or present) from: Boston Scientific; Enterra, Greatbatch; The International Neuromodulation Society; Medtronic; Nevro; St Jude; Stimwave; The Donlin & Harriett Long Family Charitable Gift Fund; The NANS Foundation; The Neuromodulation Foundation, Inc. (WIKISTIM's parent organization); The North American Neuromodulation Society; and the following individuals: Thomas Abell, MD; James Brennan, MD; David Cedeno, PhD and Pilar Mejia, PhD; Kenneth Chapman, MD; Terry Daglow; Hemant Kalia, MD,

MPH, FIPP; SuEarl McReynolds; Richard B. North, MD; Louis Raso, MD, PA; B. Todd Sitzman, MD, MPH; Konstantin Slavin, MD, PhD.

Learning Objectives: 1. Improve access to primary neurostimulation data.
2. Improve the evaluation and comparative analysis of published data in the field of neurostimulation.
3. Improve the generation and reporting of data in the field of neurostimulation by encouraging use of WIKISTIM data sheets for study design and manuscript preparation.

Financial Disclosures: Dr. North's and Ms. Shipley's previous employers, including Johns Hopkins University, as well as the charitable nonprofit Neuromodulation Foundation, of which he is an unpaid officer and Ms. Shipley is an employee, have received grant support and income from industry, including Abbott, Boston Scientific, Enterra, Medtronic, Nevro, Nuvectra, and Stimwave. Dr. North holds over 30 patents in the field of neuromodulation, and receives royalties from Abbott. His spouse holds equity in Stimwave.

Disclosure: No significant relationships.

358

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

OBJECTIVE ASSESSMENT OF PAIN USING DIGITAL PHONE APP AND WEARABLE TECHNOLOGY

Manish Ranjan, MD[1], Ali Rezai, MD[1], Victor Finomore, PhD[1], Mathew Tenan, PhD[1], Richard Vaglienti, MD[2]
[1]WVU Rockefeller Neuroscience Institute, Morgantown, United States of America, [2]WVU Center for Integrative Pain Management, Morgantown, United States of America

Introduction: Chronic pain is a major public health problem, affecting millions of people worldwide. Chronic pain can have a significant impact on a person's quality of life, affecting their ability to work, socialize, and enjoy everyday activities thus a complex phenomenon that is influenced by a variety of factors, including physical, psychological, and social factors. A major issue with the treatment and assessment of pain is that it is a subjective experience which is prone to bias and lacks objective assessments that traditionally relies on self-report questionnaires and clinician assessment. Wearable technology such as smart wearable devices and phone apps offer a promising new way to assess chronic pain by measuring bio-physiological and neurocognitive parameters. The objective of this pilot study is to develop a data infrastructure to measure and quantify patients with chronic lower back pain.

Materials / Methods: Adult patients with chronic pain secondary to low back pain and/or lower leg pain, who were evaluated for spinal cord stimulation (SCS) at West Virginia University (WVU) were recruited for the study. Participants were provided with a commercially available wearable device, the Oura ring (Oura Health Oy, Finland). Participants downloaded the WVU Rockefeller Neuroscience Institute (RNI) Health App, a smartphone application that presented daily questionnaires and cognitive tasks. Patients were enrolled prior to implantation of the SCS and continuously monitored after the procedure. The wearable device monitored participants' daily heart rate, heart rate variability, and sleep metrics. The RNI Health App measured daily wellness questions related to pain level, pain interference, fatigue, depression, and stress. Additionally, cognitive tasks were also administered on the RNI Health App to measure working memory, attention, and fatigue.

Results: A total of 53 of participants (mean age 54.6 years) were enrolled. Several features from the wearable device and RNI Health App were statistically correlated with subjective pain ratings. Higher pain score was statistically significantly ($p < 0.05$) associated with higher resting heart rate, lower HRV, lower sleep scores, lower wellness metrics, and lower cognitive attention.

Discussion: The information derived from the wearable technology and the RNI Health Apps may provide clinicians continuous and objective assessment of pain. This approach may provide objective assessment of pain and the potential opportunity to monitor treatment response beyond conventional subjective scales remotely and in the clinical setting.

Conclusions: Our study demonstrates the feasibility of objective assessment of pain using wearable technology and smartphone app through biophysiological and neurocognitive assessment.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: Reproducible and objective assessment of pain with wearable technology and digital app.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

359

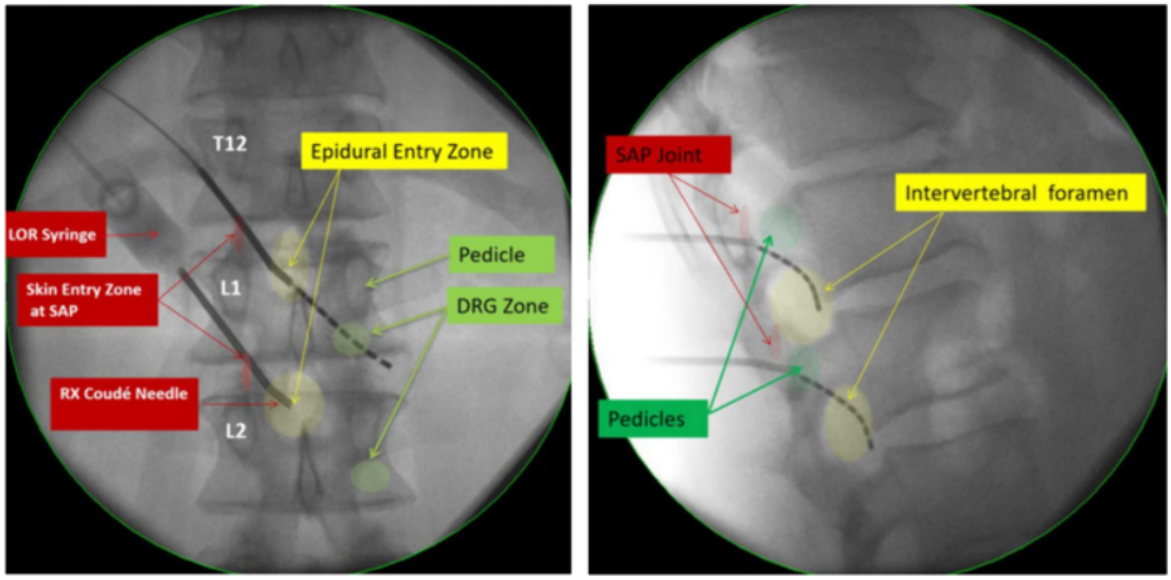
Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

SAFETY AND EFFICACY OF TRANSGRADE APPROACH TRANSFORAMINAL STIMULATION (TFS) : A RETROSPECTIVE SINGLE-CENTRE ANALYSIS

Matthew Stubbs, MBBS[1], Mario Cibelli, MBBS[1], Laurens Peene, MBBS[1,2], Stephany Harris, RN[1], Jonathan Royds, MBBS[1], David Pang, MBBS[1], Stefano Palmisani, MD[1], Thomas Yearwood, MD, PhD[1], Adnan Al-Kaisy, MBBS[1]
[1]Guy's & St Thomas' NHS Trust, Pain Management Department, London, United Kingdom, [2]Ziekenhuis Oost-Limburg, 2. department Of Anesthesiology, Intensive Care, Emergency Medicine And Multidisciplinary Pain Center, Genk, Belgium

Introduction: Transgrade lead placement technique has been successfully used in the stimulation of spinal transforaminal structures (root, DRG and spinal nerve) – most accurately termed transforaminal stimulation (TFS). Our aim was to assess safety and efficacy of TFS over a 6 year period at a tertiary referral neuromodulation centre in the UK.

Materials / Methods: Case-notes were reviewed for all patients who underwent full-implantation of at least one TFS lead (8x3mm contacts/1mm spacing, off-label use) by the transgrade approach (Figure 1) - with or without combined SCS, between January 2017 and December 2022. Pain intensity and patient global impression of change (PGIC) were assessed at early follow-up (within 1-month of full implantation) and extended follow-up (most recent available records - minimum 1-year post-implant). Full case-notes were assessed from time of implantation to September 2023, for potential complications.



A: AP view B: Lateral view

Figure 1: TFS lead placement by transgrade approach
Needle entry approximately at the contralateral superior articular process of the corresponding vertebra, with an initial inferio-medial trajectory to enter the epidural space at that level. Lead is then passed through the needle, directed towards the desired intervertebral foramen. Technique has been described in detail previously [1, 2].

Results: 45 patients were included (22 men, 23 women, mean age 50 yrs). All had a pre-implantation trial. Follow-up average was 4 years. Indications were neuropathic pain (24 patients) and CRPS (21 patients). 23 patients had combined SCS and TFS placed, 22 patients had TFS alone. Foraminal levels ranged from C6 to S1. Efficacy data (see figure 2): Efficacy data was available for sub-analysis in 22 patients. Average baseline pain intensity was 8.8 NRS (numerical rating scale - out of 10).

Average NRS at early follow-up was 3.2, with average 74% patient-reported reduction in pain. PGIC scores were positive (88% 'moderately improved' or better - table 1). At extended follow-up, 2 patients (9%) had a significant loss of efficacy. One was explanted, one was lost to follow-up. Results were otherwise comparable with early efficacy data. Average NRS was 4.0 (with average 62% reduction in pain from baseline). PGIC scores remained positive (77% 'moderately improved' or better - table 1). Safety data: There were no serious neurological complications. Moderate complications (5.5%): 1 patient developed post-dural puncture headache; 2 patients required revision (1 for lead migration, 1 for high impedances). Minor complications - resolved with re-programming (9%): 3 patients experienced episode(s) of overstimulation; 1 patient had minor lead migration.

Description	Early Follow-up	Extended Follow-up
Worsening	0	7%
No change	0	0
Almost the same, hardly any change at all	0	0
A little better but not noticeable change	0	14%
Somewhat better, but the change has not made any real difference	6%	0
Moderately better, and a slight but noticeable change	6%	0
Better and a definite improvement that has made a real and worthwhile difference	38%	21%
A great deal better and a considerable improvement that has made all the difference	50%	57%

Table 1: Patient Global Impression of Change (PGIC).
Scores at early (1 month) and extended (>1 year) follow-up, expressed as percentage of patients in each group.

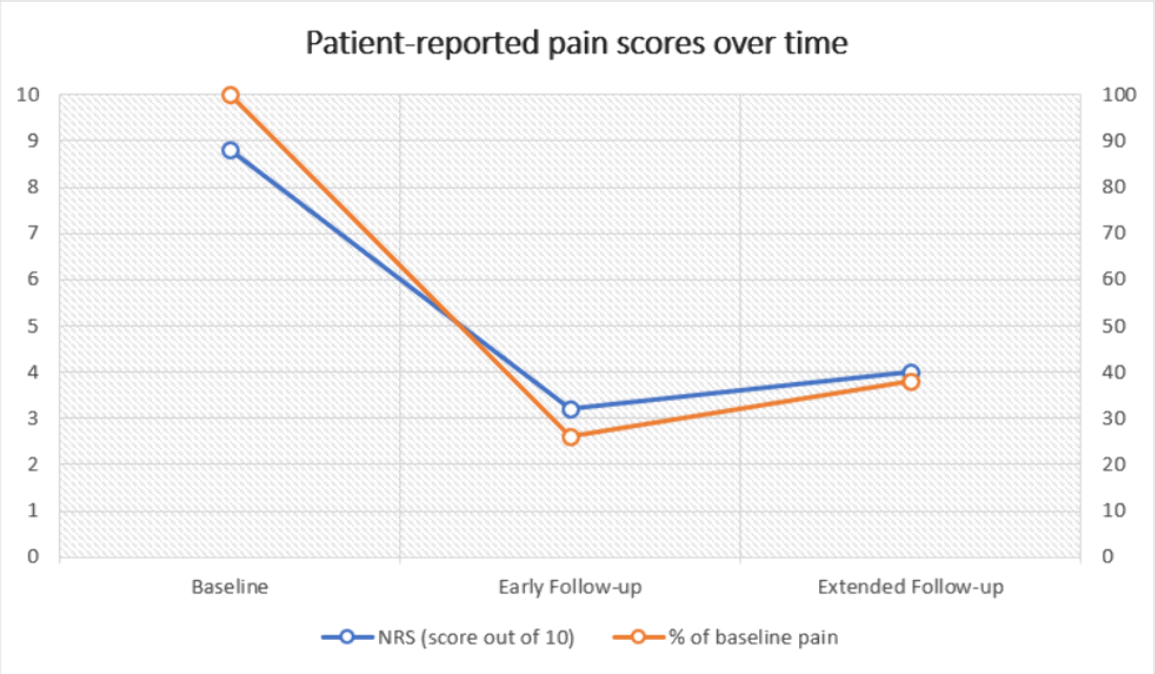


Figure 2: Patient reported pain scores over time
Average NRS (blue) and average % of baseline pain (derived from patient-reported percentage reduction in pain – orange).

Discussion: TFS has previously been shown to be effective alone [1] and in combination with SCS [2]. However, few long-term safety and efficacy data were available. This analysis has demonstrated few complications, and favourable patient-reported pain reduction and quality of life indices. Benefits were somewhat sustained at extended follow-up.

Conclusions: In our centre, transgrade approach TFS is shown to be safe and effective.

Supplemental Data:

References: [1] Al-Kaisy A, Royds J, Costanzi M, Racz G, Wesley S, Palmisani S, Pang D, Yearwood T. Effectiveness of "Transgrade" Epidural Technique for Dorsal Root Ganglion Stimulation.

A Retrospective, Single-Center, Case Series for Chronic Focal Neuropathic Pain. Pain Physician. 2019 Nov;22(6):601-611. PMID: 31775407. [2] Mullins CF, Palumbo J, Harris S, Al-Kaisy O, Wesley S, Yearwood T, Al-Kaisy A. Effectiveness of Combined Dorsal Root Ganglion and Spinal Cord Stimulation: A Retrospective, Single-Centre Case Series for Chronic Focal Neuropathic Pain Effectiveness of Combined Stimulation. Pain Med. 2023 Sep 21:pnad128. doi: 10.1093/pm/pnad128. Epub ahead of print. PMID: 37738574.

Acknowledgements: N/A

Learning Objectives: 1. To demonstrate that, in our experience, TRS devices placed using the transgrade approach are safe. 2. To demonstrate that, in our experience, TRS devices placed using the transgrade approach are effective. By and large, effectiveness is sustained at extended follow-up averaging 4 years. 3. To consider the anatomical location of of these neurostimulation leads (covering the spinal root, dorsal root ganglion, and spinal nerve) and accurately term these as transforaminal stimulation (TFS) devices.

Financial Disclosures: Stubbs M, Cibelli M, Peene L, Harris S, Royds J, Pang D, Palmisani S, Smith T, Al-Kaisy A : No significant relationships to declare. Yearwood T : Thomas Yearwood is owner of a start-up medical device company in the United Kingdom, Neuromodulation Specialists, Ltd, concerned with developing implantable devices, including SCS. He is a consultant for Neuronano, a medical device development firm in Sweden engaged in devices for DBS.

Disclosure: No significant relationships.

360

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

COMBINED CONUS MEDULLARIS & SACRAL NERVE STIMULATION IN THE MANAGEMENT OF INTERSTITIAL CYSTITIS

Laurens Peene, MBBS[1,2], Matthew Stubbs, MBBS[1], Stefano Palmisani, MD[1], Arun Sahai, MD[3], Thomas Yearwood, MD, PhD[1], Adnan Al-Kaisy, MBBS[1]
[1]Guy's and St Thomas' NHS Foundation Trust, Pain Management & Neuromodulation Center, London, United Kingdom, [2]Ziekenhuis Oost-Limburg, Department Of Anesthesiology, Intensive Care, Emergency Medicine And Multidisciplinary Pain Center, Genk, Belgium, [3]Guy's and St Thomas' NHS Foundation Trust, Urology, London, United Kingdom

Introduction: Sacral nerve stimulation (SNS) is an established minimally invasive treatment modality for functional bladder disease, including urinary incontinence, or chronic pain after interstitial cystitis. [1] Nevertheless, loss of efficacy is seen in up to 34% of all patients implanted with SNS. [2] Evidence supporting other neuromodulation techniques for functional bladder disorders remains sparse. [3]

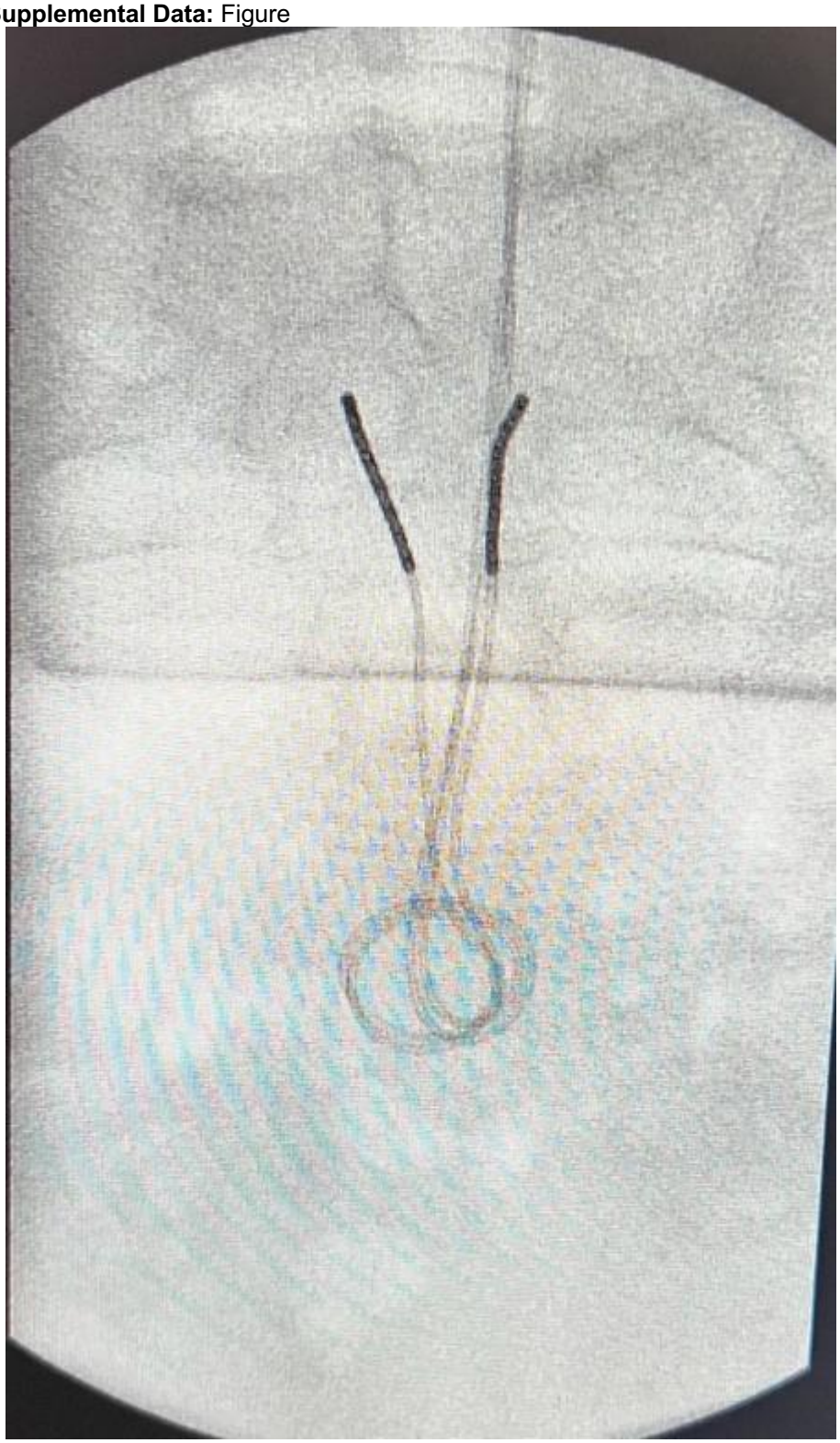
Materials / Methods: We present a case report of a 68-year-old woman, originally presenting with refractory symptoms of chronic pain in the hypogastrium combined with longstanding symptoms of urinary incontinence. All possible conservative and interventional treatments were exhausted, including a trial of right sided S3 SNS (Interstim©). Due to her debilitating symptoms, informed consent was obtained for a hybrid SNS and conus medullaris stimulation (CMS) procedure. Two octapolar leads were inserted through the sacral hiatus to stimulate the S2-S4 nerve roots (Figure 1). Additionally, two octapolar epidural leads were introduced to stimulate the conus medullaris from Th12 to L1. (Figure 2) The four leads were connected to an implantable pulse generator (Wavewriter Alpha 32©).

Results: Employed separately, SNS or CMS provide 20 – 30% pain reduction, at best. Further, urinary incontinence remained unaffected. However, the combination of SNS and simultaneous CMS resulted in 90% reported pain reduction and complete resolution of urinary incontinence. Five months after permanent implantation, the patient reported worsening urinary incontinence with maintained pain relief. After excluding lead migration and other complications, a presumed diagnosis of overstimulation was made. She was reprogrammed to intermittent stimulation (30 seconds ON – 360 seconds OFF) and experienced rapid resolution of her urinary incontinence without interrupting her pain relief.

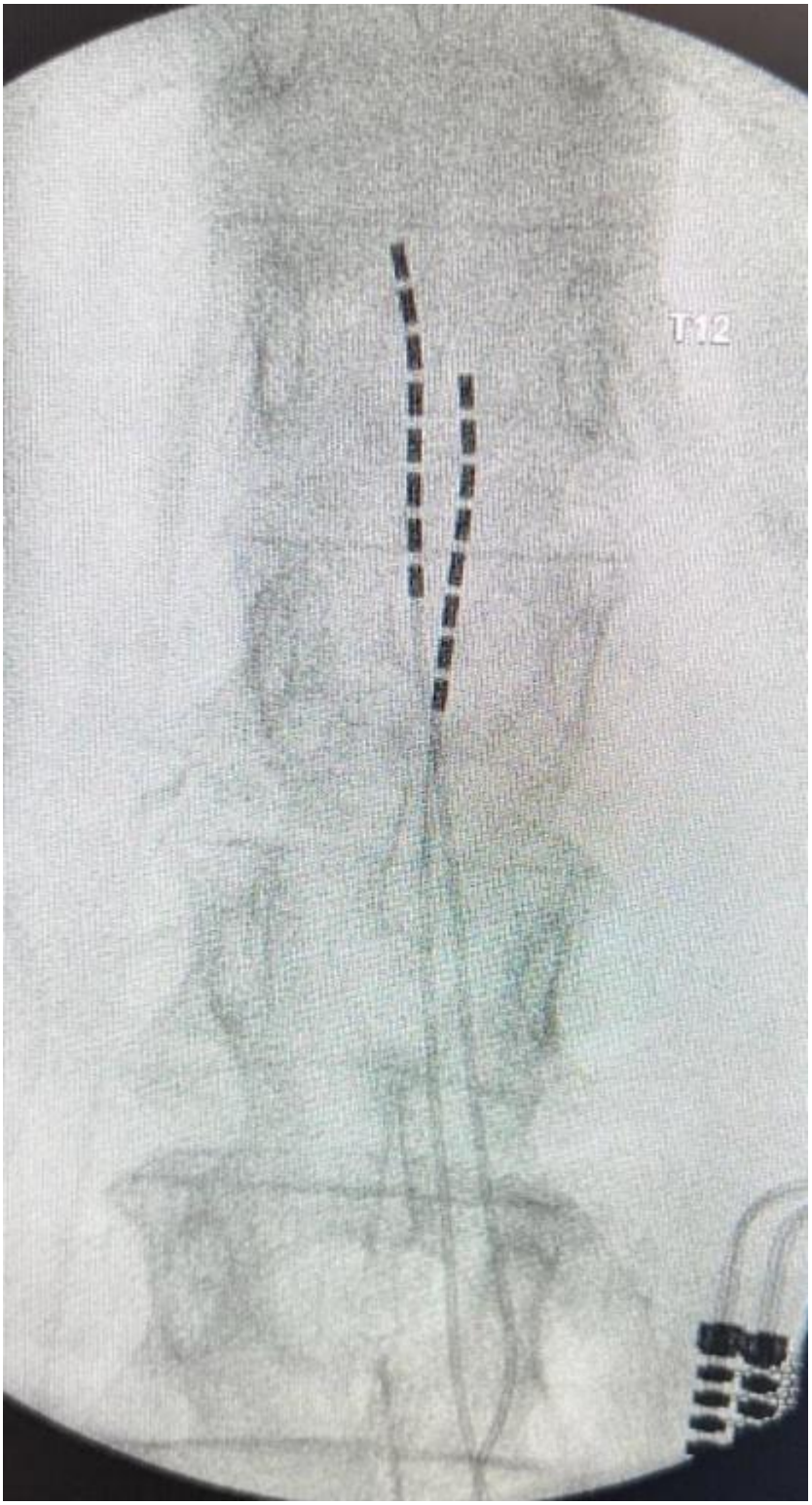
Discussion: Functional bladder symptoms and chronic pain frequently occur after interstitial cystitis and significantly impact the quality of life (QoL). In patients where SNS fails to improve outcomes, CMS could be considered. The use of CMS to treat functional bladder symptoms has been described as early as 1974. [4] Recent reports on CMS in chronic visceropelvic pain have demonstrated good clinical outcomes. [5] Our group is the first to report on the combination of SNS and CMS in these patients.

Conclusions: Using a hybrid technique of SNS with CMS can improve pain, functional outcomes, and QoL in refractory pain and bladder dysfunction after interstitial cystitis.

Supplemental Data: Figure



1 Figure

2 

References: 1. Herbison GP, Arnold EP. Sacral neuromodulation with implanted devices for urinary storage and voiding dysfunction in adults. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD004202. 2. Hernández-Hernández D, Padilla-Fernández B, Castro Romera M, Hess Medler S, Castro-Díaz D. Long-term Outcomes of Sacral Nerve Stimulation in Pelvic Floor Dysfunctions. Int Neurourol J. 2021 Dec;25(4):319-326. 3. Gish B, Langford B, Sobey C, Singh C, Abdullah N, Walker J, Gray H, Hagedorn J, Ghosh P, Patel K, Deer T. Neuromodulation for the management of chronic pelvic pain syndromes: A systematic review. Pain Pract. 2023 Sep 19. 4. Sedan R, Bourhis A, Regis H, Sarrazin L, Buffet J, Lazorthes Y, Sarramon JP, Arbus L, Zadeh J, Catte M. La stimulation électrique du cône médullaire dans les vessies neurologiques [Electrical stimulation of the conus medullaris in

neurological bladder]. Neurochirurgie. 1974 Mar-Apr;20(2):93-116. 5. Chang Chien GC, Mekhail N. Alternate Intraspinal Targets for Spinal Cord Stimulation: A Systematic Review. Neuromodulation. 2017 Oct;20(7):629-641.

Acknowledgements: None

Learning Objectives: 1. The treatment of chronic bladder pain and functional bladder symptoms can be challenging 2. While SNS is an effective treatment option, not all patients will respond in the long term. 3. Association of conus medullaris SCS to SNS can improve outcomes in well-selected patients.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

361

Poster on Board
POSTER ON BOARD: AS07. OTHER
13-05-2024 08:00 - 19:00

CHANGES IN CONDITIONED PAIN MODULATION BY ANTI-PARKINSON DRUGS AS EVALUATED BY CUTANEOUS SILENT PERIOD

Eiichiro Urasaki, MD, Yasushi Miyagi, MD
Fukuoka Mirai Hospital, Neurosurgery, Fukuoka, Japan

Introduction: The "pain inhibits pain" phenomenon, called conditioned pain modulation (CPM) in humans, is a type of endogenous pain modulation. While patients with Parkinson's disease often complain of pain, probably due to a lowered pain threshold caused by dopamine deficiency, few reports have investigated the effect of anti-Parkinson drugs on CPM. This study evaluated CPM using the cutaneous silent period (CSP) as an objective index and investigated the effect of anti-Parkinson drugs on CPM.

Materials / Methods: CSPs elicited by weak and strong stimuli were recorded in 26 patients with Parkinson's disease before deep brain stimulation surgery, both under drug-on and drug-off conditions. CSPs were recorded from the right abductor pollicis brevis muscle, and we examined the change in the CSP elicited by strong stimulation while the patient was experiencing pain by dipping the left hand in cold water (cold pressure) as a conditioned stimulus.

Results: (1) The shortened CSP duration due to cold pressure was a CPM response, which could be determined from CSP waveforms with little electromyogram contamination (17 of 26 cases). (2) The CSP duration during cold pressure and strong stimulation was decreased and was close to the CSP duration with weak stimulation without cold pressure. (3) The shortened CSP duration with cold pressure occurred in both drug-on and drug-off states ($p<0.01$). However, the rate of CSP duration shortening during cold pressure was significantly greater for the on-drug (mean 25%) than for the off-drug (mean 14%) state ($p<0.01$). (4) The CSP duration without cold pressure was significantly longer for the on-drug than the off-drug state ($p<0.01$), while the duration during cold pressure did not differ significantly between the drug-off and the drug-on states.

Discussion: Previous studies demonstrated prolonged CSP duration for strong stimulation compared with that of weak stimulation, as the former activates both Aβ and Aδ fibers, while the latter mainly activates only Aβ fibers. The shortening of the CSP duration induced by strong stimulation during cold pressure can be interpreted to result from Aδ fiber inhibition by the CPM function to suppress pain.

Conclusions: Anti-Parkinson drugs may enhance the ability to detect Aδ pain and trigger CPM, resulting in a prolonged CSP duration without cold pressure and a greater shortening rate of CSP duration under cold pressure.

Supplemental Data:

References: 1) Rossi P et al. Effect of painful heterotopic stimulation on the cutaneous silent period in the upper limbs. Clin Neurophysiol 2003; 114: 1-6. 2) Urasaki E et al. Effects of medications and subthalamic nucleus-deep brain stimulation on the cutaneous silent period in patients with Parkinson's disease. Neuromodulation 2022; 25: 854-865

Acknowledgements:

Learning Objectives: 1) Cutaneous silent period (CSP) is useful to evaluate the conditioned pain modulation (CPM). 2) Shortening of the CSP duration during cold pressure may result from Aδ fiber inhibition by the CPM function to suppress pain. 3) Anti-Parkinson drugs may enhance the ability to detect Aδ pain and trigger CPM.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

Invited Speakers

IS001

Pre-Conference Day
NON-INVASIVE BRAIN STIMULATION: FROM PAIN, TO INFLAMMATORY, TO POST-VIRAL SYMPTOMS - PART 1
12-05-2024 09:00 - 10:10

TRANSCRANIAL DIRECT CURRENT STIMULATION FOR INFLAMMATORY AND POST-INFECTION DISORDERS

Giuseppina Pilloni, PhD, Leigh Charvet, PhD
New York University Grossman School of Medicine, Neurology, New York, United States of America

Introduction and Discussion: Transcranial Direct Current Stimulation (tDCS) is a noninvasive, safe, and well-tolerated brain stimulation method, even when delivered in a home setting [1], and it involves the application of a low-intensity electric current through electrodes positioned on the scalp. tDCS is designed to shift cortical excitability of brain regions of interest to a state of excitation or inhibition for behavioral or clinical effects. Clinical trials using tDCS are now numbered in the hundreds, spanning investigation of its use for the symptom management of neurological and psychiatric conditions as well as inflammatory and post-infectious diseases [2, 3]. While research is still ongoing, some of the symptoms that have shown promising responses to tDCS include depression, fatigue, pain, motor and cognitive impairment, and emotional distress. However, the evolving nature of the field needs further large randomized clinical trials to establish tDCS dosing, like brain targeting (e.g., anatomical or functional), brain state (e.g., concurrent training activity or behavioral task), intensity of the electrical current, stimulation duration, number of sessions, and long-term efficacy. During the presentation, we will review the process behind choosing tDCS dosing parameters for distinct target symptoms such as fatigue, depression, and motor and cognitive symptoms, informed by evidence-based literature and the findings from recently completed RCTs conducted in our Neuromodulation Lab at NYU Langone Health [4, 5]. More specifically, we will go over the findings from two Class I RCTs that tested the use of tDCS to address fatigue, cognitive impairment, and motor deficits in individuals with multiple sclerosis (MS)—a chronic, progressive, and inflammatory disorder of the central nervous system. In the first double-blinded and sham-controlled trial, we enrolled n=120 participants with MS and experiencing fatigue to complete 30 sessions of 30-minute remotely supervised tDCS (RS-tDCS) paired with cognitive training. In the second trial, we enrolled n=66 participants with progressive MS and upper extremity impairment to complete 20 sessions of 20-minute RS-tDCS paired with manual dexterity training.

Supplemental Data:

References: 1. Pilloni G, Vogel-Eyny A, Lustberg M, Best P, Malik M, Walton-Masters L, George A, Mirza I, Zhovtis L, Datta A, Bikson M, Krupp L, Charvet L. Tolerability and feasibility of at-home remotely supervised transcranial direct current stimulation (RS-tDCS): Single-center evidence from 6,779 sessions. Brain Stimul. 2022 May-Jun;15(3):707-716. doi: 10.1016/j.brs.2022.04.014. Epub 2022 Apr 22. PMID: 35470019. 2. Fregni F, El-Hagrassy MM, Pacheco-Barrios K, Carvalho S, Leite J, Simis M, Brunelin J, Nakamura-Palacios EM, Marangolo P, Venkatasubramanian G, San-Juan D, Caumo W, Bikson M, Brunoni AR; Neuromodulation Center Working Group. Evidence-Based Guidelines and Secondary Meta-Analysis for the Use of Transcranial Direct Current Stimulation in Neurological and Psychiatric Disorders. Int J Neuropsychopharmacol. 2021 Apr 21;24(4):256-313. doi: 10.1093/ijnp/pyaa051. PMID: 32710772 3. Charvet L, George A, Charlson E, Lustberg M, Vogel-Eyny A, Eilam-Stock T, Cho H, Best P, Fernandez L, Datta A, Bikson M, Nazim K, Pilloni G. Home-administered transcranial direct current stimulation is a feasible intervention for depression: an observational cohort study. Front Psychiatry. 2023 Aug 22;14:1199773. doi: 10.3389/fpsyt.2023.1199773. PMID: 37674552 4. Pilloni G, Choi C, Shaw MT, Coghe G, Krupp L, Moffat M, Cocco E, Pau M, Charvet L. Walking in multiple sclerosis improves with tDCS: a randomized, double-blind, sham-controlled study. Ann Clin Transl Neurol. 2020 Nov;7(11):2310-2319. doi: 10.1002/acn3.51224. Epub 2020 Oct 20. PMID: 33080122 5. Pilloni G, Choi C, Coghe G, Cocco E, Krupp LB, Pau M, Charvet LE. Gait and Functional Mobility in Multiple Sclerosis: Immediate Effects of Transcranial Direct Current Stimulation (tDCS) Paired With Aerobic Exercise. Front Neurol. 2020 May 5;11:310. doi: 10.3389/fneur.2020.00310. PMID: 32431658

Acknowledgements:

Learning Objectives: ***1. The principles, methodology, and technology of tDCS:*** Attendees will gain a comprehensive understanding of the fundamental principles of Transcranial Direct Current Stimulation (tDCS) and its potential to address symptoms commonly associated with inflammatory and post-infectious diseases, including fatigue and depression. This will encompass practical guidance on the recommended methodology and technology essential for ensuring the safety and tolerance of tDCS sessions, whether administered in a clinical or home setting. ***2. The significance of tDCS dosing selection:*** By the end of this session, participants will be able to analyze the evolving landscape of tDCS research and identify the critical components requiring further investigation in large randomized clinical trials. Specifically, participants will develop an understanding of the necessary parameters for tDCS dosing, including considerations about brain targeting (anatomical or functional), brain state modulation (e.g., concurrent training activity or behavioral task), electrical current intensity, stimulation duration, session frequency, and the assessment of long-term efficacy. ***3. Class I RCT insights and applicability in inflammatory diseases and beyond:*** Participants will gain insights into the outcomes of two Class I RCTS, examining the effectiveness of tDCS in addressing fatigue, cognitive impairment, and motor deficits in individuals with multiple sclerosis. The session will delve into trial methodologies, enrollment criteria, and intervention protocols, highlighting the requirements for conducting Class I RCTs. Participants will be then able to expand the applicability of these findings to other inflammatory diseases, enriching their understanding of tDCS as a potential symptomatic therapeutic approach across various clinical contexts.

Financial Disclosures: GP has no significant relationships; LC has consulted for Ybrain, Neuroelectrics, Johnson & Johnson, and Biogen.

Disclosure: No significant relationships.

IS002

Pre-Conference Day
NON-INVASIVE BRAIN STIMULATION: FROM PAIN, TO INFLAMMATORY, TO POST-VIRAL SYMPTOMS - PART 1 CONT
12-05-2024 10:40 - 12:25

NON-INVASIVE BRAIN STIMULATION FOR ADDICTION MEDICINE

Hamed Ekhtiari, Dr
University of Minnesota, Psychiatry, Wayzata, United States of America

Introduction and Discussion: There is growing interest in non-invasive brain stimulation (NIBS) as a novel treatment option for substance-use disorders (SUDs). Recent momentum stems from a foundation of preclinical neuroscience demonstrating links between neural circuits and drug consuming behavior, as well as recent FDA-approval of NIBS treatments for mental health disorders that share overlapping pathology with SUDs. As with any emerging field, enthusiasm must be tempered by reason; lessons learned from the past should be prudently applied to future therapies. In this talk, I will present an overview of the state of transcranial-electrical (tES) and transcranial-magnetic (TMS) stimulation applied in SUDs. This talk provides a systematic literature review and model based meta-analyses on published data - emphasizing the heterogeneity of methods and outcome measures while suggesting strategies to help bridge knowledge gaps. The goal of this talk is to provide the community with guidelines for best practices in tES/TMS SUD research. I hope this talk will accelerate the speed at which the community translates basic neuroscience into advanced neuromodulation tools for clinical practice in addiction treatment.

Supplemental Data:

References: Ekhtiari H, Tavakoli H, Addolorato G, Baeken C, Bonci A, Campanella S, Castelo-Branco L, Challet-Bouju G, Clark VP, Claus E, Dannon PN, Del Felice A, den Uyl T, Diana M, di Giannantonio M, Fedota JR, Fitzgerald P, Gallimberti L, Grall-Bronnec M, Herremans SC, Herrmann MJ, Jamil A, Khedr E, Kouimtsidis C, Kozak K, Krupitsky E, Lamm C, Lechner WV, Madeo G, Malmir N, Martinotti G, McDonald WM, Montemitro C, Nakamura-Palacios EM, Nasehi M, Noël X, Nosratabadi M, Paulus M, Pettorruso M, Pradhan B, Praharaj SK, Rafferty H, Sahlem G, Salmeron BJ, Sauvaget A, Schluter RS, Sergiou C, Shahbabaie A, Sheffer C, Spagnolo PA, Steele VR, Yuan TF, van Dongen JDM, Van Waes V, Venkatasubramanian G, Verdejo-García A, Verveer I, Welsh JW, Wesley MJ, Witkiewitz K, Yavari F, Zarrindast MR, Zawertailo L, Zhang X, Cha YH, George TP, Frohlich F, Goudriaan AE, Fecteau S, Daughters SB, Stein EA, Fregni F, Nitsche MA, Zangen A, Bikson M, Hanlon CA. Transcranial electrical and magnetic stimulation (tES and TMS) for addiction medicine: A consensus paper on the present state of the science and the road ahead. Neurosci Biobehav Rev. 2019 Sep;104:118-140. doi: 10.1016/j.neubiorev.2019.06.007. Epub 2019 Jul 2. PMID: 31271802; PMCID: PMC7293143.

Acknowledgements: This talk is presented with support from Medical Discovery Team on Addiction (MDTA), University of Minnesota.

Learning Objectives: Participants after this talk will be able to 1. Identify the knowledge gaps in using non-invasive brain stimulation (NIBS) as a novel treatment option for substance-use disorders (SUDs) 2. Provide an overview on the state of transcranial-electrical (tES) and transcranial-magnetic (TMS) stimulation applied in SUDs and the regulatory approvals 3. Make a list of major potential targeting biomarkers for using NIBS in SUD treatment

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS004

Pre-Conference Day
NON-INVASIVE BRAIN STIMULATION: FROM PAIN, TO INFLAMMATORY, TO POST-VIRAL SYMPTOMS - PART 2
12-05-2024 13:45 - 15:30

AT-HOME TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) WITH TELEHEALTH SUPPORT FOR SYMPTOM CONTROL IN CHRONICALLY ILL PATIENTS

Helena Knotkova, PhD, PhilD[1,2]
[1]MJHS Institute for Innovation in Palliative Care, New York, United States of America, [2]Albert Einstein College of Medicine, Department Of Family And Social Medicine, And Neurology, The Bronx, United States of America

Introduction and Discussion: Transcranial direct current stimulation (tDCS) is a non-invasive neuromodulation technique that was re-introduced to modern medicine in 2000 and has gained growing interest since then [1]. The need for longer stimulation protocols spanning for several weeks or months propelled the development of the technology and procedures that enabled the tDCS application by lay persons in home settings with a remote assistance by medical/research personnel. The presentation will discuss a hands-on experience with the development of the at-home tDCS procedure remotely supervised by video and phone and will critically review patient selection criteria, as well as a successful implementation of the at-home tDCS in protocols aiming for symptom relief in patients with various chronic diseases [2-5].

Supplemental Data:

References: [1] Nitsche, M. A., and Paulus, W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. J. Physiol. 2000; 527:633–639. [2] Knotkova H, Riggs A, Patel V, Truong D, Arce D, Bernstein H, Datta A, Bikson M. A Novel approach to determining M1 tDCS montage without neuronavigational measurements, suitable for patients in home settings. Brain Stimulation, 2017; 10(4)78-80. [3] Riggs A, Patel V, Paneri B, Portenoy RK, Bikson M, Knotkova H. At-Home transcranial direct current stimulation (tDCS) with telehealth support for symptom control in chronically ill patients with multiple symptoms. Frontiers in Behavioral Science 2018, 12:93-97. [4] Gulley E, Verghese J, Blumen HM, Ayers E, Wang C, Portenoy RK, Zwerling JL, Weiss E, Knotkova H. Neurostimulation for cognitive enhancement in Alzheimer's disease (the NICE-AD study): a randomized clinical trial. Neurodegener Dis Manag. 2021 Aug;11(4):277-288. doi: 10.2217/nmt-2020-0061. Epub 2021 Jul 9. PMID: 34240627; PMCID: PMC8438943. [5] Van Zyl J, Knotkova H, Kim P, Henderson CR Jr, Portenoy RK, Berman N, Frederic MW, Reid MC. Delivery of an at-home transcranial direct current stimulation intervention to mitigate pain in patients with end-stage kidney disease receiving hemodialysis (ESKD/HD). Front Pain Res (Lausanne). 2023 Apr 5;4:1132625. doi: 10.3389/fpain.2023.1132625. PMID: 37092011; PMCID: PMC10113462.

Acknowledgements: This project has been supported by the National Institute on Aging, study #5R01AG068167-03 and by the National Institute of Diabetes and Digestive and Kidney Diseases, study #1R01DK131050-01.

Learning Objectives: 1) To critically review the facilitating factors and challenges in the process of the development and implementation of the remotely supervised at-home tDCS. 2) To learn about patient selection criteria for at-home tDCS. 3) To discuss the potential of the at-home tDCS for symptom control in chronically ill patients.

Financial Disclosures: Helena Knotkova, PhD receives funding from the National Institute on Aging, study #5R01AG068167-03 and by the National Institute of Diabetes and Digestive and Kidney Diseases, study #1R01DK131050-01.

Disclosure: No significant relationships.

IS005

Pre-Conference Day
NON-INVASIVE BRAIN STIMULATION: FROM PAIN, TO INFLAMMATORY, TO POST-VIRAL SYMPTOMS - PART 2
12-05-2024 13:45 - 15:30

A NEW DISPOSABLE ELECTROTHERAPY PLATFORM

Mohamad Fallahrad, PhD candidate
City University of New York, Biomedical Engineering Department, New York, United States of America

Introduction and Discussion: We are presenting a novel electrotherapy platform, without any electronic components, using printed abundant environmentally-benign materials. Whereas existing electrotherapy devices use an independent power source and electronics to generate and control stimulation currents, our design eliminates the need for these components, reducing manufacturing complexity and costs. Our novel platform relies only on scalable manufacturing and environmentally-benign common materials. The disposable single-use platform is activated simply by placement on the body. A prescribed electrotherapy discharge is regulated by a novel electrochemical architecture. Production is scalable by relying only on additive manufacturing and low-cost materials, and tailored to any application in a flexible package (as discreet as adhesive bandages). The single-dose nature of this platform is a categorical shift from existing approaches with durable equipment that require programming and assembly to disposable electrodes for each use. Our Wearable Disposable Electrotherapy technology can be distributed like pharmacotherapy, with indications spanning neuromodulation of brain disorders, aesthetics, wound healing, transcutaneous drug delivery, and bioelectronic medicine.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1- Familiarity with a novel platform to design electrotherapy medical devices including for neuromodulation 2- Improvement of current form factor of electrotherapy will help with wider adaption of this technology 3- With this new technology, non-invasive neuromodulation can be prescribed like pharmaceuticals

Financial Disclosures: The City University of New York has patents on neuromodulation and wearable disposable electrotherapy with MFR as inventor.

Disclosure: No significant relationships.

IS006

Pre-Conference Day
NON-INVASIVE BRAIN STIMULATION: FROM PAIN, TO INFLAMMATORY, TO POST-VIRAL SYMPTOMS - PART 2 CONT
12-05-2024 15:55 - 17:15

NON-INVASIVE BRAIN STIMULATION TO TREAT DISORDERS OF HUMAN VERTICALITY

Taiza Edwards, PhD[1,2]
[1]University of Western Australia (UWA), School Of Allied Health, Perth, Australia, [2]University of Sao Paulo-Brazil (USP); The University of Wester Australia-Australia (UWA), Usp: Ribeirao Preto Medical School, Brazil; Uwa: School Of Allied Health, Australia., Ribeirao Preto, Brazil; Perth Australia, Brazil

Introduction and Discussion: The perception of being vertical in our environment is one of the most fundamental aspects of human function. This subconscious ability that evolves during the early years of life becomes impaired in a range of neurological conditions, profoundly affects function in daily life, and impedes functional recovery from brain lesions. The multifaceted neural network that underlies this phenomenon involves a cortical hub that we and others have shown can be modulated with non-invasive stimulation. This presentation will provide an overview of evidence to date and discuss the rationale of a randomized triple-blind sham-controlled clinical trial to assess a new treatment for verticality disorder using high-definition transcranial direct current stimulation (HD-tDCS) in individuals after acute stroke.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1) Understand the methods of assessment and the neurological basis of human verticality perception. - Attendees will be able to describe how to assess verticality perception, the key brain structures involved in the perception of verticality, and how certain neurological conditions impair this fundamental aspect of human function. 2) Recognize current evidence of a neuromodulation treatment for human verticality disorder. - Participants will learn about how non-invasive brain stimulation techniques were used to modulate the cortical networks responsible for human verticality. 3) Evaluate the rationale of ongoing research to treat disorders of human verticality. - Attendees will understand the design of a randomized triple-blind sham-controlled clinical trial to assess a protocol using HD-tDCS to treat visual verticality disorder after acute stroke.

Financial Disclosures:

Disclosure: No significant relationships.

IS007

Pre-Conference Day
NON-INVASIVE BRAIN STIMULATION: FROM PAIN, TO INFLAMMATORY, TO POST-VIRAL SYMPTOMS - PART 2 CONT
12-05-2024 15:55 - 17:15

NON-INVASIVE BRAIN STIMULATION IN REHABILITATION: WHERE ARE WE AND WHERE ARE WE GOING?

Dylan Edwards, Director, Moss Rehabilitation Re[1,2]
[1]Moss Rehabilitation Research Institute, Elkins Park, United States of America, [2]Sidney Kimmel Medical College, Thomas Jefferson University, Rehabilitation Medicine, Philadelphia, United States of America

Introduction and Discussion: Non-invasive brain stimulation as a tool to promote recovery in neurorehabilitation has received significant and growing scientific and clinical interest over more than 15 years. Over this time, the methods have been refined, and the features of rational treatment prescription have advanced. This lecture will feature a presentation of several recently completed and ongoing studies centered on transcranial magnetic stimulation and transcranial direct current stimulation methods. Emphasis will be on recovery of motor function after neurological damage, one of the leading causes of adult disability. Current thinking surrounding key elements for parameter selection and clinical suitability that can impact treatment response will be discussed.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1) Define transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) 2) Provide the rationale for using an inhibitory or facilitatory neuromodulation protocol in neurorecovery 3) Describe the importance of modeling cortical electric fields with TMS and tDCS

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS008

Plenary
OPENING PLENARY SESSION
13-05-2024 08:30 - 10:30

WHY IS NEUROMODULATION EFFECTIVE IN COMPLEX REGIONAL PAIN SYNDROME (CRPS)?

Frank Huygen, MD, PhD
Erasmusmc, Centre Of Pain Medicine, Rotterdam, Netherlands

Introduction and Discussion: Introduction The International Association for the study of Pain (IASP) defines CRPS as "a syndrome characterized by persistent (spontaneous and/or evoked) regional pain that is disproportionate in duration or severity to the usual course following trauma or other lesion. The pain is regional (not in a specific nerve area or dermatome) and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor and/or trophic findings. The syndrome shows variable progression over time'. CRPS is a clinical diagnosis based on diagnostic criteria. Today it is recommended that the new IASP clinical criteria, also known as the Budapest or Harden-Bruehl criteria, be used. Guidelines show that virtually no therapy is effective in CRPS (1). Only neuromodulation repeatedly shows in studies to be an effective therapy (2,3). What is the reason that neuromodulation is effective in CRPS? Discussion In recent years, advances in CRPS research have allowed the complex syndrome to be increasingly well understood. (4). In CRPS, a normal inflammatory response to tissue damage based on a genetic susceptibility and/or an immunologically acquired abnormality runs out of control. This auto-inflammatory response is then responsible for damage in the somatosensory system both at the spinal cord and brain level and damage in a variety of other tissues such as the blood vessel wall. Currently, four CRPS phenotypes are distinguished based on the most prominent signs and symptoms: 1. fulminant, 2. vasomotor dysfunction, 3. nociplastic/neuropathic pain and 4. dystonia. In the fulminant phenotype, inflammation is in the foreground. The vasomotory phenotype is characterized by a cold and cyanotic limb. In the third phenotype, sensory changes such as nociplastic. and neuropathic pain are in the foreground. Motor disorders, such as dystonia, tremor and spasms, occur in the last phenotype. Using biomarkers (SIL6 receptor and CD 163) we can distinguish between inflammation versus residual damage such as central sensitization with nociplastic pain, motor disorders and vasomotor disorders based on endothelial dysfunction (5). Many therapies fail because they target only one of the underlying mechanisms of CRPS. Spinal cord and dorsal root ganglion stimulation are therpies that have effects on multiple underlying mechanisms, namely inflammation, pain, vasomotor and motor changes. This makes neuromodulation a logical mechanism-based therapy in CRPS.

Supplemental Data:

References: 1. Goebel A, Barker CH, Turner-Stokes L et al. Complex regional pain syndrome in adults: UK guidelines for diagnosis, referral and management in primary and secondary care. London: RCP, 2018. 2. Kemler MA, Barendse GA, van Kleef M, de Vet HC, Rijks CP, Furnée CA, van den Wildenberg FA. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. N Engl J Med. 2000 Aug 31;343(9):618-24. 3. Deer TR, Levy RM, Kramer J, Poree L, Amirdelfan K, Grigsby E, Staats P, Burton AW, Burgher AH, Obray J, Scowcroft J, Golovac S, Kapural L, Paicius R, Kim C, Pope J, Yearwood T, Samuel S, McRoberts WP, Cassim H, Netherton M, Miller N, Schaufele M, Tavel E, Davis T, Davis K, Johnson L, Mekhail N. Dorsal root ganglion stimulation yielded higher treatment success rate for complex regional pain syndrome and causalgia at 3 and 12 months: a randomized comparative trial. Pain. 2017 Apr;158(4):669-681. 4. Harden RN, McCabe CS, Goebel A, Massey M, Suvar T, Grieve S, Bruehl S. Complex Regional Pain Syndrome: Practical Diagnostic and Treatment Guidelines, 5th Edition. Pain Med. 2022 Jun 10;23(Suppl 1):S1-S53. 5. Bharwani KD, Dik WA, Dirckx M, Huygen FJPM. Highlighting the Role of Biomarkers of Inflammation in the Diagnosis and Management of Complex Regional Pain Syndrome. Mol Diagn Ther. 2019 Oct;23(5):615-626.

Acknowledgements:

Learning Objectives: 1. Understand new insights in the pathophysiology of CRPS 2. Understand how phenotyping of CRPS patients can personalize therapy and improve effecicacy 3. Understand why neuromodulation is effective in CRPS

Financial Disclosures: Frank Huygen Speaker program ABBOTT, Grunenthal, Saluda 5000-20000 USD

Disclosure: No significant relationships.

IS009

Plenary
OPENING PLENARY SESSION
13-05-2024 08:30 - 10:30

EFFECTS OF DEEP BRAIN STIMULATION ON BRAIN FUNCTION IN OBSESSIVE-COMPULSIVE DISORDER: FROM ANIMAL MODELS TO PATIENTS SPEAKER

Damiaan Denys, MD, PhD
Amsterdam University Medical Centers, Psychiatry, Amsterdam, Netherlands

Introduction and Discussion: Deep Brain Stimulation (DBS) has emerged as a promising therapeutic approach for various neuropsychiatric disorders. This abstract presents an overview of seminal contributions of the Amsterdam group led by Denys to the field of DBS, highlighting key findings from scientific papers that have significantly advanced our understanding and application of this innovative treatment modality. Their pioneering work has played a pivotal role in elucidating the mechanisms and clinical benefits of DBS, with a particular focus on obsessive-compulsive disorder (OCD) and related conditions. One of the group's' notable findings has been the demonstration of the efficacy of DBS in the treatment of severe and treatment-resistant OCD. Through meticulous clinical trials and neuroimaging studies, our work has revealed the specific neural circuits involved in OCD pathophysiology and how DBS can modulate these circuits to alleviate symptoms. Our studies have shown that DBS, when targeted to regions such as the anterior limb of the internal capsule, can result in substantial reductions in OCD symptom severity and improved functional outcomes. Moreover, our research has extended our knowledge by exploring the impact of DBS in animal models. Their scientific papers have showcased how DBS can induce neuroplasticity and reshape aberrant neural circuitry. By conducting experiments in animal subjects, we have demonstrated that DBS can lead to long-lasting changes in neural activity and behavior, shedding light on the underlying mechanisms of this therapeutic approach. In conclusion, our findings, including the targeted alleviation of OCD symptoms in humans and the modulation of neural circuitry in animals, have not only expanded our knowledge of DBS mechanisms but have also paved the way for innovative therapies in the realm of neuropsychiatric disorders. Our multidisciplinary approach, combining clinical investigations and animal studies, has laid a solid foundation for the continued development of DBS as a transformative treatment modality.

Supplemental Data:

References: van den Boom BJG, Elhazaz-Fernandez A, Rasmussen PA, van Beest EH, Parthasarathy A, Denys D, Willuhn I. Unraveling the mechanisms of deep-brain stimulation of the internal capsule in a mouse model. Nat Commun. 2023 Sep 4;14(1):5385. Fridgeirsson EA, Bais MN, Eijsker N, Thomas RM, Smit DJA, Bergfeld IO, Schuurman PR, van den Munckhof P, de Koning P, Vulink N, Figee M, Mazaheri A, van Wingen GA, Denys D. Patient specific intracranial neural signatures of obsessions and compulsions in the ventral striatum. J Neural Eng. 2023 Mar 10;20(2). Graat I, Mocking RJT, Liebrand LC, van den Munckhof P, Bot M, Schuurman PR, Bergfeld IO, van Wingen G, Denys D. Tractography-based versus anatomical landmark-based targeting in vALIC deep brain stimulation for refractory obsessive-compulsive disorder. Mol Psychiatry. 2022 Dec;27(12):5206-5212. Bergfeld IO, Ooms P, Lok A, de Rue L, Vissers P, de Knijff D, Horst F, Beute G, van den Munckhof P, Schuurman PR, Denys D. Efficacy and quality of life after 6-9 years of deep brain stimulation for depression. Brain Stimul. 2022 Jul-Aug;15(4):957-964. Fridgeirsson EA, Figee M, Luigjes J, van den Munckhof P, Schuurman PR, van Wingen G, Denys D. Deep brain stimulation modulates directional limbic connectivity in obsessive-compulsive disorder. Brain. 2020 May 1;143(5):1603-1612.

Acknowledgements:

Learning Objectives: Learning Objective: Understanding the Mechanisms of DBS in Neuropsychiatric Disorders - Explain the underlying neurobiological mechanisms of DBS and how it modulates neural circuits in the context of neuropsychiatric disorders. Describe the specific brain

regions and neural pathways targeted by DBS for conditions like obsessive-compulsive disorder (OCD) and related disorders. Summarize the neurophysiological changes induced by DBS and their impact on symptom relief in patients. **Learning Objective: Evaluating Clinical Applications of DBS in Neuropsychiatry -** Assess the clinical efficacy of DBS as a treatment option for neuropsychiatric disorders. Analyze the ethical considerations and patient selection criteria for DBS interventions in neuropsychiatry. Discuss the potential risks, benefits, and long-term outcomes associated with DBS treatments for different conditions. **Learning Objective: Conducting Animal Studies in DBS Research -** Understand the role of techniques in studying the effects of DBS. Analyze and interpret data to assess changes in brain activity and connectivity before and after DBS interventions. Design and propose research projects to investigate the neural mechanisms of DBS in neuropsychiatric disorders.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS010

Plenary
OPENING PLENARY SESSION CONT
13-05-2024 11:00 - 12:00

AN IN-DEPTH ANALYSIS OF “ASLEEP” VS. “AWAKE” DEEP BRAIN STIMULATION (DBS) – A NEUROLOGIST’S PERSPECTIVE (ARGUMENT FOR AWAKE)

Leo Verhagen Metman, MD, PhD
Northwestern University, Neurology And Neurosurgery, Chicago, United States of America

Introduction and Discussion: DBS for Parkinson’s disease was FDA approved and became a state-of-the-art procedure, based on randomized controlled trials (RCTs) of ‘awake’ DBS vs ‘best medical management’. More recently, asleep DBS has been promoted, but what exactly is ‘asleep DBS’? Asleep DBS is an umbrella-term for DBS procedures, during which the patient is not awake to participate in clinical evaluation. It refers to the level of consciousness of the patient, but not to a particular surgical method. Specifically, it does not imply that surgery is performed under image guidance only; just like “awake DBS” does not imply physiology (microelectrode recording (MER) and test stimulation) was used. In fact, asleep DBS, similar to awake DBS, can be performed with a variety of quite different techniques, making comparison of “asleep and awake DBS” flawed without specifying which technique was used. After this disclaimer, and for the sake of discussion, we will in this presentation use the term ‘asleep’ DBS to indicate DBS under general anesthesia, without feedback from the patient. On the other hand, ‘awake’ DBS will indicate that the patient is conscious while information is obtained through microelectrode recording (MER) and test stimulation. In the absence of RCTs comparing these two modes of surgery, we all rely on our opinions, biased by our own experiences, and on common sense. Using the latter, we will make a case for the value of ‘more, rather than less, information’ when performing DBS procedures. Isn’t it great to know that one is not just in the nucleus, but in the *sensorimotor* part of the nucleus, which is still not visible on MRI, but can be confirmed with MER? And is it not valuable to find out, during the procedure, that one can stimulate up to a decent amplitude and control motor symptoms such as tremor without negatively affecting speech, corticospinal/bulbar fibers, eye movements, or non-motor features? We propose that most would agree with those statements. Why then would one favor the lack of that information? The most commonly heard arguments from those in favor of ‘asleep’ surgery over ‘awake’ DBS are: increased patient comfort, accuracy, safety and ‘similar’ efficacy. These arguments will all be, if not debunked, then at least addressed and placed in today’s context, swinging the pendulum in favor of ‘awake’ DBS.

Supplemental Data:

References: none

Acknowledgements:

Learning Objectives: 1. Explain why comparing 'asleep' and 'awake' dbs, without any further specifications, is flawed. 2. Explain the value of additional information obtained during 'awake' DBS through MER and test stimulation. 3. Discuss how side effects of 'awake' surgery have diminished over the years due to technical and procedural advances.

Financial Disclosures: No relevant disclosures, no significant relationships.

Disclosure: No significant relationships.

IS011

Plenary
OPENING PLENARY SESSION CONT
13-05-2024 11:00 - 12:00

AN IN-DEPTH ANALYSIS OF “ASLEEP” VS. “AWAKE” DEEP BRAIN STIMULATION (DBS) – A NEUROSURGEON’S PERSPECTIVE (ARGUMENT FOR ASLEEP)

Kim Burchiel, MD, Shirley McCartney, PhD, Luyuan Li, MD
Oregon Health and Science University, Neurological Surgery, Portland, United States of America

Introduction and Discussion: Deep Brain Stimulation (DBS) has become an important surgical modality for the surgical treatment of movement disorders, and this technology is currently being expanded to treat numerous other conditions. Early studies on DBS relied on an awake and behaving patient intra-operatively, and typically utilized microelectrode recording (MER) to verify target acquision, with variable and additional examination and testing of the patient (1). The use of MER in this context presents unique challenges in that it typically requires an awake patient, the presence of advanced neurophysiologic expertise, and specialized equipment and intrumentation. With the development of improved MRI imaging, and sterotactic image-guidance work stations, fully image-guided surgery under general anesthesia has emerged as a viable alternative to the more traditional MER-guided approach (2). Asleep DBS appears to have a much reduced incidence of intracranial air, thus diminishing the influence of "brain shift" (3). Asleep surgery also appears to be a cost-effective approach to the placement of DBS electrodes (4). Retrospective comparisons for several studies, chiefly Parkinson's Disease (PD), but including DBS for Essential Tremor (ET), have not demonstrated a significant difference in outcomes for these differing approaches (5-12). A recent trial of MER-assisted DBS for patients with Parkinson disease, using frame-based microelectrode-guided asleep DBS was associated with similar cognitive, mood, and behavioral adverse effects compared with awake DBS. Both groups showed equal improvement in motor function and surgery under general anesthesia was faster and less burdensome for the patient (13) In another study, the outcomes of image-guided asleep DBS for PD were, in fact, superior when compared to an historical cohort which utilized MER in awake patients treated by the same surgeon (14). A sizeable body of data indicates that MER appears to introduce additional risks to the DBS procedure (15), and a population study has shown that an estimated 10-15% of patients need revision for misplacement of the electrode despite MER-guided DBS (16). As the indications for DBS expand, and white matter targets become even more important, the role of MER will likely diminish, further weakening the argument for awake DBS surgery. This presentation will highlight the evidence for asleep DBS, focussing on a recently completed systematic review of the literature on the merits of asleep and awake DBS surgery. Currently there appears to be no evidence that awake DBS surgery offers any advantage for the outcome of these procedures when compared to asleep DBS, and may present additional risk.

Supplemental Data:

References: 1. Israel, Z, BURCHIEL KJ (eds): Microelectrode Recording in Movement Disorder Surgery. Thieme, New York, 2004 2. BURCHIEL KJ, McCartney S, Lee A, Raslan AM. Accuracy of deep brain stimulation electrode placement using intraoperative computed tomography without microelectrode recording. J Neurosurg;119(2):301-306, 2013 3. Ko AL, Magown P, Ozpinar A, Hamzaoglu V, BURCHIEL KJ. Asleep Deep Brain Stimulation Reduces Incidence of Intracranial Air during Electrode Implantation. Stereotact Funct Neurosurg. 96(2):83-90, 2018. 4. Jacob RL, Geddes J, McCartney S, BURCHIEL KJ. Cost analysis of awake versus asleep deep brain stimulation: a single academic health center experience. J Neurosurg. 2016;124(5):1517-1523. 5. Chen T, Mirzadeh Z, Chapple K, Lambert M, Dhall R, Ponce FA. "Asleep" deep brain stimulation for essential tremor. J Neurosurg. 2016 Jun;124(6):1842-9. doi: 10.3171/2015.6.JNS15526. Epub 2015 Nov 27. 6. Chen T, Mirzadeh Z, Chapple K, Lambert M, Ponce FA. Complication rates, lengths of stay, and readmission rates in "awake" and "asleep" deep brain simulation. J Neurosurg. 2017 Aug;127(2):360-369. doi: 10.3171/2016.6.JNS152946. Epub 2016 Sep 23. 7. Chen T, Mirzadeh Z, Ponce FA. "Asleep" Deep Brain Stimulation Surgery: A Critical Review of the Literature. World Neurosurg. 2017 Sep;105:191-198. doi: 10.1016/j.wneu.2017.05.042. Epub 2017 May 16. 8. Chen T, Mirzadeh Z, Chapple KM,

Lambert M, Shill HA, Moguel-Cobos G, Tröster AI, Dhall R, Ponce FA.Clinical outcomes following awake and asleep deep brain stimulation for Parkinson disease. J Neurosurg. 2018 Mar 16;130(1):109-120. doi: 10.3171/2017.8.JNS17883.PMID: 29547091 9. Sheshadri V, Rowland NC, Mehta J, Englesakis M, Manninen P, Venkatraghavan L. Comparison of General and Local Anesthesia for Deep Brain Stimulator Insertion: A Systematic Review. Can J Neurol Sci. 2017 Nov;44(6):697-704. doi: 10.1017/cjn.2017.224. Epub 2017 Sep 18. Lefranc M, Zouitina Y, Tir M, Merle P, Ouendo M, Constans JM, Godefroy O, Peltier J, Krystkowiak P. 10. Asleep Robot-Assisted Surgery for the Implantation of Subthalamic Electrodes Provides the Same Clinical Improvement and Therapeutic Window as Awake Surgery. World Neurosurg. 2017 Oct;106:602-608. doi: 10.1016/j.wneu.2017.07.047. Epub 2017 Jul 19. 11. Ho AL, Ali R, Connolly ID, Henderson JM, Dhall R, Stein SC, Halpern CH. Awake versus asleep deep brain stimulation for Parkinson's disease: a critical comparison and meta-analysis. J Neurol Neurosurg Psychiatry. 2018 Jul;89(7):687-691. doi: 10.1136/jnnp-2016-314500. Epub 2017 Mar N1. 12. Lee AT, Han KJ, Nichols N, Sudhakar VR, Burke JF, Wozny TA, Chung JE, Volz MM, Ostrem JL, Martin AJ, Larson PS, Starr PA, Wang DD.Targeting Accuracy and Clinical Outcomes of Awake versus Asleep Interventional Magnetic Resonance Imaging-Guided Deep Brain Stimulation for Parkinson's Disease: The University of California, San Francisco Experience. Neurosurgery. 2022 Nov 1;91(5):717-725. doi: 10.1227/neu.0000000000002111. Epub 2022 Sep 7.PMID: 36069560 13. Holewijn RA, Verbaan D, van den Munckhof PM, Bot M, Geurtsen GJ, Dijk JM, Odekerken VJ, Beudel M, de Bie RMA, Schuurman PR. General Anesthesia vs Local Anesthesia in Microelectrode Recording-Guided Deep-Brain Stimulation for Parkinson Disease: The GALAXY Randomized Clinical Trial. JAMA Neurol. 2021 Oct 1;78(10):1212-1219. doi: 10.1001/jamaneurol.2021.2979.PMID: 34491267 14. Brodsky MA, Anderson S, Murchison C, Seier M, Wilhelm J, Vederman A, BURCHIEL K: Clinical outcomes of asleep vs awake deep brain stimulation for Parkinson disease. Neurology 89:1-7, 2017. 15. Zrinzo L, Foltynie T, Limousin P, Hariz MI: Reducing hemorrhagic complications in functional neurosurgery: a large case series and systematic review. J Neurosurg Sept 2011. DOI: 10.3171/2011.8.JNS10147 16. John D Rolston, Dario J Englot, Philip A Starr, Paul S Larson. An unexpectedly high rate of revisions and removals in deep brain stimulation surgery: Analysis of multiple databases. Parkinsonism Relat Disord 2016 Dec:33:72-77. doi: 10.1016/j.parkreldis.2016.09.014. Epub 2016 Sep 12. PMID: 27645504

Acknowledgements:

Learning Objectives: Attendees will be able to: 1. Describe the evidence that demonstrates that the motor outcomes of awake and asleep DBS for Parkinson's Disease are not significantly different 2. Discuss the evidence that microelectrode recording (MER)-guided DBS surgery introduces additional risks when compared to direct image-guided targetting not utilizing MER. 3. Describe the evidence that asleep DBS without MER guidance reduces intracranial air, and the risk of brain shift.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS012

Breakout Session
SPINE – MECHANISMS OF ACTION
13-05-2024 14:30 - 16:00

SURROUND INHIBITION MECHANISM OF ACTION

Warren Grill, Professor
Duke University, Biomedical Engineering, Durham, United States of America

Introduction and Discussion: We combined computational modeling and in vivo measurements to investigate the mechanisms of action of pain relief by low-frequency (< 200 Hz), sub-perception spinal cord stimulation (SCS). We simulated an integrated computational model of the effects of SCS on dorsal column (DC) axons and quantified subsequent downstream impact on dorsal horn (DH) neurons in a neural circuit model. We measured the responses of DC axons and DH neurons across a range of stimulation locations, frequencies, and amplitudes in urethane-anesthetized rats. DC axons responded asynchronously to 90 Hz SCS with irregular spiking. DH neurons were maximally inhibited by SCS delivered to the surround receptive field, and inhibition was greatest during low-frequency (90 Hz), low amplitude (40 % motor threshold) SCS. Decreasing the strength of inhibitory synapses in the model or application of intrathecal bicuculline in the experiments reduced the inhibition of nociceptive neuron by SCS. These results suggest that low-frequency low-amplitude SCS engages surround inhibitory mechanisms by activation of dorsal column axons that engage GABAergic mechanisms to inhibit DH nociceptive neurons and generate pain relief.

Supplemental Data:

References: None

Acknowledgements: This work was supported by a grant to Duke University from Boston Scientific Corporation.

Learning Objectives: 1. Understand the response of dorsal column axons to low-frequency low-amplitude SCS 2. Understand the response of dorsal horn neurons to low-frequency low-amplitude SCS 3. Understand the surround inhibitory mechanism of SCS

Financial Disclosures: WMG has received royalty payments from Boston Scientific Corporation for licensed I.P. WMG received compensation from Boston Scientific as a member of the Neuromodulation Scientific Advisory Board.

Disclosure: No significant relationships.

IS013

Breakout Session
SPINE – MECHANISMS OF ACTION
13-05-2024 14:30 - 16:00

ROLE OF SPIKE SYNCHRONY IN PERCEPTION IN THE OPTIMIZATION OF SPINAL CORD STIMULATION (SCS)

Steve Prescott, MD PhD
The Hospital for Sick Children, Neurosciences And Mental Health, Toronto, Canada

Introduction and Discussion: Vibrotactile stimulation activates low-threshold mechanoreceptive afferents (LTMRs), producing sensations of flutter or vibration depending on the stimulus frequency. The intensity (loudness) of the percept depends on stimulus amplitude whereas the pitch depends on stimulus frequency. Importantly, activating LTMRs also inhibits pain, as explained by gate control theory, prompting the use of spinal cord stimulus (SCS) to activate LTMRs electrically to alleviate chronic pain. As expected, conventional SCS (c-SCS) at 40-60 Hz causes paresthesia whose intensity scales with the number of activated LTMRs, as reflected in the amplitude of evoked compound action potentials (ECAPs). Yet SCS at kilohertz frequency (kf-SCS) relieves pain without causing paresthesia. If LTMR activation is responsible for the analgesic effects of SCS but normally causes paresthesia, then how does kf-SCS reduce pain without causing paresthesia. In my presentation, I will demonstrate that paresthesia is absent during kf-SCS not because axons do not spike, but because they spike less synchronously than during c-SCS. Spikes evokes by kf-SCS still phase-lock to the electrical pulses but, when pulses are repeated at an interval shorter than the axon's refractory period of about 3 ms, each axon cannot spike on consecutive pulses and instead starts responding intermittently. Different axons respond on different pulses, resulting in relatively few axons responding to each pulse, which in turn leads to smaller ECAPs and diminished paresthesia; in other words, SCS-evoked spikes desynchronize at high stimulation rates. We refer to this phenomenon as overdrive desynchronization. When stimulating with high-rate, high-amplitude pulses, responses to the first several pulses can be highly synchronized (and cause paresthesia) since it takes several cycles before neurons "get out of step". This can be avoided by ramping up the amplitude gradually so that neurons with different thresholds are activated on different pulses; this staggered start allows neurons to respond asynchronously from stimulus onset. They remain asynchronous (despite pulse amplitude eventually stabilizing at its target value) thanks to overdrive desynchronization. Unlike synchronous spikes, asynchronous spikes fail to produce paresthesia because their transmission to somatosensory cortex is blocked by feedforward inhibition. Our results demonstrate how stimulation frequency impacts synchrony based on axon properties, and how synchrony impacts sensation based on circuit properties.

Supplemental Data:

References: Sagalajev B, Zhang T, Abdollahi N, Yousefpour N, Medlock L, Al-Basha D, Ribeiro-da-Silva A, Esteller R, Ratté S, Prescott SA.
Absence of paresthesia during during high-rate spinal cord stimulation reveals importance of synchrony for sensations evoked by electrical stimulation.
Neuron, published online Nov 15, 2022, https://doi.org/10.1016/j.neuron.2023.10.021

Acknowledgements: The research was funded by a grant from Boston Scientific Neuromodulation, a Foundation Grant FDN167276 from the Canadian Institutes of Health Research, and a John Edwards Leadership Fund award CFI37493 from the Canadian Foundation for Innovation. Boriss Sagalajev, Tianhe Zhang, Nooshin Abdollahi, Noosha Yousefpour, Laura Medlock, Dhekra Al-Basha, Alfredo Ribeiro-da-Silva, Rosana Esteller, and Stéphanie Ratté all contributed to the research reported in this presentation.

Learning Objectives: 1. To better understand neural coding strategies. Specifically, neural information can be encoded by firing rate and spike timing/synchronization. Synchrony is important for if/how neural spiking is perceived and it is, therefore, important to consider the basis for and

consequences of synchronization, including how synchrony can be modulated by SCS. 2. To better appreciate how the biophysical properties of axons influence their response to electrical stimulation. Specifically, an axon's refractory period restricts spiking at short intervals (<3 ms), which directly contributes to deynchronization. Increased excitability at intermediate intervals (3-10 ms) can encourage temporal summation of subthreshold pulses, and interacts with even slower adaptation to produce bursting. 3. To better appreciate how neural circuits process information, including how that processing depends on synchrony. Specifically, feedforward inhibition tends to block synaptic relay of asynchronous spikes while selectively allowing synaptic relay of synchronous spikes.

Financial Disclosures: Boston Scientific, Consultant / Advisory Board, $5,001 - $20,000 USD Boston Scientific, Research Funding, > $100,000 USD Presidio Medical, Consultant / Advisory Board, $5,001 - $20,000 USD Presidio Medical, Research Funding, > $100,000 USD

Disclosure: No significant relationships.

IS014

Breakout Session
SPINE – MECHANISMS OF ACTION
13-05-2024 14:30 - 16:00

PHYSIOLOGICAL EFFECTS AND MECHANISMS OF ACTION OF SPINAL CORD STIMULATION TO TREAT PAIN: INSIGHTS FROM COMPUTATIONAL MODELS AND QUANTITATIVE SENSORY TESTING

Scott Lempka, Associate Professor
University of Michigan, Biomedical Engineering, Ann Arbor, United States of America

Introduction and Discussion: Spinal cord stimulation (SCS) is an established treatment for chronic pain, yet the underlying physiological mechanisms are not understood. This talk presents research utilizing both advanced computational models and empirical quantitative sensory testing (QST) to elucidate the physiological effects and mechanisms of action of SCS. We employ a hybrid computational modeling framework, combining the finite element method with multicompartment cable models, to estimate the neural response to SCS. This approach enables us to systematically dissect the influence of variable waveform parameters (such as frequency) and anatomical parameters (such as the presence of axon collaterals) on SCS-induced pain relief. In parallel, we conduct prospective clinical studies using QST to characterize the impact of SCS on sensory processing. Our computational models suggest that high-frequency stimulation reduces activation thresholds and induces asynchronous activation within the dorsal columns. These models also indicate that the pain output from the dorsal horn is sensitive to variations in spike timing and conduction failure within axon collaterals, which can occur at high stimulation frequencies. Our clinical research reveals marked improvements in several facets of chronic pain over time with SCS. Through QST, we have detected modest evidence for SCS-induced changes in sensory processing, such as a decrease in temporal summation at the primary pain site that was not observed at a non-painful control site. These findings provide limited evidence that the suppression of spinal neuron hyperexcitability may contribute to the analgesic mechanisms of SCS. Overall, this presentation will highlight the potential of integrating computational and empirical approaches to gain a deeper understanding of the complex biophysical interactions at play in SCS, ultimately aiming to refine therapeutic strategies for the treatment of chronic pain. Our integrative approach paves the way for a more precise and tailored application of SCS, potentially enhancing outcomes for patients afflicted with debilitating pain conditions.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1) Enhance understanding of spinal cord stimulation (SCS) mechanisms Desired result: Attendees will be able to articulate the key physiological processes and neural responses involved in SCS as explained through the advanced computational models presented. 2) Demonstrate the application of quantitative sensory testing (QST) in assessing SCS outcomes Desired result: Participants will understand how QST methods are used in the context of clinical research to measure changes in sensory processing due to SCS. 3) Encourage interdisciplinary approach in chronic pain treatment research Desired result: Attendees will appreciate the significance of combining computational models with empirical research for advancing SCS therapies.

Financial Disclosures: Scott Lempka, Abbott Neuromodulation, Consultant / Advisory Board, $501 - $5,000 USD Scott Lempka, CereGate, Consultant / Advisory Board and Stockholder, $1-500 USD Scott Lempka, Hologram Consultants, LLC, Stockholder Stock Value >5%, $1-500 USD Scott Lempka, Neuronoff, Inc., Stockholder, $1-500 USD Scott Lempka, Presidio Medical, Inc., Consultant / Advisory Board and Stockholder, $1-500 USD

Disclosure: No significant relationships.

IS015

Breakout Session
SPINE – MECHANISMS OF ACTION
13-05-2024 14:30 - 16:00

MECHANISM OF PERIPHERAL NERVE STIMULATION (PNS), SPINAL CORD STIMULATION (SCS): SUPRASPINAL MECHANISMS AND MECHANISMS OF ACTION (MOA)

Eellan Sivanesan, MD
Johns Hopkins, Department Of Anesthesiology, Baltimore, United States of America

Introduction and Discussion: Description: Spinal cord and peripheral nerve stimulation are being used to treat an ever-expanding array of chronic pain conditions. Furthermore, they are also being applied experimentally for treatment of non-painful conditions including movement disorders, ischemia, and other neurological disorders. A better understanding of the underlying mechanisms of these therapies may allow refinement of patient selection, improvement in treatment response, and further expansion of indications. Mechanisms can broadly be categorized as peripheral, spinal, and supraspinal. In this succinct presentation, we will explore potential supraspinal mechanisms of spinal cord and peripheral nerve stimulation.Description: Spinal cord and peripheral nerve stimulation are being used to treat an ever-expanding array of chronic pain conditions. Furthermore, they are also being applied experimentally for treatment of non-painful conditions including movement disorders, ischemia, and other neurological disorders. A better understanding of the underlying mechanisms of these therapies may allow refinement of patient selection, improvement in treatment response, and further expansion of indications. Mechanisms can broadly be categorized as peripheral, spinal, and supraspinal. In this succinct presentation, we will explore potential supraspinal mechanisms of spinal cord and peripheral nerve stimulation.

Supplemental Data:

References: Sivanesan, Eellan, Dermot P. Maher, Srinivasa N. Raja, Bengt Linderoth, and Yun Guan. "Supraspinal mechanisms of spinal cord stimulation for modulation of pain: five decades of research and prospects for the future." Anesthesiology 130, no. 4 (2019): 651-665. Parker, Tariq, Yongzhi Huang, Ashley LB Raghu, James FitzGerald, Tipu Z. Aziz, and Alexander L. Green. "Supraspinal effects of dorsal root ganglion stimulation in chronic pain patients." Neuromodulation: Technology at the Neural Interface 24, no. 4 (2021): 646-654.

Acknowledgements:

Learning Objectives: Review potential supraspinal mechanisms of spinal cord and peripheral nerve stimulation.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS016

Breakout Session
SPINE – MECHANISMS OF ACTION
13-05-2024 14:30 - 16:00

POTENTIAL MECHANISMS OF NOVEL NEUROMODULATION TECHNOLOGIES / THERAPY

Andrei Sdrulla, PhD
Oregon Health Sciences, Anesthsiology, Oregon, United States of America

Introduction and Discussion: Epidural spinal cord stimulation (SCS) has been used for over 50 years to treat refractory pain and avoid addictive opioid therapies. However, there is an incomplete understanding of how these neuromodulatory devices mediate pain relief, which has precluded effective clinical implementation. One of the mechanisms of SCS-mediated pain relief is believed to be through the activation of inhibitory superficial dorsal horn circuits, as elegantly proposed in the Gate Control Theory. This talk will focus on recent basic science advances on the modulatory effects of novel SCS waveforms on dorsal horn populations, including excitatory, inhibitory, and projection neurons. The presentation will blend information from the latest publications with data obtained from our laboratory to provide a comprehensive overview of how SCS modulates the dorsal horn. Furthermore, we will present the limitations of current models, and provide an outlook for future research.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1) Appreciate the diversity of dorsal horn populations within the context of Gate Control Theory. 2) Understand the significance of stimulation parameters on neuronal activation. 3) Describe the effects of dorsal column stimulation on dorsal horn neurons.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

IS017

Breakout Session
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 14:30 - 16:00

MICROCIRCUIT ENGAGEMENT AT THE SINGLE NEURON RESOLUTION

Luka Milosevic, PhD
University Health Network, Krembil Brain Institute, Toronto, Canada

Introduction and Discussion: Deep brain stimulation (DBS) is a chronic neuromodulatory intervention which provides symptomatic relief in a growing number of neurological indications. In this symposium, our group aims to provide a broad yet complimentary perspective of DBS mechanisms across spatiotemporal scales; from single synapses to whole-brain systems. In this talk, I will focus on scientific insights gained from intraoperative microelectrode recordings from the basal ganglia, during which we employ stimulation/recording techniques to investigate effects of DBS at the subcortical circuit level. Across various studies, we have employed a multi-modal approach combining microelectrode recordings of single-neuron and evoked potential activities, computational modelling, and high-resolution spatial mapping. Through such investigations, we demonstrate how an understanding of circuit-specific anatomical (i.e., circuit architecture) and physiological (i.e., short-term synaptic plasticity) properties can help us gain a better understanding of how current implementations of DBS may work. We show that high-frequency stimulation may depend upon reliable activation of inhibitory projections of the globus pallidus externus (GPe), which are otherwise considered to be downregulated in Parkinson's disease (PD). In other works, we show how DBS can be employed to produce long-lasting functional strengthening (i.e., long-term synaptic plasticity) of downregulated circuits, and how this approach may represent an alternative method to produce benefit which outlasts stimulation cessation. Discussion: In the context of DBS for PD, there remains debate as to how DBS may exert its therapeutic effect. Many studies have placed emphasis on the importance of antidromic activation of cortico-subthalamic fibers as having a putative role in producing benefit; however, it has been shown that this phenomenon may not directly extend to DBS of the globus pallidus internus (GPi), a stimulation target which yields benefit similar to the subthalamic nucleus (STN). As such, we argue in favour of a subcortical circuit activation phenomenon that may be able to explain the common efficacy of GPi- and STN-DBS in PD, and we provide preliminary evidence of alternative methods to produce benefit using less stimulation.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1. Discuss possible mechanisms by which DBS exerts therapeutic benefit. 2. Understand how anatomical and physiological properties jointly contribute to electrophysiological responses. 3. Discuss the potential role for long-term functional circuit manipulaitons.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS018

Breakout Session
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 14:30 - 16:00

DEEP BRAIN STIMULATION INDUCED NEUROPHYSIOLOGICAL EFFECTS TO GUIDE TREATMENT OF MOVEMENT DISORDERS

Kara Johnson, PhD[1], Jackson Cagle, PhD[1], Justin Hilliard, MD[2], Kelly Foote, MD[2], Coralie De Hemptinne, PhD[1]
[1]University of Florida, Norman Fixel Institute For Neurological Diseases, Gainesville, United States of America, [2]University of Florida, Neurosurgery, Gainesville, United States of America

Introduction and Discussion: Deep brain stimulation (DBS) targeted to the subthalamic nucleus (STN) or the globus pallidus internus (GPi) is an effective therapy to alleviate motor symptoms in select patients with Parkinson's disease (PD). However, identifying effective stimulation parameters is currently a trial-and-error process that requires extensive time and effort, especially with the advent of DBS leads capable of directional stimulation. Objective markers of therapeutic DBS are needed to tailor stimulation on a patient-specific basis and to fully leverage directional stimulation capabilities. Several neurophysiological markers to guide DBS in PD have been explored, mainly focused on neural activity in the beta frequency band (13-30 Hz) within the basal ganglia and other nodes of the motor network. Recent research has also been exploring a novel marker called evoked resonant neural activity (ERNA), a high-frequency (200-500 Hz) oscillatory evoked potential elicited by DBS in the STN region and the GPi/GPe [1]. ERNA is hypothesized to be generated through modulation of reciprocal connections within the pallido-STN circuit. Previous studies have shown that ERNA may be localized to the optimal target region and may be associated with chronic therapeutic stimulation parameters [2,3]. However, it is unclear whether ERNA is tuned to stimulating in specific directions and could guide the selection of directional parameters for chronic therapy. Our recent research has investigated the directional tuning of ERNA in the STN and GPi in patients undergoing DBS for PD. The results suggest that ERNA elicited by DBS in the GPi and STN shows spatio-directional tuning both within individuals and at a group level. Variability in directional tuning across individuals may reflect differences in stimulating contact locations relative to the ERNA "hotspot" in each of these targets. Additionally, patients seem to exhibit individualized ERNA "profiles" with variations in how ERNA responds to different stimulation contacts, amplitudes, and frequencies. In conclusion, ERNA shows promise as a marker to guide DBS for PD, given its anatomical localization, sensitivity to specific stimulation parameters (including directional stimulation), and correlation with chronic therapeutic DBS parameters and outcomes. Further prospective studies are needed to investigate the predictive power of ERNA to guide DBS for PD.

Supplemental Data:

References: [1] Sinclair NC, McDermott HJ, Bulluss KJ, Fallon JB, Perera T, Xu SS, et al. Subthalamic nucleus deep brain stimulation evokes resonant neural activity. Annals of Neurology 2018;83:1027–31. https://doi.org/10.1002/ana.25234. [2] Johnson KA, Cagle JN, Lopes JL, Wong JK, Okun MS, Gunduz A, et al. Globus pallidus internus deep brain stimulation evokes resonant neural activity in Parkinson's disease. Brain Communications 2023;5:fcad025. https://doi.org/10.1093/braincomms/fcad025. [3] Steiner LA, Crompton D, Sumarac S, Vetkas A, Germann J, Scherer M, et al. Neural signatures of indirect pathway activity during subthalamic stimulation in Parkinson's disease. Nat Commun 2024;15:3130. https://doi.org/10.1038/s41467-024-47552-6.

Acknowledgements: This research was supported by the Parkinson's Foundation and the Norman Fixel Institute for Neurological Diseases at the University of Florida.

Learning Objectives: 1. Understand the current neurophysiological markers used to guide DBS treatment of PD 2. Explain the circuit origins of evoked potentials with pallidal and STN DBS 3.

Understand the potential applications of evoked potentials and other neurophysiological markers to guide DBS for PD

Financial Disclosures: Kara A. Johnson: No significant relationships. Jackson N. Cagle: No significant relationships. Justin D. Hilliard: No significant relationships. Kelly D. Foote: Medtronic, Boston Scientific, and Functional Neuromodulation (Education/Research: $501-$5000 to the university). Coralie de Hemptinne: No significant relationships.

Disclosure: No significant relationships.

IS019

Breakout Session
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 14:30 - 16:00

ELECTROCORTICOGRAPHY IN INVESTIGATION OF CORTICO-SUBCORTICAL DYNAMICS

Philip Starr, MD, PhD
University of California San Fransisco, Neurological Surgery, San Fransisco, United States of America

Introduction and Discussion: Introduction: Despite its widespread application in movement disorders, the mechanism of action of deep brain stimulation (DBS) is still debated. Speakers in this symposium will address this at different spatiotemporal scales, from synapses and neurons to whole brain imaging. Here, I will discuss the effects of basal ganglia DBS on sensorimotor cortical function, assessed using subdural electrocorticography (ECoG). ECoG provides excellent temporal and spatial resolution, but at the expense of limited spatial coverage compared to neuroimaging. We focused on sensorimotor cortex because foundational models of movement disorders pathophysiology implicated primary or supplementary motor areas as critical sites mediating the therapeutic effects of stimulation. We utilized both acute and chronic recording paradigms. Acute studies were performed intraoperatively in awake patients, using temporary ECoG strips. Chronic studies utilized novel fully implantable bidirectional (sensing + stimulation) neural interfaces, with permanently implanted subdural strips. These allow invasive electrophysiological research, and feedback-controlled stimulation, over long periods during normal daily activities at home. In Parkinson's disease (PD), therapeutic DBS at either of the basal ganglia targets commonly implanted, subthalamic nucleus or globus pallidus, has several effects on motor cortical activity: 1) Reduction in abnormality elevated basal ganglia-cortex coherence at 13-30 Hz beta frequency bands. 2) Reduction in abnormally elevated cross frequency interactions. 3) Induction of 60-90 Hz gamma band oscillations, similar to those induced by levodopa. Of note, DBS can entrain gamma oscillations at subharmonics of the stimulation frequency, and *unilateral* stimulation can entrain *bilateral* gamma oscillations. At stimulation amplitudes higher than the therapeutic levels, entrained gamma band activity may decrease. Many of these effects can also be observed in neurostimulation for isolated dystonia. Discussion: Therapeutic DBS has profound effects on motor cortical activity at fast time scales, reducing the influence of beta band oscillatory activity, while promoting narrowband gamma activity at 60-90 Hz. These effects are broadly consistent with the hypothesis that movement disorders arise from an imbalance between antikinetic beta rhythms and prokinetic gamma rhythms. Effective therapies in PD (levodopa, pallidal ablation, and STN or pallidal DBS) act to rebalance this equation.

Supplemental Data:

References: none

Acknowledgements:

Learning Objectives: 1. Understand effects of therapeutic deep brain stimulation on cortical activity at fast time scales. 2. Discuss possible mechanisms by which DBS exerts therapeutic effecs. 3. Relate mechanisms of DBS at different spatial and temporal scales

Financial Disclosures: Philip Starr: Medtronic, Inc. provides investigational devices at no cost Philip Starr: Medtronic, Inc. and Boston Scientific Inc. provide funding to support clinical fellowships

Disclosure: No significant relationships.

IS020

Breakout Session
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 14:30 - 16:00

MODULATORY INFLUENCE ON BRAIN-WIDE NETWORK CONNECTOMICS

Barbara Hollunder, MSc[1,2,3]
[1]Charité – Universitätsmedizin Berlin, Movement Disorders And Neuromodulation Unit, Department Of Neurology With Experimental Neurology, Berlin, Germany, [2]Charité – Universitätsmedizin Berlin, Einstein Center For Neurosciences Berlin, Berlin, Germany, [3]Humboldt-Universität zu Berlin, Berlin School Of Mind And Brain, Berlin, Germany

Introduction and Discussion: Deep brain stimulation (DBS) is an effective symptomatic treatment for various brain disorders, targeted at restoring healthy circuit function (1). In this symposium, speakers aim to provide a synthesis of stimulation-invoked circuit alterations through time and space, at micro-, meso-, and macro-levels (2). My talk will focus on the role of neuroimaging-based connectomics in identifying brain-wide DBS effects at the macro-level and their implications for clinical application. This vantage point complements invasive neurophysiology techniques by extending the field of observation towards whole-brain coverage (2). To explore remote DBS effects on distributed circuitry, our group relates advanced structural or functional magnetic resonance imaging data to clinical stimulation effects as a function of the precise localization of variably placed DBS electrodes (3,4). At the cohort level, optimal whole-brain connectivity profiles of DBS electrodes can be modeled that are linked to improvements in a given behavioral or cognitive dysfunction. As such, this method allows to systematically map out what we describe as the human 'dysfunctome' – or the spatial distribution of dysfunctional connections resulting from specific circuitopathies that can be downregulated by means of successful neuromodulation (5). We applied this concept across the diverse cardinal dysfunctions present in four different brain disorders, which all profit from subthalamic DBS: dystonia, Parkinson's disease, Tourette's syndrome, and obsessive-compulsive disorder. The resulting topographical organization of dysfunction mappings followed a caudo-rostral pattern, spanning from circuits involving sensorimotor (dystonia), motor / premotor (Tourette's syndrome), supplementary motor (Parkinson's disease), toward prefrontal-most cortices (obsessive-compulsive disorder) (5). Retrospective and prospective evidence supports the potential of these findings in guiding clinical decision making. An increasing spatial resolution of such mappings promises flexibility in addressing circuit dysfunctions that extend beyond the core symptomatology of a given disorder. This can be illustrated on the example of obsessive-compulsive disorder where we identified a set of therapeutic DBS subsymptom networks relevant to the phenotypical heterogeneity within this complex condition (including symptoms such as obsessions, compulsions, depression, or anxiety). Finally, I will provide an outlook into the concept of 'symptom network blending' as a strategy for personalized targeting and stimulation parameter optimization to the heterogeneous symptom profiles of individual patients (4). In conclusion, neuromodulation-derived dysfunction mappings may bear relevance as targets for stereotactic planning and neurosurgery, and potentially for non-invasive neuromodulation, through association with prior therapeutic effectiveness. They could further play a role in managing symptoms that transcend various diagnoses, or for tailoring treatments to individual symptom constellations.

Supplemental Data:

References: 1. Neumann WJ, Horn A, Kühn AA (2023): Insights and opportunities for deep brain stimulation as a brain circuit intervention. *Trends Neurosci* 46: 472–487. 2. Neumann W-J, Steiner LA, Milosevic L (2023): Neurophysiological mechanisms of deep brain stimulation across spatiotemporal resolutions. *Brain* 146: 4456–4468. 3. Horn A, Fox MD (2020): Opportunities of connectomic neuromodulation. *Neuroimage* 221: 117180. 4. Hollunder B, Rajamani N, Siddiqi SH, Finke C, Kühn AA, Mayberg HS, *et al.* (2022): Toward personalized medicine in connectomic deep brain stimulation. *Prog Neurobiol* 210: 102211. 5. Hollunder B, Ostrem JL, Sahin IA, Rajamani N, Butenko K, Neudorfer C, *et al.* (2023): Mapping dysfunctional circuits in the frontal cortex using deep brain stimulation. *medRxiv*. https://doi.org/10.1101/2023.03.07.23286766

Acknowledgements:

Learning Objectives: 1. Understand the role of neuroimaging-based connectomics in mapping brain-wide DBS effects at the macro-level. 2. Learn how neuromodulation-derived mappings at increasing levels of granularity can be instrumental in delineating the human 'dysfunctome'. 3. Explore the clinical implications of dysfunction mappings for treatment tailored to individual symptom profiles.

Financial Disclosures: No significant relationship.

Disclosure: No significant relationships.

IS021

Breakout Session
NEUROMODULATION FOR MOVEMENT DISORDERS
13-05-2024 14:30 - 16:00

DIRECTIONALITY IN DEEP BRAIN STIMULATION (DBS) FOR MOVEMENT DISORDERS – SHOULD OMNIDIRECTIONAL STIMULATION BE ABANDONED?

Jan Vesper, MD
University Medical Center, Heinrich Heine University, Functional Neurosurgery And Stereotaxy, Duesseldorf, Germany

Introduction and Discussion: Published reports on directional Deep Brain Stimulation (DBS) have been limited to small, single-center investigations. Therapeutic window (TW) is used to describe the range of stimulation amplitudes achieving symptom relief without side effects. The PROGRESS study proofed the advantages of directional vs omnidirectional DBS in a large cohort of patients implanted with a DBS system in the subthalamic nucleus for Parkinson's disease. Futhermore a registry is undergoing regarding the outcomes from the use of directional Deep Brain Stimulation (DBS) systems equipped with Multiple Independent Current Control (MICC) in patients with Parkinson's disease (PD). Directional DBS systems can deliver specific amounts of current to each contact using MICC, and this capability has been shown to increase therapeutic window under controlled study conditions. In so doing, vertical and horizontal steering of cathodic and/or anodic current can be achieved, thereby providing flexible programming options to deliver stimulation while minimizing side effects. Directional stimulation yielded a wider TW compared to omnidirectional stimulation and was preferred by blinded subjects and clinicians. Use of directional DBS systems in clinical practice has been demonstrated to be beneficial per increases in therapeutic window and associated positive outcomes. Results from ongoing registries demonstrate sustained improvement in overall outcomes with the use of directional DBS systems. In conclusion, Omnidirectional stimulation is no longer needed.

Supplemental Data:

References: (Dembek TA, et al. 2017; Kirsch AD., 2018) Schnitzler et al, Directional Deep Brain Stimulation for Parkinson's Disease: Results of an International Crossover Study With Randomized, Double-Blind Primary Endpoint 2022 Aug;25(6):817-828. doi: 10.1111/ner.13407. Epub 2022 Feb 2. Neuromodulation

Acknowledgements:

Learning Objectives: Importance of directional DBS for outcome and battery connsumption.

Financial Disclosures: Jan Vesper paid consultant for ABBOTT, Boston Scintific, Medtronic research contracts with ABBOTT, Boston Scientific

Disclosure: No significant relationships.

IS022

Breakout Session
NEUROMODULATION FOR NEUROPSYCHIATRY: OBSESSIVE COMPULSIVE DISORDER AND DEPRESSION
13-05-2024 14:30 - 16:00

NOVEL TRANSCRANIAL MAGNETIC STIMULATION (TMS) PROTOCOLS FOR DEPRESSION

Noah Philip, MD
VA Providence, Center For Neurorestoration And Neurotechnology, Providence, United States of America

Introduction and Discussion: Transcranial Magnetic Stimulation (TMS) is an evidence-based option for treatment-resistant major depressive disorder. Using rapidly fluctuating magnetic fields, TMS induces electrical current in targeted brain areas, and as such is thought to correct pathological large-scale neural network activity implicated in depression and other psychiatric disorders. Over the last decade, there have been significant advances in TMS protocols; these started with an original 10Hz protocol using a figure-of-eight TMS coil (1), followed by H-coil systems that delivered a broader stimulation with a different protocol (2). In the time since protocols have been abbreviated or adapted to mimic endogenous theta rhythms, now called theta burst stimulation (3), and doses have been increased via either the number of pulses or administrations per day. Most recently, there has been significant attention to accelerated TMS protocols that can deliver as much as several months of TMS in a short period, achieving remission in a relatively short period of time (4). This session is designed for attendees who wish to learn more about the use of TMS for depression and catch up on some of the latest advances in the area, with a focus on accelerated TMS protocols (5). The presentation will provide a perspective on the arc of these protocols over time, various considerations for their use, and touch upon related areas of active research in the field.

Supplemental Data:

References: 1. O'Reardon, J. P., Solvason, H. B., Janicak, P. G., et al., Sampson, S., et al., (2007). Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. *Biological psychiatry*, *62*(11), 1208–1216. 2. Levkovitz, Y., Isserles, M., Padberg, F., Lisanby, S. H., et al., (2015). Efficacy and safety of deep transcranial magnetic stimulation for major depression: a prospective multicenter randomized controlled trial. *World psychiatry*, *14*(1), 64–73. 3. Blumberger, D. M., Vila-Rodriguez, F., Thorpe, K. E., Feffer, K., et al., (2018). Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): a randomised non-inferiority trial. *Lancet*, *391*(10131), 1683–1692. 4. Cole, E. J., Phillips, A. L., Bentzley, B. S., Stimpson, K. H., et al., (2022). Stanford Neuromodulation Therapy (SNT): A Double-Blind Randomized Controlled Trial. *The American journal of psychiatry*, *179*(2), 132–141. 5. van Rooij, S. J. H., Arulpragasam, A. R., McDonald, W. M., & Philip, N. S. (2023). Accelerated TMS - moving quickly into the future of depression treatment. *Neuropsychopharmacology*, 10.1038/s41386-023-01599-z. Advance online publication.

Acknowledgements: None

Learning Objectives: By the end of the presentation, participants should be able to: 1) Describe the evolution of TMS protocols for depression 2) Describe novel TMS protocols for depression, including accelerated TMS protocols 2) Discuss ongoing research in the area

Financial Disclosures: No commercial conflicts of interest related to the content of this session. Noah S. Philip MD Wave Neuro Clinical trial support through US Dept of Veterans Affairs n/a Wave Neuro Clinical trial support through US Dept of Veterans Affairs n/a Motif Neurotech Advisor <$5,000 Pulvinar Neuro Scientific Advisory Board <$5,000

Disclosure: No significant relationships.

IS023

Breakout Session
NEUROMODULATION FOR NEUROPSYCHIATRY: OBSESSIVE COMPULSIVE DISORDER AND DEPRESSION
13-05-2024 14:30 - 16:00

VAGUS NERVE STIMULATION (VNS) FOR DEPRESSION: RECOVER STUDY

Charles Conway, MD
Washington University in St. Louis, Psychiatry, St. Louis, United States of America

Introduction and Discussion: Introduction: Numerous studies demonstrate therapeutic Vagus Nerve Stimulation (VNS) antidepressant efficacy in treatment-resistant major depression (TRD)[1]. The US FDA approved VNS for TRD in 2005. In 2007, the US Centers for Medicare and Medicaid Services (CMS) issued a "non-coverage decision", which limited access to VNS for TRD in the USA. In 2017, a large open-label trial comparing the antidepressant efficacy of adjunctive VNS versus treatment as usual (defined as any antidepressant treatment including electroconvulsive therapy) demonstrated that adjunctive VNS had superior cumulative and more rapid antidepressant response/remission rates, and these advantages held for both unipolar and bipolar TRD[2]. In 2019, CMS requested a "coverage with evidence trial" to study VNS efficacy in Medicare TRD patients. Entitled the RECOVER Trial, this large, multi-center (84 US sites), randomized, double-blind, sham-controlled trial assesses VNS efficacy over 12 months[3]. **Discussion:** The RECOVER trial is the largest double-blind, device-based trial ever conducted for a psychiatric illness. TRD participants must fail four chart-verified, adequate dose-duration antidepressant (AD) trials and have either recurrent or chronic (> 2 years in duration) major depressive disorder (MDD) or a bipolar major depressive episode (MDE). The trial is independently powered for unipolar and bipolar disorder (N=500 max/group). To date, 500 unipolar patients are randomized, with a median age of 58.0 years, moderate-severe baseline depressive symptomology (median Montgomery-Asberg Depression Rating Scale [MADRS] of 34.5). Using the Clinical Global Impression (CGI), the sample was clinically judged as moderately ill (CGI = 4; 19.2%) or severely ill (CGI ≥ 5; 80.6%). The median age of MDE onset in the sample is 25.0, with a median of 18.7 years in MDE (36% lifetime spent in MDE). The sample has high suicidal ideation (77% positive), with 40% having a history of suicide attempt(s). Median failed lifetime AD treatments is 11.0; a median of 10.0 failed AD medications. Most (71%) of the sample had received aggressive AD treatments in the current MDE: repetitive transcranial magnetic stimulation (50%), electroconvulsive therapy (38%), and ketamine (24%); 40% had received 2 of these three treatments, 10% had received all three. To date, 330 unipolar patients (including withdrawals) have completed the trial's first year. **Conclusions:** VNS is an effective treatment for TRD. The RECOVER trial will provide clearer understanding of VNS responsivity (e.g., onset of response, baseline outcome predictors, among others).

Supplemental Data:

References: [1]Berry, S. M., Broglio, K., Bunker, M., Jayewardene, A., Olin, B., & Rush, A. J. (2013). A patient-level meta-analysis of studies evaluating vagus nerve stimulation therapy for treatment-resistant depression. *Medical Devices: Evidence and Research*, 17-35. [2]Aaronson, S. T., Sears, P., Ruvuna, F., Bunker, M., Conway, C. R., Dougherty, D. D., ... Zajecka, J. M. (2017). A 5-year observational study of patients with treatment-resistant depression treated with vagus nerve stimulation or treatment as usual: comparison of response, remission, and suicidality. *American Journal of Psychiatry*, *174*(7), 640-648. [3]Conway, C. R., Olin, B., Aaronson, S. T., Sackeim, H. A., Bunker, M., Kriedt, C., ...Rush, A. J. (2020). A prospective, multi-center randomized, controlled, blinded trial of vagus nerve stimulation for difficult to treat depression: a novel design for a novel treatment. *Contemporary Clinical Trials*, *95*, 106066.

Acknowledgements: The research and travel support of LivaNova, and research support of the US Committee on Medicare and Medicaid Services is gratefully acknowledged.

Learning Objectives: The listener will better understand the clinical history of vagus nerve stimulation (VNS) in treatment-resistant depression. The listener will better understand how the VNS stimulation device is implanted, its stimulation patterns, and how the stimulation impacts the afferent pathway of the vagus. The listener will learn about the ongoing RECOVER trial, which is the largest device-based, blinded trial conducted in psychiatry to date.

Financial Disclosures: Charles Richard Conway, LivaNova, PLC, consulting relationship, research funding through Washington University, and is the Lead Investigator of the RECOVER Trial.

Disclosure: No significant relationships.

IS024

Breakout Session
NEUROMODULATION FOR NEUROPSYCHIATRY: OBSESSIVE COMPULSIVE DISORDER AND DEPRESSION
13-05-2024 14:30 - 16:00

A DECADE OF CLINICAL AND TRANSLATIONAL EXPERIENCE OF SUPEROLATERAL MEDIAL FOREBRAIN BUNDLE DEEP BRAIN STIMULATION (DBS) IN DEPRESSION AND OBSESSIVE COMPULSIVE DISORDER (OCD)

Volker Coenen, MD
University Freiburg - Medical Centre, Dept. Of Stereotactic And Functional Neurosurgery, Freiburg, Germany

Introduction and Discussion: Major depression and obsessive compulsive disorders are prevalent diseases that can be treated with a combination of drugs and psychotherapy. Despite the distinctive classification of the diseases, symptomatology and treatments point to common networks which are then distinctively affected. Treatment resistant major depression (TR-MD) and obsessive compulsive disorders (TR-OCD) are debilitating and create an important individualö and socioeconomic burden. TR-MD amounts to 30 % of all MD patients treated , TR-OCD ranges as high as 30-40% (1). For a sub-proportion of these patients deep brain stimulation (DBS) might present as a treatment option. In all psychiatric indications, DBS has to be regarded as experimental. More than a decade ago we introduced a new target structure, the superolateral branch of the medial forebrain bundle (slMFB), for the treatment of TR-MD (2) and TR-OCD (3). Meanwhile, we have successfully treated 88 patients (TR-MD: 69, TR-OCD: 19), mostly in clinical trials (2,4) but also in published case series (5). This talk will illustrate the journey form the first idea of reward system modulation, via the development of tractography assisted slMFB-DBS surgery (6,7) to our current understanding of how the slMFB facilitates flexible behavior and decision making in the human brain (8).

Supplemental Data:

References: 1. Atmaca M. Treatment-refractory obsessive compulsive disorder. Prog Neuro-Psychopharmacol Biol Psychiatry. 2016;70:127–33.
2. Schlaepfer TE, Bewernick BH, Kayser S, Mädler B, Coenen VA. Rapid effects of deep brain stimulation for treatment-resistant major depression. Biological psychiatry. 2013 Jun 15;73(12):1204–12.
3. Coenen VA, Schlaepfer TE, Goll P, Reinacher PC, Voderholzer U, Elst LT van, et al. The medial forebrain bundle as a target for deep brain stimulation for obsessive-compulsive disorder. CNS spectrums. 2016 Jun 8;493(03):1–8.
4. Coenen VA, Bewernick BH, Kayser S, Kilian H, Boström J, Greschus S, et al. Superolateral medial forebrain bundle deep brain stimulation in major depression: a gateway trial. Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology. 2019 Mar 13;26(9):587.
5. Meyer DM, Spanier S, Kilian HM, Reisert M, Urbach H, Sajonz BEA, et al. Efficacy of superolateral medial forebrain bundle deep brain stimulation in obsessive-compulsive disorder. Brain Stimul. 2022;15(3):582–5.
6. Coenen VA, Sajonz B, Reisert M, Bostroem J, Bewernick B, Urbach H, et al. Tractography-assisted deep brain stimulation of the superolateral branch of the medial forebrain bundle (slMFB DBS) in major depression. NeuroImage: Clinical. 2018;20:580–93.
7. Coenen VA, Schlaepfer TE, Reinacher PC, Mast H, Urbach H, Reisert M. Machine learning—aided personalized DTI tractographic planning for deep brain stimulation of the superolateral medial forebrain bundle using HAMLET. Acta Neurochir [Internet]. 2019 May 29;161(8):1559–69. 8. Coenen VA, Schlaepfer TE, Sajonz BEA, Reinacher PC, Döbrössy MD, Reisert M. "The Heart Asks Pleasure First"—Conceptualizing Psychiatric Diseases as MAINTENANCE Network Dysfunctions through Insights from slMFB DBS in Depression and Obsessive–Compulsive Disorder. Brain Sci. 2022;12(4):438.

Acknowledgements: This is an invited talk by INS

Learning Objectives: 1. to understand the motivation ofr reward sytem DBS in OCD and MDD 2. to understand anatomy and physiology of the slMFB 3. to understand stimulation effects of slMFB DBS

Financial Disclosures: V.A.C. as an employee of University of Freiburg, listed by the institution as inventor, has filed a U.S. provisional patent application generally related to highly focused DBS in the treatment of OCD (U.S. Patent Application Number 63/253740). He receives a collaborative grant from BrainLab (Munich, Germany). He is a consultant for Ceregate (Munich, Germany), Cortec (Freiburg, Germany) and Inbrain (Barcelona, Spain). He has an ongoing IIT with Boston Scientific (USA) and has received personal honoraria and travel support for lecture work from Boston Scientific (USA), ALEVA, UNEEG and PRECISIS.

Disclosure: No significant relationships.

IS025

Breakout Session
NEUROMODULATION FOR NEUROPSYCHIATRY: OBSESSIVE COMPULSIVE DISORDER AND DEPRESSION
13-05-2024 14:30 - 16:00

EFFICACY OF DEEP BRAIN STIMULATION FOR TREATMENT-RESISTANT OBSESSIVE COMPULSIVE DISORDER (OCD): SYSTEMIC REVIEW AND METAANALYSIS

Sameer Sheth, MD
Baylor College of Medicine, Neurosurgery, Houston, United States of America

Introduction and Discussion: Deep brain stimulation (DBS) is an increasingly established intervention for treatment-resistant obsessive-compulsive disorder (TROCD). We assessed current evidence on the efficacy of DBS in alleviating OCD and comorbid depressive symptoms including newly available evidence from recent trials and a deeper risk of bias analysis than previously available. PubMed and EMBASE databases were systematically queried using PRISMA guidelines. We included studies reporting primary data on multiple patients who received DBS therapy with outcomes reported through the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). Primary effect measures included Y-BOCS mean difference and percent reduction as well as responder rate (≥35% Y-BOCS reduction) at last follow-up. Secondary effect measures included standardized depression scale reduction. Risk of bias assessments were performed on randomized controlled (RCTs) and non-randomized trials. Thirty-four studies from 2005 to 2021, nine RCTs (n = 97) and 25 non-RCTs (n = 255), were included in systematic review and meta-analysis based on available outcome data. A random effects model indicated a meta-analytic average 14.3 point or 47% reduction ($p < 0.01$) in Y-BOCS scores without significant difference between RCTs and non-RCTs. At last follow-up, 66% of patients were full responders to DBS therapy. Sensitivity analyses indicated a low likelihood of small study effect bias in reported outcomes. Secondary analysis revealed a 1 standardized effect size (Hedges g) reduction in depressive scale symptoms. Both RCTs and non-RCTs were determined to have a predominantly low risk of bias. A strong evidence-base supports DBS for TROCD in relieving both OCD and comorbid depression symptoms in appropriately selected patients.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: Describe criteria used to select patients as candidates for DBS for OCD. Indicate evidence base for DBS for OCD therapy in terms of meta-analytic outcome data. Describe the methodology of meta-analysis, including fixed and random effects models.

Financial Disclosures: Consultant: Zimmer Biomet, Neuropace, Boston Scientific, Koh Young, Sensoria Therapeutics, Varian Medical Co-founder: Motif Neurotech

Disclosure: No significant relationships.

IS026

Breakout Session
NEUROMODULATION FOR REHABILITATION AFTER STROKE
13-05-2024 14:30 - 16:00

THE CURRENT STATE OF NON-INVASIVE NEUROMODULATION FOR POST-STROKE REHABILITATION

Dylan Edwards, Director, Moss Rehabilitation Re[1,2]
[1]Moss Rehabilitation Research Institute, Elkins Park, United States of America, [2]Sidney Kimmel Medical College, Thomas Jefferson University, Rehabilitation Medicine, Philadelphia, United States of America

Introduction and Discussion: Non-invasive electromagnetic stimulation can modulate neuronal function and has received increasing interest over the past several decades for diagnostic, prognostic, and treatment applications. Safety and training guidelines have been developed, and a range of neurological disorders studied. Adult stroke is a prevalent condition often resulting in hemiparesis that does not fully recover. This causes reduced quality of life for those affected and also has substantial general socioeconomic impacts. Neuromodulation in stroke motor recovery has predominantly used repetitive transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS), coupled with motor practice. With numerous past trials, both successful and unsuccessful, the circumstances under which these methods might augment the training-induced recovery (parameter and patient selection) are beginning to emerge. Modern technological advances enable more robust and rational prescription of these methods. Current and recent trials will be discussed.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1) Define transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) 2) Provide the rationale for targeting and parameter selection in for TMS/tDCS in post-stroke motor recovery 3) Describe the importance of modeling cortical electric fields with TMS and tDCS

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS027

Breakout Session
NEUROMODULATION FOR REHABILITATION AFTER STROKE
13-05-2024 14:30 - 16:00

VAGUS NERVE STIMULATION AS A STRATEGY TO AUGMENT STROKE REHABILITATION

Seth Hays, PhD
The University of Texas at Dallas, Bioengineering, Richardson, United States of America

Introduction and Discussion: Loss of motor and somatosensory function after stroke and spinal cord injury is common, debilitating, and lacks effective interventions. It is widely held that enhancing synaptic plasticity in spared circuits represents a means to improve recovery. We developed one such approach that uses brief bursts of closed-loop vagus nerve stimulation (VNS) concurrent with exercises during rehabilitation to engage neuromodulatory networks and facilitate synaptic plasticity. VNS therapy recently received FDA approval as the first neuromodulation-based intervention to promote upper limb recovery after chronic stroke. Here, we present the studies that built the foundation for VNS therapy, including studies that reveal the mechanisms engaged by VNS and ongoing efforts to develop other VNS-based interventions. Additionally, we will discuss our ongoing clinical trials applying this strategy to individuals with spinal cord injury. Finally, we will explore efforts to optimize VNS therapy through improvements in the device and parameters of stimulation.

Supplemental Data:

References: None

Acknowledgements: We gratefully acknowledge funding from The National Institute for Neurological Disorders and Stroke (UG3/UH3 NS109497 and R01 NS094384), Wings for Life, and the Defense Advanced Research Projects Agency (N66001-17-2-4011) to suppoprt the work described in the presentation.

Learning Objectives: 1. Define the current applications of VNS to enhance motor and sensory recovery after neurological injury, including stroke and SCI. 2. Describe the neural mechanisms that underlie VNS-dependent recovery of motor and sensory function. 3. Apply neuroscience and engineering principles to optimize VNS therapy to maximally improve motor and sensory recovery.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

IS028

Breakout Session
NEUROMODULATION FOR REHABILITATION AFTER STROKE
13-05-2024 14:30 - 16:00

SPINAL CORD AND PERIPHERAL NERVE STIMULATION FOR MOTOR REHABILITATION

Douglas Weber, Professor[1], Nikhil Verma, BSc (Hons)[1], Luigi Borda, MSc[1], Prakarsh Yadav, BSc (Hons)[1], Roberto De Freitas, PhD[2], Erick Carranza, BSc (Hons)[2], Erynn Sorensen, BSc (Hons)[2], Amy Boos, MSc[2], Peter Gerszten, MD[3], Daryl Fields, MD[3], George Wittenberg, MD[4], Lee Fisher, PhD[2], Elvira Pirondini, PhD[2], Marco Capogrosso, PhD[2]
[1]Carnegie Mellon University, Department Of Mechanical Engineering And The Neuroscience Institute, Pittsburgh, United States of America, [2]University of Pittsburgh, Rehab Neural Engineering Labs, Pittsburgh, United States of America, [3]UPMC, Neurological Surgery, Pittsburgh, United States of America, [4]UPMC, Neurology, Pittsburgh, United States of America

Introduction and Discussion: Every year, half of the 800,000 people that suffer a stroke in the US will experience permanent paralysis that is generally unresponsive to standard treatments. To address this unmet need, neuromodulation interventions are being developed to improve recovery of arm and hand function for people with chronic hemiplegia [1]. While vagal nerve stimulation (VNS) is used in conjunction with activity-based stroke rehabilitation, VNS does not directly target sensorimotor circuits but enhances the neuroplasticity needed to support functional recovery [2]. On the contrary, epidural spinal cord stimulation (eSCS) produces immediate effects on muscle activation by activating primary afferent neurons that synapse directly and indirectly on spinal motor neurons [3]. We are exploring the immediate and sustained effects of eSCS for improving arm and hand function in people with chronic deficits post-stroke (NCT04512690). Preliminary results from our first 2 participants showed that eSCS of the cervical spinal cord produced significant increases in strength and dexterity with stimulation, and Fugl-Meyer Assessment scores for both participants were higher at the end of the 4-week study [4]. To date, six people have been implanted with a pair of 8-contact eSCS leads (PN 977A260, Medtronic) in the cervical spinal cord ipsilateral to the paretic arm. Participants performed planar and 3D reaching tasks and joint torques were measured isometrically using a dynamometer (Humac Norm, Computer Sports Medicine, Inc.). Muscle activation was measured using high-density surface electromyography (HDsEMG, SAGA+, TMSI, Inc.). The HDsEMG recordings were used to decompose single-motor unit (MU) activity. Peri-stimulus time histograms of MU firing showed an increased spike probability of motor unit firing at approximately 7-15 ms latency following each SCS pulse, demonstrating that SCS provides transient excitatory drive to the motoneurons that allows the residual cortical inputs to gain volitional motor neuron control. The duration and magnitude of facilitation varied across the recorded motor units, perhaps reflecting differences in the synaptic strength across the pool of motor neurons. We also tested different methods of tuning SCS to improve motor control. The participants were able to perform faster and smoother movements with tonic SCS than without. Further improvements in reach kinematics were achieved by tuning SCS parameters for flexion and extension phases of the movement. These results offer new insights into the neurophysiological mechanisms underlying the therapeutic effects of eSCS in facilitating the recovery of arm function after chronic stroke.

Supplemental Data:

References: [1] Dawson, J., Abdul-Rahim, A. H., and Kimberley, T. J., 2024, "Neurostimulation for Treatment of Post-Stroke Impairments," Nat. Rev. Neurol. [2] Meyers, E. C., Solorzano, B. R., James, J., Ganzer, P. D., Lai, E. S., Rennaker, R. L., Kilgard, M. P., and Hays, S. A., 2018, "Vagus Nerve Stimulation Enhances Stable Plasticity and Generalization of Stroke Recovery," Stroke, 49(3), pp. 710–717. [3] Pirondini, E., Carranza, E., Balaguer, J.-M., Sorensen, E., Weber, D. J., Krakauer, J. W., and Capogrosso, M., 2022, "Poststroke Arm and Hand Paresis: Should We Target the Cervical Spinal Cord?," Trends Neurosci., 45(8), pp. 568–578. [4] Powell, M. P., Verma, N., Sorensen, E., Carranza, E., Boos, A., Fields, D. P., Roy, S., Ensel, S., Barra, B., Balzer, J., Goldsmith, J., Friedlander, R. M., Wittenberg, G. F., Fisher, L. E., Krakauer, J. W.,

Gerszten, P. C., Pirondini, E., Weber, D. J., and Capogrosso, M., 2023, "Epidural Stimulation of the Cervical Spinal Cord for Post-Stroke Upper-Limb Paresis," Nat. Med., 29(3), pp. 689–699.

Acknowledgements: This work was supported by a grant from the NIH BRAIN initiative UG3NS123135.

Learning Objectives: 1. Introduce spinal cord stimulation as a novel neuromodulation strategy for promiting recovery of arm and hand function in people with chronic hemiplegia post-stroke. 2. Understand the neurophysiological mechanisms underlying the effects of SCS in facilitating activation of motor neurons. 3. Understand how spinal cord stimulation is programmed to maximize recovery.

Financial Disclosures: Drs. Weber, Powell, Gerszten, and Capogrosso are founders and shareholders of Reach Neuro, Inc., a startup company focused on neuromodulation therapies for stroke rehabilitation.

Disclosure: No significant relationships.

IS029

Breakout Session
NEUROMODULATION FOR REHABILITATION AFTER STROKE
13-05-2024 14:30 - 16:00

DEEP BRAIN STIMULATION FOR POST-STROKE REHABILITATION

Introduction and Discussion: Upper-extremity impairment after stroke remains a major therapeutic challenge and a target of neuromodulation treatment efforts. We have previoulsy shown that deep brain stimulation (DBS) targeting the dentate nucleus (DN) promotes rehabilitation in the rodent post-stroke model, along with increments in perilesional excitability, perilesional cortical reorganization and increased expression of markers of long-term potentiation. We have now completed the first-in-man translation of this work and report on the complete outcomes of this phase I clinical trial, along with mechanistic examination with positrron emission tomograph and cerebello-cortical electrophysiology. These outcomes have been recently published in Nature Medicine. Twelve patients with chronic (>1yr post-MCA-stroke) moderate-to-severe upper-extremity hemiparesis underwent implantation of an 8-channel DBS lead targeting the contralesional DN. All patients underwent 3 months of structured rehabilitation prior to activation of DBS, in an effort to establish a new, post-therapy, baseline. All participants received up to 8 months of DBS combined with physicial rehabilitation, after which DBS was turned OFF in order to study carry-over effects of treatment. The study accumulated 168 participant-months of DBS implant experience and 72 months of DN stimulation experience, with no device failures and no study-related, serious adverse events throughout the trial. When pooling all data, participants showed a 7-point median improvement in FM-UE scores in response to DN DBS combined with rehabilitation. Nine of 12 participants (75%) exceeded MCID. Individuals who entered the study with at least minimal residual preservation of distal motor function (7/12) demonstrated a significantly greater median improvement of 15 points on the FM-UE. Finally, the median FM-UE score for the full cohort again remained unchanged at the end of the long-term follow-up phase, supporting the durability of previously-realized, treatment-related gains. These results support DN DBS as a promising treatment for patients with post-stroke hemiparesis. A prospective, multi-site, double-blinded, randomized, sham-controlled phase II trial (FDA-IDE # G150237) is underway to further evaluate this emerging therapy and address the limitations inherent to phase I trials.

Supplemental Data:

References: Baker KB, Plow EB, Nagel S, Rosenfeldt AB, Gopalakrishnan R, Clark C, Wyant A, Schroedel M, Ozinga J 4th, Davidson S, Hogue O, Floden D, Chen J, Ford PJ, Sankary L, Huang X, Cunningham DA, DiFilippo FP, Hu B, Jones SE, Bethoux F, Wolf SL, Chae J, Machado AG. Cerebellar deep brain stimulation for chronic post-stroke motor rehabilitation: a phase I trial. Nat Med. 2023 Sep;29(9):2366-2374. doi: 10.1038/s41591-023-02507-0. Epub 2023 Aug 14. PMID: 37580534; PMCID: PMC10504081.

Acknowledgements: The support of the National Institutes of Health and Enspire DBS are gratefully acknowledged.

Learning Objectives: 1. Evaluate Dentate Nucleus Deep Brain Stimulation as a therapeutic modality for post-stroke rehabilitation 2. Examine the outcomes data for the Phase I clinical trial 3. Examine positron-emission tomography data associated with clinical improvements.

Financial Disclosures: The presenting authors has distribution rights intellectual property written at Cleveland Clinic, as well as options from Enspire DBS for serving as the Chief Scientific / Medical Officer

Disclosure: No significant relationships.

IS030

Plenary
PLENARY SESSION 02
14-05-2024 09:30 - 11:00

INSIGHTS INTO DISEASE AND MECHANISMS OF NEUROMODULATION FROM INVASIVE NEUROPHYSIOLOGY

Nader Pouratian, MD, PhD
University of Texas Southwestern Medical Center, Dallas, Not Hispanic/Latino/Latina/Latinx, United States of America

Introduction and Discussion: Neuromodulation aims to modify brain function in order to treat symptoms of neurological and psychiatric disease. Given the focus on improving brain function, studies that shed light both on the neurophysiological underpinning of disease and therapeutic mechanisms of neuromodulation are critical to both improving the efficacy of current therapies and expanding indications for neuromodulatory interventions. While non-invasive techniques brain mapping techniques have moved the field, these are often limited in either spatial or temporal resolution or spatial sampling. Neurosurgical interventions, such as deep brain stimulation and intracranial monitoring for epilepsy, provide a unique opportunity to attain disease- and symptom-relevant neurophysiological signals. Using these “opportunistic” approaches, studies from our research group have shed light on motor control and regulatory mechanisms, the network basis of Parkinsonian symptoms such as bradykinesia, therapeutic mechanisms of pallidal brain stimulation using both conventional and novel stimulation paradigms, and brain mechanisms underlying consciousness. Building on the strength of and insights garnered from these “opportunistic” studies, we now see an emerging era of neuromodulatory clinical trials that are specifically designed to record network-wide signals and biophysical response to neurostimulation in patients who otherwise would not undergo such surgical interventions. These novel clinical trials, which often include a phase of stereotactic EEG or intracranial monitoring, offer unparalleled opportunity to expand our understanding of disease in the target population and opportunities to bring novel neuromodulatory treatments to fruition. This new era of neuromodulatory clinical trials has begun to shed light on neurophysiological biomarkers of treatment resistant depression and biophysical responses to visual cortex stimulation, and opened doors to investigating neuromodulation for novel diseases, like schizophrenia.

Acknowledgements:

Learning Objectives: 1. Describe techniques for recording and interpreting signals during neurosurgical procedures to understand disease and therapeutic mechanisms
2. Explain key physiological features that may be critical for understanding the pathophysiology of disease and mechanisms of therapy
3. Detail limitations of intraoperative neurophysiological studies to understand disease as well as opportunities

Financial Disclosures: NP Abbott - Consultant/Advisory Board - $5,001-$20,000 Sensoria Therapeutic - Consultant, Stck Options - $501-$5,000

Disclosure: No significant relationships.

IS031

Plenary
PLENARY SESSION 02
14-05-2024 09:30 - 11:00

CAN SPINAL CORD STIMULATION ALTER THE DISEASE OF CHRONIC PAIN?

Yun Guan, PhD, MD
Johns Hopkins University, Department Of Anesthesiology And Critical Care Medicine, Baltimore, United States of America

Introduction and Discussion: Chronic pain is a complex disease that affects millions of people worldwide. This debilitating condition, which can be caused by various factors such as injury, chemotherapy, disease, or nerve damage, remains a challenge to treat. Spinal cord stimulation (SCS) has been an effective alternative treatment for several chronic pain conditions, improving the quality of life for many over the decades. SCS works by delivering mild electrical pulses to the spinal cord, which interfere with the transmission of pain signals to the brain. However, the detailed mechanisms underlying SCS-induced pain inhibition remain partially understood. Historically, SCS was thought to merely attenuate pain symptoms, such as reducing pain intensity, without addressing the underlying etiology of chronic pain. Recent findings, however, have illuminated the potential of SCS as a disease-modifying therapy that may help treat the root causes of chronic pain, such as neuronal plasticity, nerve injury, and inflammation. In this talk, we will delve deeper into the mechanisms of SCS. We will provide a brief background introduction of SCS and, importantly, review preclinical and clinical evidence for different SCS paradigms to address both neuronal mechanisms (e.g., central sensitization, altered gene transcription in the spinal cord and dorsal root ganglion, nerve injury), and non-neuronal mechanisms (e.g., gliosis, neuroinflammation) underlying chronic pain. The potential of SCS to prevent the development of certain chronic pain conditions, achieve long-term pain inhibition, and even promote nerve regeneration and repair is a promising avenue of research. However, the question of whether SCS can alter the disease of chronic pain remains highly debatable. More research and clinical trials are needed to determine whether SCS is more than just a palliative treatment. It is also important to consider whether SCS should be applied earlier in the treatment process, rather than being the last resort after patients have exhausted other pharmacological and non-surgical pain management options.

Supplemental Data:

References: None

Acknowledgements: None

Learning Objectives: 1. Is it possible for spinal cord stimulation to modify gene expression within the dorsal root ganglion and spinal cord? Yes. 2. Can spinal cord stimulation attenuate neuronal plasticity induced by nerve injury? Yes. 3. Can spinal cord stimulation influence glial cell function and neuroimmune interaction? Yes.

Financial Disclosures: Dr. Guan received research grant support from Medtronic, Inc, TissueTech, Inc.

Disclosure: No significant relationships.

IS032

Plenary
PLENARY SESSION 02 CONT
14-05-2024 11:30 - 12:30

HOW NEUROMODULATION CHANGED THE LANDSCAPE OF EPILEPSY SURGERY

Arthur Cukiert, PhD
Clinica Cukiert, Neurosurgery, São Paulo, Brazil

Introduction and Discussion: Combined Neuromodulation for Refractory Epilepsy Abstract Thirty percent of people with epilepsy would be refractory to anti-seizure medications. Resective and disconnective epilepsy surgery had been a relevant therapeutic option in their treatment, with high success rates. On the other hand, a significant amount of them are not good candidates for resective/disconnective surgery. Neuromodulation added new and effective alternatives for treatment of people with epilepsy who are not candidates for conventional treatment or are not willing to do so. Current techniques include both extracranial (VNS) and intracranial hardware (DBS, RNS). Different targets have been explored according to each epileptic syndrome. Quite extensive experience and controlled studies are available for each of them, although we lack adequate direct comparisons between them. More recently, combined neuromodulation (i.e., using more than one target or device in the same patient) has been implemented more widely. It follows the same paradigm as rational drug polytherapy, trying to use devices with different mechanisms of action or different targets. The better understanding of the behavior of each potential neuromodulation target during the interictal and ictal periods would lead to further developments in multi-site/multi-technique neuromodulation.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1- na 2- na 3- na

Financial Disclosures: no significant relationships

Disclosure: No significant relationships.

IS033

Plenary
PLENARY SESSION 02 CONT
14-05-2024 11:30 - 12:30

CONTROVERSIES IN ETHICS RELATED TO NEUROTECHNOLOGIES

Zelma Kiss, MD, PhD[1], Ari Rotenberg, MSc[2], Stacey Anderson-Redick, BSc (Hons)[1], Judy Illes, [2]
[1]University of Calgary, Clinical Neurosciences, Calgary, Canada, [2]UBC, Medicine, Vancouver, Canada

Introduction and Discussion: While there are innumerable possible controversies in neuroethics related to neuromodulation, we have focused on one specific aspect: patenting of medical methods. We examined patents already granted in the field of neurotechnology – analysed them for their legal viability, and explored perspectives from experts about their potential benefits and risks to individuals, patients and society. According to the Organisation for Economic Co-operation and Development (OECD), between 2008 and 2016, 16,273 patents representing a health-related neurotechnology were filed worldwide. Of these 63% were related to devices/methods for performing neuromodulation. While pure medical methods, or techniques without an associated novel device, are ineligible for patent protections in most countries, they are patentable in the US, leading to many international inventors patenting there. Based on preliminary analysis of the patent landscape we conducted up to the year 2016 (Nature Biotech 2017), we extended our analysis of neuromodulation patents to 2020. We developed a novel, customized search algorithm to mine Lens.org, an open-access patent database. We based our approach on the presence of combinations of terms associated with the nervous system or its modulation in the text of claims. We applied a content analytical procedure to facilitate a standard review of the claims, with each meeting inclusion criteria pertaining to nervous tissue and health-related applications. A total of 779 patents arose from this data mining, 571 of which involved electrical (64%), magnetic (10%), radiation (9%), or ultrasound (5%) therapies. Pain was the commonest condition targeted comprising 28% of patents, with cognitive and psychiatric indications a close second at 21% of patents. Sensorimotor, autonomic, epilepsy, and sleep disorders completed the therapeutic claims. Sensing neurological states made up 7% of the patents. Four percent of patents granted had non-medical applications. Ethical analysis included identifying concerns related to scientific validity, moral principles, and those patents designed to interfere with cognition or behaviour. Nine patents were problematic from these perspectives, 5 involving human dignity and autonomy. Further in-depth analysis will involve following the future of these patents as they are licensed or marketed, because several are held by industry leaders and physicians/scientists. In summary, patent protections may put best practice at risk. A framework for patenting and marketing new invasive and non-invasive neurotechnologies that balances medical and commercial value, autonomy, and human use protections is critical. Proactive guidance from within the profession is essential to achieve this balance.

Supplemental Data:

References: Roskams-Edris D, Anderson-Redick S, Kiss ZH, Illes J. Situating brain regions among patent rights and moral risks. Nat Biotechnol. 2017 Feb 8;35(2):119-121. doi:10.1038/nbt.3782. PMID: 28178252. Roskams-Edris D, Anderson-Redick S, Illes J, Kiss ZHT. Medical methods patents in neuromodulation. Neuromodulation. 2019 Jun;22(4):398-402. doi:10.1111/ner.12919. PMID: 30748045.

Acknowledgements: Funding provided by CIHR/INMHA in partnership with ERA-NET(Ethical legal and social aspects of neuroscience) for NEURON, the Network of European Funding for Neuroscience Research), *#ERN-174185 (*JI)

Learning Objectives: After the presentation the audience will be able to: 1. describe the principles of medical methods patents. 2. outline the breadth of patenting of implantable neurotechnologies. 3. apply ethical principles to such patents.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

IS034

Breakout Session
SPINAL CORD STIMULATION FOR PAIN CLINICAL UPDATE
14-05-2024 14:30 - 16:00

DATA ON NON-SURGICAL BACK AND EXPERIENCE WITH DIFFERENT WAVEFORMS

Timothy Deer, MD
Pain, Charleston, United States of America

Introduction and Discussion: Low back pain (LBP) is a highly prevalent musculoskeletal problem and a leading cause of disability, affecting millions of people worldwide in all sociodemographic classes. Treatment paradigms have traditionally been classified as conservative, interventional or surgical. Evidence for therapies has typically been growing, and we are entering a 'golden age' of the diagnosis and treatment of low back pain, both PSPS type 1 and 2, with numerous evidence-based treatment options available. (1) The exclusion criteria for further 'surgical' options used to lie exclusively in the domain of the spine surgeon. However, with the advent of more evidence-based MIS techniques the definition of "non-surgical back pain" is evolving and is now best understood to include "no options for surgically correctable symptoms, inclusive of MIS options." This review will outline the evidence for different neuromodulation therapies in this "non-surgical treatment option" group. Overall, many studies have been done over the last several years on this population with axial low back pain, which until recently was felt to be challenging. Recent studies using tonic, BurstDR and HF SCS systems uniformly show favorable outcomes and acceptable complication rates. The selection of these non-operated patients for neuromodulation is a recent development in the spine space, and collaborative work between spine surgeons and pain specialists remains to determine optimal patient selection. The largest study in this space enrolled 270 patients with chronic debilitating back pain lasting more than a decade. The DISTINCT study results indicate that passive recharge B-SCS is superior to CMM for these patients. Primary and secondary end points show dramatic improvements in pain, function, pain-related emotional distress, day to-day pain interference, and a greater PGIC. Greater improvements with passive recharge B-SCS therapy are noted, using fewer injection and RF ablation procedures and accompanied by reductions in opioid use. Strengths of the study included the combination of orthopedic spine surgery, neurosurgery, and interventional pain investigator sites, and the inclusion of patients with long-standing, refractory axial spine without corrective surgical indications.

Supplemental Data: Table 1.

Company	**Abbott**	**Medtronic**		**Nevro**				**Boston Scientific**
Study Name	DISTINCT	HIDENS		Al-Kaisy Pooled Analysis (Senza-RCT/EU)		Kapural (Retrospective Efficacy & Cost-contain..)	Kapural (pragmatic … RCT)	SOLIS
Study size (n)	270	20		26	20	90	159	60
Arms	BurstDR vs CMM	HD-SCS (1KHz)		10KHz		10KHz	10Khz vs CMM	Combo Therapy vs CMM
Primary Endpoints	6 mo.	3 mo.	12 mo.	3 mo.	12 mo.	12 mo.	3 mo.	3 mo.
Pain Relief (NRS, mean)	69.7%	40.9%	48.8%	-	-	-	-	
Pain Relief NRS Responder Rate	85.6% (ITT)		30%	-	-	-	-	89.5%
Pain Relief (VAS)	-	-	-	-	5.6 cm	4.38cm	4.33cm	

Pain Relief								
VAS Responder Rate	-	-	-	73%	62%	-	80.9%	
Secondary Endpoints	6 mo.	3 mo.	12 mo.	3 mo.	12 mo.	-	-	
ODI Change (mean)	30.6	19.49	15.73	-	15.7	-	24.2	28
PCS Responder Rate	86.4%	-	-	-	-	-	-	-
PGIC	-	4.90	5.40	-	-	-	-	-
PGIC Responder Rate	77.8%	-	-	-	-	-	70.8%	86%
Pain Interference (% change)	18.1%	-	-	-	-	-	-	-
Physical function (% change)	28.0%	-	-	-	-	-	-	-
PSQ-3 (% change)	-	47.1%	50.6%	-	-	-	-	-

References: Sayed D, Grider J, Strand N, Hagedorn JM, Falowski S, Lam CM, Tieppo Francio V, Beall DP, Tomycz ND, Davanzo JR, Aiyer R, Lee DW, Kalia H, Sheen S, Malinowski MN, Verdolin M, Vodapally S, Carayannopoulos A, Jain S, Azeem N, Tolba R, Chang Chien GC, Ghosh P, Mazzola AJ, Amirdelfan K, Chakravarthy K, Petersen E, Schatman ME, Deer T. The American Society of Pain and Neuroscience (ASPN) Evidence-Based Clinical Guideline of Interventional Treatments for Low Back Pain. *J Pain Res*. 2022;15:3729-3832 https://doi.org/10.2147/JPR.S386879 Deer TR, et al. DISTINCT Treatment of Refractory Low Back Pain Using Passive Recharge Burst in Patients Without Options for Corrective Surgery: Findings and Results From the DISTINCT Study, a Prospective Randomized Multicenter Controlled Trial. Neuromodulation 2023 Mehta V, et al. Effectiveness of high dose spinal cord stimulation for non-surgical intractable lumbar radiculopathy -HIDENS Pain Practice 2022. Mekhail N, Levy RM, Deer TR, Kapural L, Li S, Amirdelfan K, Hunter CW, Rosen SM, Costandi SJ, Falowski SM, Burgher AH, Pope JE, Gilmore CA, Qureshi FA, Staats PS, Scowcroft J, Carlson J, Kim CK, Yang MI, Stauss T, Poree L; Evoke Study Group. Long-term safety and efficacy of closed-loop spinal cord stimulation to treat chronic back and leg pain (Evoke): a double-blind, randomised, controlled trial. Lancet Neurol. 2020 Feb;19(2):123-134. doi: 10.1016/S1474-4422(19)30414-4. Epub 2019 Dec 20. PMID: 31870766. Al-Kaisy A, Van Buyten JP, Kapural L, Amirdelfan K, Gliner B, Caraway D, Subbaroyan J, Edgar D, Rotte A. 10 kHz spinal cord stimulation for the treatment of non-surgical refractory back pain: subanalysis of pooled data from two prospective studies. Anaesthesia. 2020 Jun;75(6):775-784. doi: 10.1111/anae.15036. PMID: 32383509; PMCID: PMC7384077.

Acknowledgements: The author appreciates the support and assistance of Ashley G. Comer in preparing this presentation.

Learning Objectives: The attendee will learn the demographics and data surrounding those with non surgical back pain. The attendee will learn the waveform options that have been used for the treatment of non surgical back pain. The attendee will be given the statistical data needed to access the success of various spinal cord stimulation options to treat this complex group.

Financial Disclosures: TRD Abbott, Consultant. 20 to 100k Saluda, Consultant 5 to 20k, Stock options less than 5% SPR, Consultant 1 to 5k, Stock options less than 5% Spinal Simplicity, Stock options less than 5% Vertos, Consultant 5 to 20k Painteq, Consultant 1 to 5k, Stock options less than 5% Cornorloc, Consultant. Stock options less than 5% Spinethera, Consultant, Stock Options less than 5%

Disclosure: No significant relationships.

IS035

Breakout Session
SPINAL CORD STIMULATION FOR PAIN CLINICAL UPDATE
14-05-2024 14:30 - 16:00

RESTORATIVE STIMULATION FOR CHRONIC NONSURGICAL LOW BACK PAIN

Christopher Gilligan, MD
Robert Wood Johnson University Hospital, Pain Medicine, New Brunswick, United States of America

Introduction and Discussion: Introduction: Mechanical chronic low back pain (mCLBP), concomitant with dysfunctional neuromuscular control (NMC), is often caused by underlying multifidus muscle dysfunction.[1] The ReActiv8-B randomized sham-controlled pivotal trial (Clinicaltrials.gov Identifier: NCT02577354) utilized an implantable multifidus neurostimulation system to bilaterally stimulate L2 dorsal rami medial branch nerves for up to 30 minutes twice daily to override chronic multifidus inhibition and facilitate NMC restoration.[2,3] This trial has safety, effectiveness, and durability evidence of this therapy over 5 years. Prospective neuromodulation trials with shared outcomes beyond two years are rare. **Methods:** The RCT open label phase prospectively followed participants implanted with the system (ReActiv8®, Mainstay Medical, Inc., Dublin, Ireland) through 5 years during conduction in the United States (US), Australia, and Europe following compliance with US Food and Drug Administration regulations, ISO 14155, International Conference on Harmonization, and Declaration of Helsinki. Consented participants (N=204, age=47±9yrs; F110; BMI=28±4kg/m^2; pain duration=14.2±10.6yrs; no surgery indications; failed physical therapy; positive prone instability test; pain on 97±8% of days in the pre-enrollment year; 100% failed medications with 37% on opioids at baseline) were implanted over 21 months and randomized. Prespecified outcome measures included visual analog scale (VAS), Oswestry Disability Index (ODI), and quality of life (EQ-5D-5L) documented at intervals to 5 years. Completer analysis and mixed-effects models for repeated measures for missing data imputations were conducted. Treatment success was a composite of ODI and VAS improvements. **Results:** At 5 years, 126 complete records showed improved mean(±SE) VAS by 4.9(±0.2)cm (71.8% with ≥50% improvement), ODI by 22.7(±1.4) (61.1% with ≥20-point improvement), and EQ-5D-5L by 0.231±0.018 (P<0.0001 for all outcomes). mCLBP resolved in 66.9% (VAS≤2.5 cm), and 88% of participants “definitely satisfied” with treatment. Successful treatment was indicated in 78.2%. Those consuming opioids at baseline either discontinued (46%) or decreased (23%) opioid consumption. Overall safety profile was favorable including no lead migrations. **Discussion:** Five-year data from this multi-center RCT revealed significant reductions in mCLBP symptoms, improved function, and quality of life. **Conclusion:** This is the first prospective study of chronic low back pain neurostimulation treatment with 5-year durability data. Patients suffering with severe mCLBP have a proven effective, durable, and safe option over 5 years. Long-duration implantable multifidus neurostimulation should be considered within standard of care for these patients.

Supplemental Data: N/A

References: 1. Goubert, D., Van Oosterwijck, J., Meeus, M. & Danneels, L. Structural Changes of Lumbar Muscles in Non-specific Low Back Pain: A Systematic Review. *Pain Physician* **19**, E985–E1000 (2016). 2. Gilligan, C. *et al.* An implantable restorative-neurostimulator for refractory mechanical chronic low back pain: a randomized sham-controlled clinical trial. *Pain* **162**, 2486–2498 (2021). 3. Russo, M. *et al.* Muscle Control and Non-specific Chronic Low Back Pain. *Neuromodulation* **21**, 1–9 (2018).

Acknowledgements: The support of Mainstay Medical, Inc. for this project is gratefully acknowledged.

Learning Objectives: 1. By the end of this presentation, the audience will be able to differentiate mechanical nociceptive chronic low back pain (mCLBP) from other categories of chronic low back pain (i.e., neuropathic pain). 2. By the end of this presentation, the audience will be able to summarize 5-year data from the ReActiv8-B trial. 3. By the end of this presentation, the audience will be able to

interpret how neuromuscular electrical stimulation of the L2 dorsal ramus medial branch nerve is effective in mCLBP treatment with a high probability of clinically significant pain reduction, functional improvement, and quality of life for patients.

Financial Disclosures: Dr. Gilligan reports stock-options received from Mainstay, personal fees from Mainstay ($20,001-$100K), Saluda ($5,001-$25K), Persica ($5,001-$25K), and Iliad Lifesciences ($5,001-$25K), expert witness testimony personal fees, and serves as Editor in Chief of Pain Practice.

Disclosure: No significant relationships.

IS036

Breakout Session
SPINAL CORD STIMULATION FOR PAIN CLINICAL UPDATE
14-05-2024 14:30 - 16:00

IS THERE ANY INDICATION FOR SPINAL CORD STIMULATION (SCS) AND DORSAL ROOT GANGLION (DRG) IN REFRACTORY BRACHIAL PLEXUS PAIN?

Jan Vesper, MD
University Medical Center, Heinrich Heine University, Functional Neurosurgery And Stereotaxy, Duesseldorf, Germany

Introduction and Discussion: Dorsal root ganglia stimulation (DRG-S) has established its role as a very effective alternative treatment to traditional spinal cord stimulation in focal pain conditions or where a specific nerve is affected. While primarily used in the lumbar region, recent literature has shown that DRG-S can be effectively used in the upper thoracic and cervical region with slight alterations of the surgical approach.In the REALITY postmarket-study, a total of 20 subjects at 5 European sites were identified with leads implanted at C6 through T9 spinal levels. Of those, 9 subjects had completed their 6-months follow-up visits.There was only 1 reported device-related adverse event (a lead fracture) across all 20 upper extremity subjects. However other reposrts reveal significant side effects (machnical and neurological with high cervical DRG). DRG stimulation therapy has exceptional value in the treatment of CRPS of the upper extremities by reducing Numerical Rating Scale (NRS) pain scores and minimizing opioid therapies.

Supplemental Data:

References: Piedade GS, Vesper J, Chatzikalfas A, Slotty PJ. Cervical and High-Thoracic Dorsal Root Ganglion Stimulation in Chronic Neuropathic Pain. Neuromodulation. 2019;22(8):951-955. doi:10.1111/ner.12916 Mateusz J Graca [1], Timothy R Lubenow [2,] Update to "Efficacy and Safety of Cervical and High-Thoracic Dorsal Root Ganglion Stimulation Therapy for Complex Regional Pain Syndrome of the Upper Extremities"Neuromodulation. 2023 Oct 5:S1094-7159(23)00738-9. doi: 10.1016/j.neurom.2023.08.005. Online ahead of print.

Acknowledgements:

Learning Objectives: Reason to offer DRG-S for cervical and high-thoracic indications Alternatives

Financial Disclosures: J is consultant for ABBOTT, BSCI, MDT

Disclosure: No significant relationships.

IS037

Breakout Session
BRAIN: EPILEPSY
14-05-2024 14:30 - 16:00

NEUROMODULATION FOR REFRACTORY EPILEPSY: PROGRESS TOWARDS LESS INVASIVE APPROACHES

Andreas Schulze-Bonhage, MD
University Hospital Freiburg, Epileptology, Freiburg, Germany

Introduction and Discussion: Neuromodulatory approaches for the treatment of epilepsy have originated with deep brain stimulation of the cerebellum, the subthalamic and thalamic nuclei, with the intention to induce net inhibitory network effects on the brain and thus counteract the hyperexcitabilty which characterizes chronic epilepsy. Whereas initial clinical trials with low numbers of participants resulted in inconsistant results, first convincing evidence of antiseizure effects resulted from stimulation of the vagus nerve (1) and indirect modulation of brainstem nuclei like the locus coeruleus and the raphe nuclei; so far, vagus nerve stimulation has remained the most frequent neuromodulatory intervention in epilepsy. In 2010 and 2011, two invasive approaches with deep brain stimulation of the anterior nuclei of the thalamus (2) and responsive neurostimulation of the epileptic focus (3) with implantable devices were introduced and proved growing efficacy over time until now. In parallel with these approaches, non-invasive techniques like transcranial magnetic stimulation and transcranial electricel stimulation were repeatedly tested. Transcranial magnetiv stimulation was particularly used with low-frequency (0.1-1 Hz).stimulation protoculs and unclear efficacy until now. In contrast, kathodal transcranial DC stimulation over epileptogenic regions showed efficacy in reducing interictal spiking or seizure frequency in a serious of independent studies; remarkable overlasting effects of 20 minutes of kathodal stimulation or even shorter periods of trancranial stimulation were found (4). Recently, a combination of DC-like stimulation and high frequency stimulation has become available using an implantable device with an electrode array positioned epicranially over the epileptogenic focus area (5). Thus, strategies tested non-invasively are becomig available as implantable, yet minimally invasive devices for long-term application. This may also contribute to clarifying the role of low frequency stimulation and long-term depression as a potential strategy for epilepsy treatment in the next future.

Supplemental Data:

References: 1. The Vagus Nerve Stimulation Study Group. A randomized con- trolled trial of chronic vagus nerve stimulation for treatment of medically intractable seizures. Neurology. 1995;45:224–30 2. Fisher R et al. ; SANTE Study Group. Electrical stimulation of the anterior nucleus of thalamus for treatment of refractory epilepsy. Epilepsia. 2010;51:899-908. 3. Morrell MJ; RNS System in Epilepsy Study Group. Responsive cortical stimulation for the treatment of medically intractable partial epilepsy. Neurology. 2011 Sep 27;77(13):1295-304. doi: 10.1212/WNL.0b013e3182302056. Epub 2011 Sep 14. PMID: 21917777. 4. San-Juan D et al. Transcranial Direct Current Stimulation in Mesial Temporal Lobe Epilepsy and Hippocampal Sclerosis. Brain Stimul. 2017;10:28-35. 5. Schulze-Bonhage A et al. EASEE Study Group. Focal Cortex Stimulation With a Novel Implantable Device and Antiseizure Outcomes in 2 Prospective Multicenter Single-Arm Trials. JAMA Neurol. 2023;80:588-596. d

Acknowledgements:

Learning Objectives: 1. To understand different pathophysiological strategies to counteract hyperexcitability in neurostimulation for epilepsy 2. To knwo results from transcranial stimulation techniques and from implantable devices for neurostimulation in epilepsy 3. To learn about differential indications for approved neuromodulation approaches.

Financial Disclosures: Andreas Schulze-Bonhage has received personal honoraria for lectures or advice from Angelini Pharma, Bial, Desitin, Eisai, JAZZ Pharma, Precisis, UCB and UNEEG during the last three years.

Disclosure: No significant relationships.

IS038

Breakout Session
BRAIN: EPILEPSY
14-05-2024 14:30 - 16:00

MULTITARGET NEUROMODULATION FOR EPILEPSY

Andrew Yang, Director of Epilepsy Surgery
Barrow Neurological Institute, Neurosurgery, Phoenix, United States of America

Introduction and Discussion: Recent randomized controlled trials (RCT) have demonstrated efficacy of deep brain stimulation (DBS) of the anterior nucleus of the thalamus[1] (ANT) and responsive brain stimulation[3] in focal epilepsy. DBS of the centromedian[2] (CM) nucleus appears to be most suitable in well-defined generalized epilepsy syndromes, specifically Lennox-Gastaut Syndrome (LGS). However, there remains limited data to inform clinical decision making for neuromodulation in patients who did not fit the populations represented in these trials, such as those with multifocal, diffuse-onset, posterior-onset, generalized, or both focal and generalized seizures. We discuss multitarget neuromodulation, whereby stimulation electrodes are surgically implanted in more than one distinct brain structure, with personalized selection of targets based on the individual patient's epileptic network. Targets utilized in this emerging approach have included, in addition to the widely-used targets[4–10] (ANT, CM, cortical/quasi-cortical seizure-onset zone [SOZ]), less-studied thalamic nuclei[5,10,11] (pulvinar, mediodorsal), and basal ganglia structures (subthalamic nucleus,[5] nucleus accumbens[12]). Implant configurations reported in the literature consist of two types: 1) multiple distinct targets within subcortical regions; 2) the cortical/quasi-cortical SOZ in addition to thalamic nuclei. Multitarget neuromodulation is a procedurally-feasible treatment strategy to multiplicatively increase the parameter space for electrical stimulation. In spite of the added complexity to device programming, this approach is – at least theoretically – anticipated to maximize seizure outcomes with neuromodulation in patients with complex epilepsy. Future RCTs should assess the benefits of simultaneous multitarget stimulation, over and above monotarget stimulation.

Supplemental Data:

References: 1. Fisher, R. *et al.* Electrical stimulation of the anterior nucleus of thalamus for treatment of refractory epilepsy. *Epilepsia* **51**, 899–908 (2010). 2. Dalic, L. J. *et al.* DBS of Thalamic Centromedian Nucleus for Lennox-Gastaut Syndrome (ESTEL Trial). *Ann Neurol* **91**, 253–267 (2022). 3. Morrell, M. J. & RNS System in Epilepsy Study Group. Responsive cortical stimulation for the treatment of medically intractable partial epilepsy. *Neurology* **77**, 1295–1304 (2011). 4. Alcala-Zermeno, J. L. *et al.* Centromedian thalamic nucleus with or without anterior thalamic nucleus deep brain stimulation for epilepsy in children and adults: A retrospective case series. *Seizure* **84**, 101–107 (2021). 5. Yang, A. I., Isbaine, F., Alwaki, A. & Gross, R. E. Multitarget deep brain stimulation for epilepsy. *Journal of Neurosurgery* **1**, 1–8 (2023). 6. Elder, C., Friedman, D., Devinsky, O., Doyle, W. & Dugan, P. Responsive neurostimulation targeting the anterior nucleus of the thalamus in 3 patients with treatment-resistant multifocal epilepsy. *Epilepsia Open* **4**, 187–192 (2019). 7. Fields, M. C. *et al.* A multicenter retrospective study of patients treated in the thalamus with responsive neurostimulation. *Front. Neurol.* **14**, (2023). 8. Roa, J. A. *et al.* Responsive Neurostimulation of the Thalamus for the Treatment of Refractory Epilepsy. *Front Hum Neurosci* **16**, 926337 (2022). 9. Burdette, D. E. *et al.* Brain-responsive corticothalamic stimulation in the centromedian nucleus for the treatment of regional neocortical epilepsy. *Epilepsy & Behavior* **112**, 107354 (2020). 10. Beaudreault, C. P. *et al.* Responsive Neurostimulation Targeting the Anterior, Centromedian and Pulvinar Thalamic Nuclei and the Detection of Electrographic Seizures in Pediatric and Young Adult Patients. *Front Hum Neurosci* **16**, 876204 (2022). 11. Burdette, D., Mirro, E. A., Lawrence, M. & Patra, S. E. Brain-responsive corticothalamic stimulation in the pulvinar nucleus for the treatment of regional neocortical epilepsy: A case series. *Epilepsia Open* **6**, 611–617 (2021). 12. Kowski, A. B. *et al.* Nucleus accumbens stimulation in partial epilepsy--a randomized controlled case series. *Epilepsia* **56**, e78-82 (2015).

Acknowledgements:

Learning Objectives: 1) Explain the subset of patients with epilepsy who may be considered for multitarget neuromodulation 2) Describe patient factors that inform target selection for implantation and active contact configurations 3) Describe the clinical rationale and goals of multitarget neuromodulation

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS039

Breakout Session
BRAIN: EPILEPSY
14-05-2024 14:30 - 16:00

INTRACRANIAL NEUROMODULATION IN CHILDREN WITH REFRACTORY EPILEPSY

George Ibrahim, MD
Institute of Biomedical Engineering, University Of Toronto, Toronto, Canada

Introduction and Discussion: Epilepsy is the most common serious neurological disorder of childhood. For one-third of children, medications are not sufficient to control seizures and this population of children with drug-resistant epilepsy is at higher risk of death and psychosocial disadvantage. Neuromodulation is increasingly considered in the treatment of epilepsy when resective or disconnection procedures cannot be performed. Extracranial (i.e vagus nerve) and intracranial (deep brain or responsive neurostimulation) may be considered. Evidence for intracranial neuromodulation in children will be presented along with expected benefits and potential complications. Novel connectomic-based tools to stratify patients presurgically based on expected response to therapy will be discussed. Emerging neuromodulation tools to treat comorbidities of epilepsy will be introduced. The session will provide a discussion of emerging therapies in children with broad application in epilepsy and beyond.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1. Describe the role of intracranial neuromodulation therapies for drug resistant epilepsy. 2. Appreciate connectomic-based tools to identify responders to neuromodulation 3. Introduce emerging applications for neuromodulatory tools to treat comorbidites of epilepsy.

Financial Disclosures: LivaNova Inc. Advisory Board - 501-5000 USD LivaNova Inc Education/Research Grant - >100,000 USD Synergia Inc Advisory Board - 1-500 USD Medtronic Inc Advisory Board - 501-5000 USD

Disclosure: No significant relationships.

IS040

Breakout Session
BRAIN: EPILEPSY
14-05-2024 14:30 - 16:00

VAGAL NERVE STIMULATION IN REFRACTORY AND SUPER-REFRACTORY EPILEPTIC STATUS IN CHILDREN

Andrea Landi, MD
Università di Padova, Neuroscience, Padova, Italy

Introduction and Discussion: Background: Status epilepticus is a life-threatening condition which is defined refractory (RSE) when the seizure activity continues despite treatment with benzodiazepine and a second appropriate treatment. Super refractory status epilepticus (SRSE) is a RSE that persists or recurs for ≥ 24 hours. Usually these patients support a complex multi-drug therapy, often associated with ketogenic diet. The outcome in terms of brain function and of survival is generally poor. Recently, have been reported cases of new onset epileptic seizures (NORSE) following un-identified febrile status (FIRES), particularly in children and young patients. NORSE in the case of FIRES may be associated with SRSE, difficult to treat. Moreover, few papers deal with the outcomes of patients affected by RSE and SRSE treated with neuromodulator therapies. Vagus nerve stimulation (VNS) is an approved treatment for drug resistant epilepsy both in adults and in children. To improve the knowledge of the potentiality of neuromodulation in the treatment of SRSE, we present our personal experience of paediatric patients treated with VNS for SRSE. Methods: Case series of 7 consecutive paediatric patients treated with VNS for SRSE since 2012 by a single surgeon in Monza and Padua. SRSE were of different aetiologies and in 3 cases were consequent to a FIRES. VNS surgery was conducted as usual on the left vagus trunk. A rapid titration of the stimulation was started soon after implantation. We considered electro clinical data before and after VNS implantation and at the last follow-up. Results: We achieved the resolution of SRSE in 5 out of 7 patients in a mean time of two weeks. At the last follow up (mean 15 months) these patients showed a significant reduction of seizure burden without any relapse of SE. Their functional outcome was excellent in 3 cases and satisfactory in the other, measured with QOL scores. Two patients did not benefit from VNS (one case of genetic SRSE and another after FIRES). Conclusions: Based on our experience, we suggest that VNS could be considered as a valid and safe adjuvant treatment for SRSE, considering neuromodulation as a new strategy for this challenging condition.

Supplemental Data:

References: Bonardi CM, Furlanis GM, Toldo I, et al. Myoclonic super-refractory status epilepticus with favourable evolution in a teenager with FIRES: Is the association of vagus nerve stimulation and cannabidiol effective? *Brain Dev*. 2023;45(5):293-299. doi:10.1016/j.braindev.2023.01.004 Dibué-Adjei M, Brigo F, Yamamoto T, Vonck K, Trinka E. Vagus nerve stimulation in refractory and super-refractory status epilepticus - A systematic review. Brain Stimul. 2019 Sep-Oct;12(5):1101-1110. doi: 10.1016/j.brs.2019.05.011. Epub 2019 May 14. PMID: 31126871. Grioni D, Landi A, Fiori L, Sganzerla EP. Does emergent implantation of a vagal nerve stimulator stop refractory status epilepticus in children? Seizure. 2018 Oct;61:94-97. doi: 10.1016/j.seizure.2018.08.008. Epub 2018 Aug 11. PMID: 30118931.

Acknowledgements:

Learning Objectives: 1. To clarify the value of neuromodulation in the treatment of difficult to treat epilepsy 2. To suggest possible use of Vagal neve stimulation in the treatment of Status epilepticus 3 To increase the collection of case series in this specific pathology

Financial Disclosures: Andrea Landi Livanova Consultant/Advisory board 500 - 5000 USD

Disclosure: No significant relationships.

IS041

Breakout Session
BRAIN: NEUROPSYCHIATRY: NOVEL APPLICATIONS IN BEHAVIORAL NEUROMODULATION
14-05-2024 14:30 - 16:00

DEEP BRAIN STIMULATION OF THE NUCLEUS ACCUMBENS IN THE TREATMENT OF SEVERE ALCOHOL USE DISORDER: A PHASE I PILOT TRIAL

Nir Lipsman, MD
Sunnybrook Health Sciences Centre, Toronto, Canada

Introduction and Discussion: Alcohol use disorder (AUD) is a prevalent, often refractory, and among the most challenging conditions to treat. The symptoms of AUD are driven by dysfunction in circuits centered on the nucleus accumbens (NAc). Case reports and animal studies suggest NAc-DBS may be an effective harm-reduction treatment in severe AUD. Six patients with severe, refractory AUD underwent NAc-DBS. Safety metrics and clinical outcomes were recorded. Positron emission tomography (FDG-PET) was used to measure glucose metabolism in the NAc at baseline and 6 months. Functional magnetic resonance imaging (fMRI) was used to characterize postoperative changes in NAc functional connectivity to the rest of the brain, as well as NAc and dorsal striatal reactivity to alcoholic visual cues. All patients experienced a reduction in craving. There was a significant reduction in alcohol consumption, alcohol-related compulsivity, and anxiety at 12 months. There was no significant change in depression. FDG-PET analysis demonstrated reduced NAc metabolism by 6 months, which correlated with improvements in compulsive drinking behaviors. Clinical improvement correlated with reduced functional connectivity between the NAc and the visual association cortex. Active DBS was associated with reduced activation of the dorsal striatum during passive viewing of alcohol-containing pictures. NAc-DBS is feasible and safe in patients with severe, otherwise refractory AUD. It is associated with a reduction in cravings and addictive behavior. A potential mechanism underlying this process is a down-regulation of the NAc, a disruption of its functional connectivity to the visual association cortex, and interference of cue-elicited dorsal striatum reactivity.

Supplemental Data:

References: Davidson B, Giacobbe P, George TP, Nestor SM, Rabin JS, Goubran M, Nyman AJ, Baskaran A, Meng Y, Pople CB, Graham SJ, Tam F, Hamani C, Lipsman N. Deep brain stimulation of the nucleus accumbens in the treatment of severe alcohol use disorder: a phase I pilot trial. Mol Psychiatry. 2022 Oct;27(10):3992-4000.

Acknowledgements: Funding was supplied from the Harquail Centre for Neuromodulation, and philanthropic support to the Sunnybrook Foundation

Learning Objectives: 1. Describe the challenge of treatments for alcohol use disorder, and the link to disordered brain circuitry 2. Describe the nature of deep brain stimulation as a circuit modulation strategy 3. Review the results of a prospective pilot trial of DBS in AUD, describing next steps for the field

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS042

Breakout Session
BRAIN: NEUROPSYCHIATRY: NOVEL APPLICATIONS IN BEHAVIORAL NEUROMODULATION
14-05-2024 14:30 - 16:00

DEEP BRAIN STIMULATION OF THE NUCLEUS ACCUMBENS IN TREATMENT-RESISTANT ALCOHOL USE DISORDER: A DOUBLE-BLIND RANDOMIZED CONTROLLED MULTI-CENTER TRIAL

Jens Kuhn, MD
University of Cologne and Alexianer GmbH Cologne, Psychiatry And Psychotherapy, Cologne, Germany

Introduction and Discussion: The introduction of deep-brain stimulation (DBS) by Benabid in the mid-1980s marked the beginning of a whole new era of therapy for movement disorders .Owing to its high evidence-based efficacy, this procedure has, in the meantime, been applied to more than 250,000 patients with Parkinson's disease worldwide. The knowledge and success gained through the application of DBS in Parkinson's disease has been leveraged for the treatment of non-motor disorders, including psychiatric diseases. Considering enormous socio-economic problems associated with addictive disorders and the absent of reliable and effective therapeutic interventions it is perhaps obvious that DBS has, in the case of therapy resistance, also be considered as a treatment for one of the most frequent psychiatric diseases – addiction due to psychoactive substance use. In the context of the lecture, the development of DBS for addiction will be presented via positive individual cases and animal studies. In addition, the results of the world's first blinded multicenter study on DBS for alcohol addiction will be presented and discussed.

Supplemental Data:

Learning Objectives: 1 Development of DBS in the field of addiction 2 Insight into the application and research status of DBS for alcohol addiction. 3 Recruitment and cost problems

Financial Disclosures: The presented study was supported by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation Bo 799/8-1). Jens Kuhn was PI in Investigator initiated trials supported by Medtronic.

Disclosure: No significant relationships.

IS043

Breakout Session
BRAIN: NEUROPSYCHIATRY: NOVEL APPLICATIONS IN BEHAVIORAL NEUROMODULATION
14-05-2024 14:30 - 16:00

CORTICAL STIMULATION FOR ADDICTIVE DISORDERS

Dirk De Ridder, MD
University of Otago, Surgical Sciences (neurosurgery), Dunedin, New Zealand

Introduction and Discussion: Substance use disorder (SUD) has a large impact on both the medical system and society. Stress, craving and triggers lead to relapse in 85% patients with alcohol SUD within one year of traditional treatments. The DLPFC has been most targeted for non-invasive transcranial stimulation, and the insula may be an emerging target. Meta-analyses of non-invasive high frequency rTMS of the left DLPFC and bifrontal tDCS demonstrate beneficial effects on craving and consumption. The ACC has been targeted to reduce craving and stress in different addictive disorders, both by lesioning and neuromodulation. Neuromodulation of the ACC has been performed with non-invasive transcranial magnetic stimulation and transcranial direct current stimulation, as well as invasively by implanted electrodes. But no meta-analysis has been performed. An addiction/craving network can be targeted at multiple parts of the cortex, including the DLPFC, ACC, and insula.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. understand the cortical brain network of addiction 2. understand the targets of the main non-invasive neuromodulation treatments 3. understand the main targets of the main surgical neuromodulation treatments

Financial Disclosures: Dirk De Ridder, Abbott, speakers' bureau, consultant

Disclosure: No significant relationships.

IS044

Breakout Session
BRAIN: NEUROPSYCHIATRY: NOVEL APPLICATIONS IN BEHAVIORAL NEUROMODULATION
14-05-2024 14:30 - 16:00

COGNITIVE AND QUALITY-OF-LIFE RELATED FACTORS OF BODY MASS INDEX (BMI) IMPROVEMENT AFTER DEEP BRAIN STIMULATION IN THE SUBCALLOSAL CINGULATE AND NUCLEUS ACCUMBENS IN TREATMENT-REFRACTORY CHRONIC ANOREXIA NERVOSA

Gloria Villalba, MD, PhD[1,2,3], Matilde Elices, DPsych[4], Purificacion Salgado, MD[4], Jose Maria Gines, MD[4], Maria J Portella, PhD[5], Rocio Guardiola, DPsych[4], Maria Polo, DPsych[4], Carlos Cedron, DPsych[4], Rosa Maria Manero, DPsych[6], Ignacio Delgado, MD[7], Victor Perez-Sola, PhD[4]
[1]Research Institute Hospital del Mar, Systems Neurologics And Neurotherapeutics Group, Barcelona, Spain, [2]Hospital del Mar, Neurosurgery, Barcelona, Spain, [3]Pompeu Fabra University, Medicine, Barcelona, Spain, [4]Hospital del Mar, Psychiatry, Barcelona, Spain, [5]Hospital de Sant Pau, Psychiatry, Barcelona, Spain, [6]Hospital del Mar, Neurology, Barcelona, Spain, [7]Universitat Autonoma Barcelona, Fisiology, Barcelona, Spain

Introduction and Discussion: It is unknown the effect that deep brain stimulation (DBS) may have on cognitive status in patients with anorexia nervosa (AN). The results of a study where 8 patients with chronic and severe AN are treated with DBS in the subgeniculate cingulum (SGC) and in the nucleus accumbens (NAcc) are presented (Clinicaltrials.gov: NCT03168893). Preoperatively and 6 months after DBS, the following clinical aspects were evaluated: Cognitive status (executive functions, attention, memory, visuospatial deficits, processing speed), Core psychophatology, General psychophatology, Quality of life and Body mass index (BMI). As with other mental illnesses, DBS is cognitively safe. It is of interest that the improvement in some cognitive and psychopathology aspects is related or not to the improvement in BMI. Because the sample studied is small, a common problem in studies of DBS and mental illness, the results cannot be extrapolated, but it is the first time that the cognitive effect of DBS is collected in a series of patients with AN.

Supplemental Data:

References: Reville MC, Frampton I, O'connor L (2016). Literature review of cognitive neuroscience and anorexia nervosa. *Current Psychiatry Reports* , *18*(18), 1–8 Mole JA , Prangnell SJ (2017) Role of clinical neuropsychology in deep brain stimulation: Review of the literature and considerations for clinicians. *Applied Neuro- psychology: Adult*, *26*(3), 283–296. Lipsman N, Lam E, Volpini M et al (2017). Deep brain stimulation of the subcallosal cingulate for treatment-refractory anorexia nerv- osa: 1 year follow-up of an open-label trial. *The Lancet Psy- chiatry*, *4*(4), 285–294 Liu W , Zhan S , Li D et al (2020). Deep brain stimulation of the nucleus accumbens for treatment-refractory anorexia nervosa: a long-term follow-up study. *Brain Stimul.* 13, 643–64 Scaife J, Eraifek J, Green A et al (2022) Deep brain stimulation of the nucleus accumbens in severe enduring Anorexia Nervosa: a pilot study. Frontiers in Behavioral Neuroscience, 16,article 842184

Acknowledgements:

Learning Objectives: It is the first time that the relationship between cognitive status, psychopathology, quality of life and body mass index has been reported in a group of patients with anorexia nervosa treated with DBS.

Financial Disclosures: Instituto de Salud Carlos III, Grant/Award : PI16/00382(Spanish Goverment); Grant/Award : 2017 SGR 134 (Catalan Goverment), Grant/Award : 2017 SGR1343 (European Union funds)

Disclosure: No significant relationships.

IS045

Breakout Session
BRAIN: NEUROPSYCHIATRY: NOVEL APPLICATIONS IN BEHAVIORAL NEUROMODULATION
14-05-2024 14:30 - 16:00

POSTSURGICAL MORBIDITY AND MORTALITY FAVORABLY INFORMS DEEP BRAIN STIMULATION FOR NEW INDICATIONS INCLUDING SCHIZOPHRENIA AND SCHIZOAFFECTIVE DISORDER

Judith Gault, PhD[1], Patrick Hosokawa, MSc[2], Daniel Kramer, MD[2], Elyn Saks, PhD[3], Paul Appelbaum, MD[4], John Thompson, PhD[2,5], Ann Olincy, MD[6], Nicola Cascella, MD[7], Akira Sawa, MD[8], Wayne Goodman, MD[9], Nidal Moukaddam, MD[9], Sameer A Sheth, MD[9], William Anderson, MD[10], Rachel A Davis, MD[11]
[1]University of Colorado AMC, Neurosurgery And Psychiatry, Aurora, United States of America, [2]University of Colorado AMC, Neurosurgery, Aurora, United States of America, [3]University of Southern California, Gould School Of Law, Los Angeles, United States of America, [4]Columbia University, Psychiatry, New York, United States of America, [5]University of Colorado AMC, Aurora, United States of America, [6]VA Eastern Colorado Medical Center, Psychiatry, Aurora, United States of America, [7]Johns Hopkins University, Psychiatry, Baltimore, United States of America, [8]Johns Hopkins University, Baltimore, United States of America, [9]Baylor College of Medicine, Menninger Department Of Psychiatry And Behavioral Sciences, Houston, United States of America, [10]Johns Hopkins University, Neurosurgery, Baltimore, United States of America, [11]University of Colorado AMC, Psychiatry And Neurosurgery, Aurora, United States of America

Introduction and Discussion: Deep brain stimulation (DBS) is promising for new indications like treatment-refractory schizophrenia/schizoaffective disorder (SZ/SAD) based on initial clinical trials. Despite effective treatment of psychosis, in the first DBS clinical trial for treatment refractory schizophrenia, one of the eight subjects experienced both a symptomatic hemorrhage and an infection requiring device removal.[1] Now, ethical concerns about higher surgical risk in SZ/SAD have impacted clinical trial progress. However, insufficient numbers of cases precludes conclusions regarding DBS risk in SZ/SAD. Here, we directly compared adverse surgical outcomes for all surgical procedures between SZ/SAD and Parkinson's disease (PD) cases to infer relative surgical risk relevant to indirectly gauging DBS risks in subjects with SZ/SAD. In the primary analysis through the TriNetX Research Network™, browser-based statistical analysis software, TriNetX Live (trinetx.com TriNetX LLC, Cambridge, MA), for Measures of Association using the Z-test was used to compare frequencies of postsurgical morbidity and mortality after matching for ethnicity, over 39 surgical risk factors, and 19 CPT 1003143 coded surgical procedures from over 35,000 electronic medical records (EMR), over 19 years, from 48 United States health care organizations (HCOs). Diagnoses were based on ICD-10 codes. In the final analysis, logistic regression was used to determine relative frequencies of outcomes among 21 diagnostic groups/cohorts currently treated with or considered for DBS and 3 control cohorts. Postsurgical mortality was 1.01–4.11% lower in SZ/SAD compared to the matched PD cohort at 1 month and 1 year after any surgery, while morbidity was 1.91–2.73% higher related in part to postsurgical noncompliance with medical treatment. Hemorrhages and infections were not higher. Across the 21 cohorts compared unmatched, PD and SZ/SAD were among eight cohorts with fewer surgeries, nine cohorts with higher postsurgical morbidity, and fifteen cohorts within the control-group range for 1-month postsurgical mortality. Given that the subjects with SZ or SAD, along with most other diagnostic groups examined, had lower postsurgical mortality than the PD cohort, it is reasonable to apply existing ethical and clinical guidelines to identify appropriate surgical candidates for inclusion of these patient populations in DBS clinical trials.[2]

Supplemental Data:

References: 1 Corripio, I. *et al.* Deep brain stimulation in treatment resistant schizophrenia: A pilot randomized cross-over clinical trial. *EBioMedicine* **51**, 102568 (2020). https://doi.org:10.1016/j.ebiom.2019.11.029 2 Gault, J. M. *et al.* Postsurgical morbidity and mortality favorably informs deep brain stimulation for new indications including schizophrenia and schizoaffective disorder. *Frontiers in Surgery* **10** (2023). https://doi.org:10.3389/fsurg.2023.958452

Acknowledgements: The support of University of Colorado, Department on Neurosurgery and NIMH MH121362 is gratefully acknowledged.

Learning Objectives: 1) Use of surgical outcomes for all surgical procedures to infer surgical risk relevant to gauging DBS risks for 16 new diagnostic indications relative to 5 diagnoses currently treated with DBS. 2) Diagnosis-related surgical risks associated with all surgical procedures combined will be discussed for 21 DBS-related diagnoses. 3) Disparities in the frequency of surgical procedures across 21 DBS-related diagnoses will be discussed.

Financial Disclosures: SAS is a consultant for Boston Scientific, Zimmer Biomet, Neuropace, Abbott. WKG received honorarium from Biohaven Pharmaceuticals, royalties from NView, LLC, and donated devices from Medtronic for an NIH funded research study. RAD provides paid Ad Hoc consultation for Medtronic. JMG owns Pfizer stock. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Disclosure: No significant relationships.

IS046

Breakout Session
NEUROPROSTHETICS AND NEUROREGENERATION
14-05-2024 14:30 - 16:00

OPTIMIZING PHYSIOLOGICAL CLOSED-LOOP CONTROLLERS (PCLC) IN CLOSED-LOOP NEUROMODULATION

Tim Denison, PhD
Oxford University, Institute Of Biomedical Engineering, Oxford, United Kingdom

Introduction and Discussion: The advent of “smart” systems technology using machine learning is revolutionizing many facets of everyday life – from self-driving cars to digital home assistants. However, experiences from this nascent field also provide lessons on the importance of including risk management in core systems design. Lessons range from the innocuous, such as algorithms performing odd behavior like spontaneously laughing digital assistants, to the severe, such as crashes resulting from compromised algorithms or the user being overly reliant on their performance. As the medical field adapts similar automated technologies, it is worth considering how engineers and clinicians can work together to mitigate risks with deploying intelligent systems through thoughtful system design. This talk provides an overview of how risk should be considered in *physiological control loops* that strive for semi-to-fully automated operation. I will first provide an overview of current use cases in neuromodulation, which both motivates a framework for the design of closed-loop controllers and highlights safety considerations. I will then discuss specific risk areas and their potential mitigations, drawing from historical medical device examples to illustrate the key concepts. I will put special focus on how we can make these systems safe and adapted to real physiologic dynamics. Finally, I will provide a general design checklist framed through the overview of an adaptive bidirectional brain-machine-interface currently undergoing human clinical studies.

Supplemental Data:

References: Gunduz A, Opri E, Gilron R, Kremen V, Worrell G, Starr P, Leyde K, Denison T. Adding wisdom to 'smart' bioelectronic systems: a design framework for physiologic control including practical examples. Bioelectron Med (Lond). 2019 Mar;2(1):29-41. doi: 10.2217/bem-2019-0008. Epub 2019 May 30. PMID: 33868718; PMCID: PMC7610621.

Acknowledgements:

Learning Objectives: 1. Provide a framework and common language for physiologic closed-loop controllers (PCLCs) 2. Use example from sensing-based domains to provide intuition for PCLC operation, and the problems they help solve, as template for any system using adaptive technology 3. Reinforce key terms and concepts for safe sensing-based systems from FDA guidance documents and PCLC standards (e.g. risk, 60601-1-10) for robust design and safe use – design template

Financial Disclosures: •paid consultant for Cortec Neuro, Inspire, and Synchron •I have intellectual property in this space (currently licensed to Medtronic, Amber) •Director/shares in Amber Thx Ltd for a research system I am designing and using (DyNeuMo) for use in adaptive systems

Disclosure: No significant relationships.

IS047

Breakout Session
NEUROPROSTHETICS AND NEUROREGENERATION
14-05-2024 14:30 - 16:00

HIGH PERFORMANCE SPEECH NEUROPROSTHESIS

Daniel Rubin, Neurologist
Massachusetts General Hospital, Neurology, Boston, United States of America

Introduction and Discussion: In many conditions that cause anarthria, including brainstem stroke, muscular dystrophy, and amyotrophic lateral sclerosis (ALS), the cortical substrate of language is intact but is disconnected from motor systems that actuate communication.[1–4] The ability to communicate with depth and nuance is one of our most defining characteristics as humans, and whether an individual will retain or regain the ability to communicate is often a determining factor in the decision to continue or withdraw life- sustaining care.[1,5–8] Existing augmentative and alternative communication (AAC) devices may allow patients to communicate by adapting residual volitional motor control (e.g., eye gaze, sip and puff), but such systems are often cumbersome and require substantial effort on the part of both the patient and caregiver.[9] As a result, these devices are often abandoned due to the need for frequent caregiver-based re-calibration, low communication rates, and technical failure.[10] Brain computer interfaces (BCIs) link the brain's electrical signals directly to an external device and can restore function by bypassing the site of pathology within the nervous system.[11] Previous research with intracortical BCI (iBCI) systems for communication has focused mainly on point-and-click communication; paralyzed users imagine or attempt to move their hand and decoding algorithms translate the measured neural activity into the control signal for a computer cursor.[12–15] People have used iBCI systems to type at 30-40 correct characters per minute (approximately 8 words per minute),[13] and this rate doubles when handwritten characters of the alphabet are decoded.[16] While a potentially life changing improvement for many, this is nonetheless far from fluent conversational speech (90-170 words per minute). In this talk, we describe a more natural and faster approach to restoring communication using an iBCI that analyzes the neural signals controlling the muscles of speech production, rather than hand movement, to decode the user's attempted speech directly. The BrainGate clinical trial (ClinicalTrials.gov Identifier: NCT00912041) enrolls adults with tetraplegia and/or anarthria in a study of the efficacy and safety of an iBCI that utilizes microelectrode arrays implanted directly in motor cortex.[17] Through research sessions focused on understanding the neural activity underlying the production of speech, we have developed a real-time speech-decoding iBCI that can return intuitive, near-fluent communication to people with severe speech motor impairments.[18,19]

Supplemental Data:

References: 1. Lulé D, Zickler C, Häcker S, et al. Life can be worth living in locked-in syndrome. Prog Brain Res 2009; 177: 339–51. PMID: 19818912. 2. Branco MP, Pels EGM, Sars RH, et al. Brain-Computer Interfaces for Communication: Preferences of Individuals With Locked-in Syndrome. Neurorehabil Neural Repair 2021; 35: 267–79. PMCID: PMC7934157. 3. Bach JR. Amyotrophic lateral sclerosis. Communication status and survival with ventilatory support. Am J Phys Med Rehabil 1993; 72: 343–9. PMID: 8260126. 4. Hochberg LR, Cudkowicz ME. Locked in, but not out? Neurology 2014; 82: 1852–3. PMID: 24789868. 5. Mayer SA, Kossoff SB. Withdrawal of life support in the neurological intensive care unit. Neurology 1999; 52: 1602–1602. PMID: 10331685. 6. Côte N, Turgeon AF, Lauzier F, et al. Factors associated with the withdrawal of life-sustaining therapies in patients with severe traumatic brain injury: A multicenter cohort study. Neurocrit Care 2013; 18: 154–60. PMID: 23099846. 7. Turgeon AF, Lauzier F, Burns KEA, et al. Determination of neurologic prognosis and clinical decision making in adult patients with severe traumatic brain injury: A survey of canadian intensivists, neurosurgeons, and neurologists. Crit Care Med 2013; 41: 1086–93. PMID: 23385104. 8. Adil MM, Larriviere D. Family discussions on life-sustaining interventions in neurocritical care. Handb Clin Neurol. 2017, 2017 DOI:10.1016/B978-0-444-63600-3.00022-2. PMID: 28187812. 9. Laureys S, Pellas F, Van Eeckhout P, et al. The locked-in syndrome : what is it like to be conscious but paralyzed and voiceless? Prog Brain Res. 2005: 495–611. PMID: 16186044. 10. Wolpaw JR, Bedlack RS, Reda DJ, et al. Independent home use of a brain-computer interface by people with

amyotrophic lateral sclerosis. Neurology 2018; 91: e258–67. PMCID: PMC6059033. 11. Brandman DM, Cash SS, Hochberg LR. Review: Human Intracortical Recording and Neural Decoding for Brain-Computer Interfaces. IEEE Trans. Neural Syst. Rehabil. Eng. 2017; 25: 1687–96. PMCID: PMC5815832 12. Hochberg LR, Serruya MD, Friehs GM, et al. Neuronal ensemble control of prosthetic devices by a human with tetraplegia. Nature 2006; 442: 164–71. PMID: 16838014. 13. Pandarinath C, Nuyujukian P, Blabe CH, et al. High performance communication by people with paralysis using an intracortical brain-computer interface. Elife 2017; 6: 1–27. PMCID: PMC5319839. 14. Brandman DM, Burkhart MC, Kelemen J, Franco B, Harrison MT, Hochberg LR. Robust closed-loop control of a cursor in a person with tetraplegia using Gaussian process regression. Neural Comput 2018; 30: 2986–3008. PMCID: PMC6685768. 15. Brandman DM, Hosman T, Saab J, et al. Rapid calibration of an intracortical brain-computer interface for people with tetraplegia. J Neural Eng 2018; 15: 1–26. PMCID: PMC5823702. 16. Willett FR, Avansino DT, Hochberg LR, Henderson JM, Shenoy K V. High-performance brain-to-text communication via handwriting. Nature 2021; 593: 249–54. PMCID: PMC8163299. 17. Rubin DB, Ajiboye AB, Barefoot L, Bowker M, Cash SS, Chen D, Donoghue JP, Eskandar EN, Friehs G, Grant C, Henderson JM, Kirsch RF, Marujo R, Masood M, Mernoff ST, Miller JP, Mukand JA, Penn RD, Shefner J, Shenoy KV, Simeral JD, Sweet JA, Walter BL, Williams ZM, Hochberg LR. Interim Safety Profile From the Feasibility Study of the BrainGate Neural Interface System. Neurology. 2023 Mar 14;100(11):e1177-e1192. PMCID: PMC10074470. 18. Wilson GH, Stavisky SD, Willett FR, et al. Decoding spoken English from intracortical electrode arrays in dorsal precentral gyrus. J Neural Eng 2020; 17: 066007. PMCID: PMC8293867. 19. Willett FR, Kunz EM, Fan C, Avansino DT, Wilson GH, Choi EY, Kamdar F, Glasser MF, Hochberg LR, Druckmann S, Shenoy KV, Henderson JM. A high-performance speech neuroprosthesis. Nature. 2023 Aug;620(7976):1031-1036. doi: 10.1038/s41586-023-06377-x. Epub 2023 Aug 23. PMID: 37612500; PMCID: PMC10468393.

Acknowledgements: This work has been supported by: NINDS K23 DC021297, NINDS U01NS098968, NIDCD U01DC017844, NIDCD U01DC019430, NIDCD DP2DC021055, Office of Research and Development, Rehabilitation R&D Service, Department of Veterans Affairs (N2864C, A2295R, A3803R), AAN Clinical Research Training Scholarship, Harvard Catalyst KL2/CMeRIT, NINDS K23 DC021297, AHA's Second Century Early Faculty Independence Award, Stanford Wu Tsai Neurosciences Institute, Howard Hughes Medical Institute, Larry and Pamela Garlick, Simons Foundation Collaboration on the Global Brain, A.P. Giannini Postdoctoral Fellowship, DOD CDMRP ALS Pilot Clinical Trial Award (AL220043), Pilot Award from the Simons Collaboration for the Global Brain (872146SPI), Searle Scholars Program, Career Award at the Scientific Interface from the Burroughs Wellcome Fund, UC Davis Early Career Faculty Award for Creativity and Innovation. *The content does not necessarily represent the official views of the Department of Veterans Affairs or the U.S. Government. CAUTION: Investigational Device. Limited by Federal Law to Investigational Use.*

Learning Objectives: 1. To understand recent progress in brain computer interface technology for communication 2. To describe cutting edge applications of machine learning in real-time neural decoding 3. To inform practitioners, researchers, and patient advocates about potential research opportunities

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS048

Breakout Session
NEUROPROSTHETICS AND NEUROREGENERATION
14-05-2024 14:30 - 16:00

BIOHYBRID REGENERATIVE INTERFACE

Damiano Barone, MD, PhD
University of Cambridge, Clinical Neurosciences, Cambridge, United Kingdom

Introduction and Discussion: The development of electronics for interfacing with the nervous system is rapidly advancing, with applications spanning basic science to clinical translation. Neural interfaces and cell transplantation have been powerful strategies for the restoration of neurological function, targeting dysfunctional regions to either electrically stimulate or record from healthy neural circuitry, or provide new cells to replace damaged tissue. Traditionally considered independently, the concept of biohybrid interfaces—implantable neural interfaces containing cells that integrate into the host tissue—offers novel opportunities for treatment. Biohybrid implants, which combine electrode arrays with cultured cells, enhance tissue integration and long-term stability. These devices, designed for in vitro studies or in vivo implantation, mediate the electrode-tissue interface by integrating the cells within the implants into the surrounding tissue. This integration facilitates a natural interaction between the device and the nervous system, potentially reducing the foreign body response and improving the implant's longevity and functionality. Furthermore, the use of cells in these biohybrid systems opens up possibilities for dynamic interactions with the nervous system, such as the release of neurotrophic factors or the modulation of local neural activity. Building on this concept, we have developed a first application that employs induced pluripotent stem cell (iPSC)–derived myocytes as biological targets for peripheral nerve inputs, grafted onto flexible electrode arrays. This biohybrid device, demonstrated in freely moving rats, shows long-term survival and functional integration with the forearm nerve bundle, enhancing resolution and electrical recording in vivo. This advancement represents a significant step toward restorative therapies using regenerative bioelectronics, addressing critical challenges in biocompatibility and tissue-electronics interface resolution.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. **Understanding Biohybrid Implants**: Attendees should gain a comprehensive understanding of the concept of biohybrid implants, including their design, how they integrate cultured cells with electrode arrays, and their potential to enhance tissue integration and long-term stability in neural interfaces. 2. **Exploring Biohybrid Implants**: Participants should learn about the innovative approach of combining neural interfaces with cell transplantation to create biohybrid systems. They should understand how this integration facilitates natural interactions between the device and the nervous system, potentially improving the functionality and longevity of the implant. 3. **Applications of Biohybrid Implants**: Attendees should become familiar with the latest advancements in restorative therapies using regenerative bioelectronics, particularly the development of a biohybrid device that employs iPSC-derived myocytes for enhanced resolution and electrical recording in vivo for amputated nerves. They should understand the significance of this advancement in addressing critical challenges in biocompatibility and the tissue-electronics interface.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS049

Breakout Session
NEUROPROSTHETICS AND NEUROREGENERATION
14-05-2024 14:30 - 16:00

HIGH RESOLUTION EMG-BASED PROSTHETIC CONTROL

James Fitzgerald, MB ChB, PhD
University of Oxford, Nuffield Department Of Surgical Sciences, Oxford, United Kingdom

Introduction and Discussion: Traditional electromyogram (EMG) based control of prosthetics (myoelectrics) is a decades-old technology based on low resolution capture of EMG signals from residual musculature above an amputation. The user has to learn to generate control signals with muscle twitches and can typically generate only two or three such signals that the system can discern. This leads to poor control with a very limited repertoire of movements available, no simultaneous joint movements and no gradation of force. Output is position sensitive and degraded by perspiration, and use is cognitively burdensome, and these factors together lead to high rates of prosthesis abandonment. Several solutions to the problem of better prosthesis control have been suggested and are at various stages of development. Amongst these are implanted peripheral nerve interfaces of several types, and targeted muscle reinnervation. Implants are ultimately likely to provide a definitive solution in many cases, but they do have problems that presently limit their translatability and longevity, and there remains a clear place for improved noninvasive solutions. To provide better control information requires an increase in EMG bandwidth. High density surface EMG (HD-sEMG) involves recording large numbers of EMG signals from an array of electrodes. Translation of this data into movement intent is a pattern recognition task well suited to Deep Learning techniques, and we have developed RPC-Net (Recursive Prosthetic Control Network) to do this. This uses a regression-based approach to translate proximal forearm HD-sEMG signals from a 96-contact array into hand kinematics in a way that is computationally efficient. RPC-Net outperforms other methods with equivalent computational requirements. Importantly, this deep learning based method is robust to reductions in the number of electrodes, providing significant redundancy in input, and to input signal length, suggesting potential for further reduction in computational cost. Importantly, the control signals are derived from musculature that is activated in the normal fashion, removing the excess cognitive load from the user. This and similar methods pave the way for more natural and functional prosthetic control.

Supplemental Data:

References: Decomposition into dynamic features reveals a conserved temporal structure in hand kinematics. Keogh C, FitzGerald JJ. iScience 2022;25(11):105428. Developing RPC-Net: leveraging high-density electromyography and machine learning for improved hand position estimation. Rolandino G, Gagliardi M, Martins T, Cerone GL, Andrews B, FitzGerald JJ. IEEE Trans Biomed Eng 2023 doi: 10.1109/TBME.2023.3346192.

Acknowledgements:

Learning Objectives: To understand how deep learning techniques may improve noninvasive prosthetic control solutions.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS051

Plenary
PLENARY SESSION 03 CONT
15-05-2024 11:30 - 12:00

INTRATHECAL DRUG DELIVERY (ITDD) SHALL REMAIN AN RCT FREE ZONE: THE CHALLENGES OF RESEARCH IN ITDD – ITDD DAY

Sam Eldabe, FRCA[1,2]
[1]James Cook Hospital, Pain Department, Middlesbrough, United Kingdom, [2]James Cook University Hospital, Middlesbrough, United Kingdom

Introduction and Discussion: Introduction: The technique of intrathecal drug delivery (ITDD) is based on the principle that effective analgesia can be achieved by the action of some drugs at the dorsal horn of the spinal cord where adequate concentrations cannot be achieved by systemic administration, or only by high systemic doses. Delivery of the drug by the intrathecal (spinal) route is a means of achieving enhanced therapeutic effects. The smaller doses needed for intrathecal administration also allow a reduction in side effects compared to systemic administration. There is evidence to support this technique. Discussion: There are three major indications namely: • chronic non-malignant pain (CNMP) • pain associated with cancer • spasticity • For CNMP there are large scale randomised controlled trials (RCTs) relating to the use of ziconotide and two supportive small RCTs as well as several prospective single-arm studies. • For pain in patients with cancer there is RCT evidence. • For spasticity there are well designed single-arm studies in adult and paediatric populations for clinical and cost effectiveness assessment. There is RCT evidence for stroke related spasticity. The speaker will discuss the difficulty in setting up and conducting RCT to evidence ITDD in both cancer and CNMP. While the obstacles to conduct of an RCT in cancer pain may be obvious such as limited life expectancy, willingness to be randomised, etc... the obstacles for the conduct of an RCT in the domain of CNMP are less obvious but perhaps more difficult to overcome as evidenced by the recently published Pope et al trial.

Supplemental Data:

References: Yaksh TL, Rudy TA. Narcotic analgesia produced by a direct action on the spinal cord. Science 1976; 192: 1357-8. Hayek SM, Deer TR, Pope JE, Panchal SJ, Patel VB. Intrathecal therapy for cancer and non-cancer pain. Pain Physician 2011; 14(3):219-248. Atli A, Theodore BR, Turk DC, Loeser JD. Intrathecal opioid therapy for chronic nonmalignant pain: a retrospective cohort study with 3-year follow-up. Pain Med 2010; 11(7):1010-1016. Hamza M, Doleys D, Wells M, Weisbein J, Hoff J, Martin M, Soteropoulos C, Barreto J, Deschner S, Ketchum J. Prospective study of 3-year follow-up of low-dose intrathecal opioids in the management of chronic nonmalignant pain. Pain Med 2012; 13(10): 1304-1313. Duarte RV, Raphael JH, Sparkes E, Southall JL, LeMarchand K, Ashford RL. Long-term intrathecal drug administration for chronic non-malignant pain. J Neurosurg Anesthesiol 2012; 24(1):63-70. Grider JS, Etscheidt MA, Harned ME, Lee J, Smith B, Lamar C, et al. Trialing and maintenance dosing using a low-dose intrathecal opioid method for chronic nonmalignant pain: a prospective 36-month study. Neuromodulation 2016;19(2):206-219. Raphael JH, Duarte RV, Southall JL, Nightingale P, Kitas GD. Randomised, double-blind controlled trial by dose reduction of implanted intrathecal morphine delivery in chronic non-cancer pain. BMJ Open 2013; 3(7):e003061. Pope JE, Jassal N, Sayed D, Patterson D, McDowell G, Bux A, Lim P, Chang E, Nairizi A, Grodofsky S, Deer TR. A post-market, randomized, controlled, prospective study evaluating intrathecal pain medication versus conventional medical management in the non-cancer, refractory, chronic pain population (PROSPER). Expert Rev Med Devices 2022; 19(11):895-904.

Acknowledgements:

Learning Objectives: Learn about the existing evidence for ITDD in pain management. Learn about RCT for ITDD in pain management. Understand the obstacles to conducting more large-scale RCTs in the field ITDD as opposed to SCS

Financial Disclosures: S Eldabe has received speaker fees from ECMT a not for profit charity wholly funded by Medtronic S Eldabe has a consulting agreement with Medtronic S Eldabe's department has received research funding from Medtronic

Disclosure: No significant relationships.

IS052

Breakout Session
CURRENT STATUS OF INTRATHECAL DRUG DELIVERY SYSTEMS FOR CANCER-RELATED PAIN
15-05-2024 14:30 - 16:00

INTRATHECAL DRUG DELIVERY (ITTD) FOR CANCER-RELATED PAIN: PATHOPHYSIOLOGICAL CHANGES AND CHEMOSENSITIVITY AFTER ITDD

Eellan Sivanesan, MD
Johns Hopkins, Department Of Anesthesiology, Baltimore, United States of America

Introduction and Discussion: Description: Cancer-related pain is a frequent and disabling occurrence. This pain may be due to the mass effect of the primary cancer or metastasis, neural invasion, secreted products, or side effects of cancer treatment (e.g., chemotherapy, tumor resection or other surgery, or radiation therapy). While pain treatment in these settings typically relies on pharmacologic therapies, refractory pain may be treated via interventional modalities. Interventional modalities include targeting nerve or neuraxial injections, sympathethic blockade, electrical stimulation, or intrathecal drug delivery. Despite the accepted use of intrathecal drug delivery for refractory cancer pain, its effects on tumor growth and chemosensitivity are not well understood. Thus, we will explore theoretical effects of intrathecal analgesia on chemosensitivity and cancer pain.

Supplemental Data:

References: De Andres, Jose, Salim Hayek, Christophe Perruchoud, Melinda M. Lawrence, Miguel Angel Reina, De Andres-Serrano, Ruben Rubio-Haro, Mathew Hunt, and Tony L. Yaksh. "Intrathecal drug delivery: Advances and applications in the management of chronic pain patient." Frontiers in Pain Research 3 (2022): 900566. Yaksh, Tony L., Gilson Goncalves Dos Santos, Julia Borges Paes Lemes, and Kaue Malange. "Neuraxial drug delivery in pain management: an overview of past, present, and future." Best Practice & Research Clinical Anaesthesiology 37, no. 2 (2023): 243-265.

Acknowledgements:

Learning Objectives: Discuss how neuromodulation may affect chemosensitivity and cancer pain neurobiology.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

IS053

Breakout Session
CURRENT STATUS OF INTRATHECAL DRUG DELIVERY SYSTEMS FOR CANCER-RELATED PAIN
15-05-2024 14:30 - 16:00

INTRATHECAL DRUG DELIVERY FOR CANCER-RELATED PAIN: A SYSTEMATIC REVIEW AND META-ANALYSIS OF CLINICAL STUDIES

Rui Duarte, PhD[1,2]
[1]University of Liverpool, Institute Of Population Health, LIVERPOOL, United Kingdom, [2]Saluda Medical, Artarmon, Australia

Introduction and Discussion: Intrathecal drug delivery systems (IDDS) and spinal cord stimulation (SCS) have been proposed and assessed for the management of cancer pain; however, such treatments remain underused. A systematic review was conducted to evaluate the effectiveness and safety of IDDS and SCS for cancer pain.[1] The electronic databases MEDLINE, CENTRAL, EMBASE, and WikiStim were searched from 1988 to March 2021. Randomized controlled trials and observational studies of adults with pain related to cancer or its treatment who received an implantable IDDS or SCS were eligible for inclusion. The primary outcome of the review was change in pain intensity from baseline to the last available follow-up, measured using a visual analog scale or numerical rating scale. The protocol for this review was registered on PROSPERO (CRD42021240717). A total of 22 studies (24 reports) were included with a total of 3043 participants who received either IDDS or SCS for cancer pain. Eight studies reporting data for 405 participants with an IDDS could be included in the meta-analysis of pain intensity that showed a statistically significant reduction at the latest post-treatment follow-up time compared with baseline (mean difference [MD], -3.31; 95% CI, -4.18 to -2.45; $p < 0.001$). Six studies reporting data for 325 participants with an IDDS could be included in the meta-analysis of pain intensity that showed a statistically significant reduction up to one month after treatment compared with baseline (MD, -3.53; 95% CI, -4.06 to -3.00; $p < 0.001$). A meta-analysis including studies of participants with either an IDDS or an SCS device showed similar results. Improvements in other outcomes following implantation of IDDS also were observed. Postdural puncture headache was the most reported complication, whereas urinary retention, nausea, and vomiting were commonly reported side effects. The findings from this sytematic review suggest that IDDS is effective in reducing pain intensity for patients with cancer pain when compared with pre-treatment. Results from additional systematic reviews and recent studies of IDDS will be dicussed.

Supplemental Data:

References: 1. Duarte R, Copley S, Nevitt S, Maden M, Al-Ali AM, Dupoiron D, Eldabe S. Effectiveness and Safety of Intrathecal Drug Delivery Systems for the Management of Cancer Pain: A Systematic Review and Meta-Analysis. *Neuromodulation* 2023; 26(6): 1126-1141.

Acknowledgements:

Learning Objectives: 1. Intrathecal drug delivery systems (IDDS) for cancer pain remain underused 2. The evidence suggests that IDDS is safe and effective in reducing pain intensity for patients with cancer pain 3. Conclusions from additional systematic reviews are in agreement on the value of IDDS for the management of cancer pain

Financial Disclosures: Employee of Saluda Medical. The employer had no role in the current study.

Disclosure: No significant relationships.

IS054

Breakout Session
CURRENT STATUS OF INTRATHECAL DRUG DELIVERY SYSTEMS FOR CANCER-RELATED PAIN
15-05-2024 14:30 - 16:00

INTRATHECAL DRUG DELIVERY FOR CANCER-RELATED PAIN: TRUNK AND LIMB PAIN

Shane Brogan, Professor of Anesthesiology
University of Utah, Department Of Anesthesiology, Salt Lake City, United States of America

Introduction and Discussion: Intrathecal drug delivery for cancer pain has an established role in treating challenging clinical scenarios including refractory pain and intolerance to analgesics. This session will review the rationale for intrathecal drug delivery with an emphasis on optimizing clinical outcomes in pain of the trunk and limbs. The clinical science behind intrathecal drug selection, dosing, and optimal intrathecal catheter tip placement will be discussed. Additional topics covered will include practical advice on appropriate patient selection, side effect management, and management of coexisting systemic analgesics.

Learning Objectives: 1. Understand the principles behind when to proceed with intrathecal therapy. 2. Understand the basics of rational drug selection and dosing. 3. Understand how to successfully wean patients off systemic opioids onto exclusively intrathecal drug delivery.

Financial Disclosures: Dr. Brogan has worked as a consultant for Medtronic Inc. in the past.

Disclosure: No significant relationships.

IS055

Breakout Session
CURRENT STATUS OF INTRATHECAL DRUG DELIVERY SYSTEMS FOR CANCER-RELATED PAIN
15-05-2024 14:30 - 16:00

INTRATHECAL DRUG DELIVERY FOR CANCER-RELATED PAIN: HEAD AND NECK PAIN

Denis Dupoiron, MD[1,2]
[1]Institut de Cancerologie de l'Ouest - Angers, Anesthesiology And Pain Medicine, Angers, France, [2]Institut de Cancerologie de l'Ouest-Angers, Anesthesiology And Pain Medicine, Angers, France

Introduction and Discussion: Pain remains the first symptom in cancer population at an advance stage of the disease (1). Intrathecal drug delivery systems (IDDS) are efficient to relieve pain refractory to comprehensive medical management (2) and plays a key role for patients suffering intractable cancer pain. Intrathecal drug distribution is highly localized around the catheter tip. Limited intrathecal diffusion has been proven in animal models as well as in simulations using flows like those delivered by programmable intrathecal infusion devices. However, IDDS for head and neck cancer pain, requiring a cervical catheter tip implantation, have been poorly described in medical literature. The main challenge in implanting such patients is reaching the right level with the catheter tip. Cervical placement has traditionally been described using surgical cervical approaches, thoracic laminotomy or through thoracic percutaneous placement. A direct suboccipital approach was used twice in the literature. Although for a decade now, devices have enabled placement of cervical catheters percutaneously from the lumbar spine, but the lumbar percutaneous approach was performed only for few recent case reports. A recent follow up study including 98 patients evaluated the outcomes of cervical IDDS for Cancer pain (3). the selection was based on a multidisciplinary meeting discussion. After a complete withdrawal of systemic opioids, IDDS-treated patients were prescribed a combined intrathecal regimen (morphine, ropivacaine and ziconotide) through a catheter placed behind the cervical spinal cord. The more frequent locations of the catheter tip were at the C1 vertebral body level (24.44%), C4 (22.45%) and C5 (17.35%). At least a 50% reduction in pain NRS was achieved in 93% of patients after 1 week despite a complete withdrawal of all systemic opioids. IDDS provided pain relief compared to initial pain score with a significant statistical difference after 1 week, 1 month, 2 and 3 months ($p < 0.01$). Mean NRS pain score before surgery was 8.01 ± 0.24. No implantation failure was observed by lumbar route. The most frequent complications were infection (3.05 %). Only one requiring a device removal and hematoma. Two pumps flipping, one catheter dislodgement and one sub-dural hematoma were also observed. No granuloma formation was observed in this study, probably because high flow rates were required. The outcomes suggest that long-term IDDS placement of cervical catheter through percutaneous lumbar access is suitable and is a pertinent option for head and neck refractory cancer pain.

Supplemental Data:

References: 1-van den Beuken : Update on Prevalence of Pain in Patients With Cancer - JPSM. 2016;51(6) 2-Smith TJ : Randomized clinical trial of IDDS -JCO 2002;20(19) 3- Dupoiron D, Bienfait F, Carvajal et al, RAPM 2023

Acknowledgements:

Learning Objectives: To understand 1- the indications, 2- feasabilty 3 - efficacy of Intrathecal drug delivery systems for Head and Neck refractory cancer pain

Financial Disclosures: Dr Dupoiron received consultation fees from Medtronic and Esteve

Disclosure: No significant relationships.

IS056

Breakout Session
CUTTING EDGE RESEARCH IN NONINVASIVE BRAIN STIMULATION (NIBS)
15-05-2024 14:30 - 16:00

TRANSCRANIAL MAGNETIC STIMULATION OF THE VISUAL CORTEX: AN UPDATE

Ivete Ferrraz, MSc
Dra.Ivete Contieri Ferraz Clinic, Psychiatric, Curitiba, Brazil

Introduction and Discussion: INTRODUCTION: Transcranial Magnetic Stimulation (TMS) is a non-invasive brain stimulation technique used to induce longer-lasting neuroplastic changes in a variety of cortical and subcortical regions, including the visual cortex. The visual cortex can be divided into neural pathways, V1, V2, V3, V4, and V5, and its stimulation may hold promise for low vision rehabilitation. **OBJETIVES**: To analyze the main results in the different visual functions in the use of TMS in the visual cortex. **METHOD**: This was a systematic review of the literature in the last five years in the Pubmed databases, using the keywords TMS, visual cortex, occipital cortex, transcranial magnetic stimulation, neuromodulation, contrast sensitivity" neuromodulation occipital cortex", visual rehabilitation. **RESULTS:** Fifteen studies were included (13 trials and 02 literature reviews). Results were grouped into diferentes targets of visual pathways, V1, V2, V3, V4 e V5 and its effects on amblyopia, blind vision, Sprague Effect, hemianopsias, and visual loss after stroke. **CONCLUSION:** There are significant effects of visual cortex TMS on contrast sensitivity, on visual perception, on visual processing, on blind vision and on word recognition. Future studies with robust experimentals designs are needed to extend these findings to populations with vision loss.

Supplemental Data:

References: 1. Tuna AR, Pinto N, Brardo FM, Fernandes A, Nunes AF, Pato MV. Transcranial Magnetic Stimulation in Adults With Amblyopia. J Neuroophthalmol. 2020 Jun;40(2):185-192. doi: 10.1097/WNO.0000000000000828. PMID: 31453915.

2. Donkor R, Silva AE, Teske C, Wallis-Duffy M, Johnson AP, Thompson B. Repetitive visual cortex transcranial random noise stimulation in adults with amblyopia. Sci Rep. 2021 Feb 4;11(1):3029. doi: 10.1038/s41598-020-80843-8. PMID: 33542265; PMCID: PMC7862667.

3. Rafique SA, Steeves JKE. Modulating intrinsic functional connectivity with visual cortex using low-frequency repetitive transcranial magnetic stimulation. Brain Behav. 2022 Feb;12(2):e2491. doi: 10.1002/brb3.2491. Epub 2022 Jan 20. PMID: 35049143; PMCID: PMC8865167.

4. El Nahas N, Elbokl AM, Abd Eldayem EH, Roushdy TM, Amin RM, Helmy SM, Akl AZ, Ashour AA, Samy S, Amgad A, Emara TH, Nowara M, Kenawy FF. Navigated perilesional transcranial magnetic stimulation can improve post-stroke visual field defect: A double-blind sham-controlled study. Restor Neurol Neurosci. 2021;39(3):199-207. doi: 10.3233/RNN-211181. PMID: 34024791.

5. Railo H, Hurme M. Is the primary visual cortex necessary for blindsight-like behavior? Review of transcranial magnetic stimulation studies in neurologically healthy individuals. Neurosci Biobehav Rev. 2021 Aug;127:353-364. doi: 10.1016/j.neubiorev.2021.04.038. Epub 2021 May 8. PMID: 33965459.

6: Tuna AR, Pinto N, Fernandes A, Brardo FM, Pato MV. Theta burst stimulation in adults with symmetric and asymmetric visual acuity. Int Ophthalmol. 2022 Sep;42(9):2785-2799. doi: 10.1007/s10792-022-02269-7. Epub 2022 Mar 30. PMID:35353292.

7: Räty S, Ruuth R, Silvennoinen K, Sabel BA, Tatlisumak T, Vanni S. Resting-state Functional Connectivity After Occipital Stroke. Neurorehabil Neural

Repair. 2022 Feb;36(2):151-163. doi: 10.1177/15459683211062897. Epub 2021 Dec 23. PMID: 34949135.

8: Mazzi C, Savazzi S, Silvanto J. On the "blindness" of blindsight: What is the evidence for phenomenal awareness in the absence of primary visual cortex (V1)? Neuropsychologia. 2019 May;128:103-108. doi: 10.1016/j.neuropsychologia.2017.10.029. Epub 2017 Oct 24. Erratum in: Neuropsychologia. 2020 Sep;146:107548. PMID: 29079397.

9: Silson EH, Gouws AD, Legge GE, Morland AB. In a case of longstanding low vision regions of visual cortex that respond to tactile stimulation of the finger with Braille characters are not causally involved in the discrimination of those same Braille characters. Cortex. 2022 Oct;155:277-286. doi: 10.1016/j.cortex.2022.07.012. Epub 2022 Aug 11. PMID: 36054997.

10: Koenig L, Ro T. Dissociations of conscious and unconscious perception in TMS-induced blindsight. Neuropsychologia. 2019 May;128:215-222. doi: 10.1016/j.neuropsychologia.2018.03.028. Epub 2018 Mar 26. PMID: 29588224.

11: Sabel BA, Hamid AIA, Borrmann C, Speck O, Antal A. Transorbital alternating current stimulation modifies BOLD activity in healthy subjects and in a stroke patient with hemianopia: A 7 Tesla fMRI feasibility study. Int J Psychophysiol. 2020 Aug;154:80-92. doi: 10.1016/j.ijpsycho.2019.04.002. Epub 2019 Apr 9. PMID:30978369.

12: Yeo JM, Carson A, Stone J. Seeing again: treatment of functional visual loss. Pract Neurol. 2019 Apr;19(2):168-172. doi: 10.1136/practneurol-2018-002092. PMID: 30872460.

13: Rafique SA, Steeves JKE. Assessing differential effects of single and accelerated low-frequency rTMS to the visual cortex on GABA and glutamate concentrations. Brain Behav. 2020 Dec;10(12):e01845. doi: 10.1002/brb3.1845. Epub 2020 Sep 23. PMID: 32964685; PMCID: PMC7749615.

14: Poh EZ, Harvey AR, Makowiecki K, Rodger J. Online LI-rTMS during a Visual Learning Task: Differential Impacts on Visual Circuit and Behavioral Plasticity in Adult Ephrin-A2A5^{-/-} Mice. eNeuro. 2018 Feb 14;5(1):ENEURO.0163-17.2018. doi: 10.1523/ENEURO.0163-17.2018. PMID: 29464193; PMCID: PMC5815844.

15: Hurme M, Koivisto M, Revonsuo A, Railo H. V1 activity during feedforward and early feedback processing is necessary for both conscious and unconscious motion perception. Neuroimage. 2019 Jan 15;185:313-321. doi: 10.1016/j.neuroimage.2018.10.058. Epub 2018 Oct 23. PMID: 30366074.

16: Coldea A, Veniero D, Morand S, Trajkovic J, Romei V, Harvey M, Thut G. Effects of Rhythmic Transcranial Magnetic Stimulation in the Alpha-Band on Visual Perception Depend on Deviation From Alpha-Peak Frequency: Faster Relative Transcranial Magnetic Stimulation Alpha-Pace Improves Performance. Front Neurosci. 2022 Jun 1716:886342. doi: 10.3389/fnins.2022.886342. PMID: 35784849;PMCID: PMC9247279.

17. Ro T, Koenig L. Unconscious Touch Perception After Disruption of the Primary Somatosensory Cortex. Psychol Sci. 2021 Apr;32(4):549-557. doi: 10.1177/0956797620970551. Epub 2021 Feb 26. PMID: 33635728.

18. Sanders RD, Banks MI, Darracq M, Moran R, Sleigh J, Gosseries O, Bonhomme V,Brichant JF, Rosanova M, Raz A, Tononi G, Massimini M, Laureys S, Boly M Propofol-induced unresponsiveness is associated with impaired feedforward connectivity in cortical hierarchy. Br J Anaesth. 2018 Nov;121(5):1084-1096. doi: 10.1016/j.bja.2018.07.006. Epub 2018 Aug 21. PMID: 30336853; PMCID: PMC6208295.

Acknowledgements: Mario Aloisio Ferraz Filho – Biomedical at the Lab
Amanda Ferraris – Family Doctor at the Neuromood Lab
Claudia Dettmer – Ophalmologist at the Neuromood Lab

Learning Objectives: Evaluate the diferente forms of neuromodulation in the visual cortes and compare the results and convergents effects.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS057

Breakout Session
CUTTING EDGE RESEARCH IN NONINVASIVE BRAIN STIMULATION (NIBS)
15-05-2024 14:30 - 16:00

TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) FOR DEPRESSION: THE LAST TEN YEARS AND THE NEXT FIVE

Andre Brunoni, MD
University of São Paulo Medical School, Psychiatry, São Paulo, Brazil

Introduction and Discussion: Major depressive disorder (MDD) is a prevalent and debilitating condition with limited treatment options. Despite the availability of antidepressant drugs, cognitive-behavioral therapy, and non-invasive brain stimulation techniques, many patients continue to experience treatment resistance or face challenges with access to these interventions. Transcranial direct current stimulation (tDCS) has emerged as a promising non-invasive brain stimulation modality for MDD, offering advantages in portability, affordability, and minimal adverse effects. TDCS uses a low-intensity, direct current that is applied through two electrodes placed over the patient's scalp in order to change the cortical excitability of underlying brain areas, particularly the prefrontal cortex. Over tthe last decade, several clinical trials have been conducted to address the efficacy of this technique. Here, we will discuss the results of these pivotal trials, which attested the safety of the technique, but presented mixed results in terms of the efficacy of the technique. In fact, these results suggested that tDCS has its greatest potential for low-treatment resistant samples, such as patients in the initial depressive episode. In the next years, opportunities have been emerging in terms of scalability, precision, and augmentation. Regarding scalability, it is important to underscore that conventional tDCS protocols require daily applications at clinical settings, posing logistical challenges and limiting its widespread adoption. Home-use tDCS devices offer the potential to address these limitations by enabling patients to administer treatment in the comfort of their own homes. Notwithstanding, a recent clinical trial from our group found no significant differences between active, home-use tDCS vs. placebo. In terms of precision, several groups are tackling the issue of the "one-size-fits-all" approach. In other words, individualized tDCS dosage, which would be based either in adjusting the position of the electrodes or the current intensity using electric field simulations of the current distribution in the brain, holds promise as a new and viable strategy to enhance tDCS response. In this context, machine learning approaches have also been used to estimate which groups of patients are more likely to respond to tDCS. Finally, another promising avenue would be to combine tDCS with prefrontal-focused neuropsychological tasks that could enhance the efficacy of tDCS through cortical excitability of specific areas related to working memory and cognitive control, which are impaired in depression. Notwithstanding, the main challenge of this approach is to develop the specific neuropsychological protocol, considering the complexity of delivering the task concomitantly to the tDCS application.

Supplemental Data:

References: 1. **Brunoni et al.,** Trial of Electrical Direct- Current Stimulation Therapy versus Escitalopram for Depression. *New England Journal of Medicine*, 2017. **2. Borrione et al.,** Efficacy and Safety of Portable Transcranial Electrical Stimulation and Internet-based Behavioral Therapy for Major Depressive Disorder: a Randomized Clinical Trial, *JAMA Psychiatry*, 2024 (in press). **3. Valiengo et al.,** TDCS for treating negative symptoms in schizophrenia: a randomized, double-blinded, sham controlled trial. *JAMA Psychiatry*, 2020. **4. Sampaio-Junior et al.,** Efficacy and Safety of Transcranial Direct Current Stimulation as an Add-on Treatment for Bipolar Depression: a randomized clinical trial. *JAMA Psychiatry*, 2018. **5. Brunoni et al.,** The sertraline vs. electrical current therapy for treating depression clinical study: results from a factorial, randomized, controlled trial. *JAMA Psychiatry*, 2013.

Acknowledgements: None

Learning Objectives: 1. To provide an overview of the results of recent clinical trials for transcranial direct current stimulation for depression 2. to discuss why results have been so heterogenous and variable accross clinical trials 3. to describe the challenges and opportunities of the field in the next 5 years

Financial Disclosures: Andre Brunoni: Flow Neuroscience, consultant / advisory board and stock options, in-kind support for research. MagVenture, education / research, in-kind support for research. Soterix Medical, education / research, in-kind support for research.

Disclosure: No significant relationships.

IS058

Breakout Session
CUTTING EDGE RESEARCH IN NONINVASIVE BRAIN STIMULATION (NIBS)
15-05-2024 14:30 - 16:00

LEVERAGING NEUROMODULATION-INDUCED BRAIN PLASTICITY FOR IMPROVEMENT IN ATTENTION AND WORKING MEMORY IN MILD TRAUMATIC BRAIN INJURY

Lars Hungerford, PhD[1,2,3]
[1]Traumatic Brain Injury Center of Excellence, Traumatic Brain Injury, San Diego, United States of America, [2]General Dynamics Information Technology, Falls Church, United States of America, [3]Naval Medical Center San Diego, San Diego, United States of America

Introduction and Discussion: Non-invasive brain-stimulation techniques have been utilized for human performance optimization in both non-clinical and rehabilitation research to modulate neuronal firing and improve cognitive training. Transcranial Direct Current Stimulation (tDCS) applies a low-intensity direct current to the cortex using two electrodes on the scalp. Anodal stimulation (cortical excitability occurs through depolarization of underlying cortical neurons) is applied to a brain region for 5-30 minutes, with a current between 1-4 mA. This increases regional cortical activity, with short-term effects lasting a few hours and long-term effects up to several months. Cognitive training can be completed either during, or after, stimulation to enhance the effects of the procedure. tDCS is safe and non-invasive, making it a popular choice for modulating cortical excitability, enhancing neuronal firing, and promoting long-term plasticity. Ulam et al.,[1] in a recent double-blind, placebo-controlled clinical study of TBI patients, applied tDCS over the left DLPFC in patients with TBI for 10 consecutive days. Increased cortical excitability was demonstrated as improvements in working memory and attention were associated with increased power in the alpha frequency band and decreased power in the delta and theta frequency bands. Observed EEG changes were also associated with improved neurocognitive performance. tDCS over DLPFC has also demonstrated dramatic/durable reduction in impulsivity in a veteran population.[2] These results suggest that tDCS application to DLPFC may demonstrate significant improvements in working memory and attention within mTBI populations. Neurocognitive optimization is critical following traumatic brain injury, which is a leading cause of injury within the military—over 450,000 since 2000. The majority of these TBIs are classified as mild according to current DOD/VA criteria. This study is motivated by the high rates of TBI and the relative dearth of treatment options available to return Service Members back to optimal neurocognitive functioning. The proposed talk will describe and provide preliminary data from the first 30 participants from an ongoing double-blind, randomized, placebo (sham) controlled study. A sample of 60 Active Duty Service Members with a history of mild traumatic brain injury (most with a history of blast exposure or blast TBI) will be recruited and randomly assigned to receive either active or sham tDCS, both paired with cognitive training tasks. Intake will involve a full pre-assessment of symptoms, neurocognitive performance, electrophysiology baseline, and resting state fMRI (for a subset of participants). Training/tDCS sessions occur twice daily over five consecutive days. Post-assessment occurs at 4 days and six-weeks following the five-day sessions.

Supplemental Data:

References: Anas R. Alashram, Elvira Padua & Giuseppe Annino (2023) Noninvasive brain stimulation for cognitive rehabilitation following traumatic brain injury: A systematic review, Applied Neuropsychology: Adult, 30:6, 814-829, DOI: 10.1080/23279095.2022.2091440 Andrews SC, Hoy KE, Enticott PG, Daskalakis ZJ, Fitzgerald PB. Improving working memory: the effect of combining cognitive activity and anodal transcranial direct current stimulation to the left dorsolateral prefrontal cortex. Brain Stimul. 2011 Apr;4(2):84-9. doi: 10.1016/j.brs.2010.06.004. Epub 2010 Jul 11. PMID: 21511208. Gilmore, C. S., Dickmann, P. J., Nelson, B. G., Lamberty, G. J., & Lim, K. O. (2018). Transcranial Direct Current Stimulation (tDCS) paired with a decision-making task reduces risk-taking in a clinically impulsive sample. *Brain stimulation*, *11*(2), 302-309.

Acknowledgements: The support of the International Neuromodulation Society for this project is gratefully acknowledged.

Learning Objectives: 1. Upon completion of the session, delegates will be able to discuss the proposed mechanisms of action underlying improvement in attention and working memory in mild TBI patients. Desired result: Increased understanding of neuroplasticity and targets of interest. 2. Upon completion, delegates will have a better understanding of gold-standard research design for neuromodulation studies of attention and working memory. Desired result: Increased knowledge of research methods to enable researchers to design and implement powerful randomized controlled trials in neuromodulation. 3. Upon completion of the session, delegates will be able to discuss relevant findings related to the most recent studies using transcranial direct current stimulation for improving attention and working memory. Desired result: Increased visibility and understanding of the state of the science related to improving cognition and symptoms following mild traumatic brain injury.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

IS059

Breakout Session
CUTTING EDGE RESEARCH IN NONINVASIVE BRAIN STIMULATION (NIBS)
15-05-2024 14:30 - 16:00

TRANSCRANIAL ELECTRICAL STIMULATION IN NEUROPATHIC PAIN

Helena Knotkova, PhD, PhilD[1,2]
[1]MJHS Institute for Innovation in Palliative Care, New York, United States of America, [2]Albert Einstein College of Medicine, Department Of Family And Social Medicine, And Neurology, The Bronx, United States of America

Introduction and Discussion: The presentation will focus on transcranial direct current stimulation and its efficacy and clinical potential in patients with neuropathic pain syndromes.Transcranial direct current stimulation (tDCS) is a non-invasive neuromodulation technique that was re-introduced to modern medicine in 2000 [1] and has gained growing interest in various field of medicine, including pain management [2]. In the past two decades, numerous studies have explored the potential of tDCS for the treatment of neuropathic pain in difficult-to-treat conditions, such as phantom limb pain, complex regional pain syndrome, or multiple sclerosis. The presentation will critically review the level of evidence on tDCS efficacy in major neuropathic pain syndromes and discuss the patient selection process and safety. Further, the presentation will briefly discuss remotely-supervised tDCS protocols delivered in home settings and a potential of the at-home tDCS for management of neuropathic pain [3].

Supplemental Data:

References: [1] Nitsche, M. A., and Paulus, W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. J. Physiol. 2000; 527:633–639. [2] Knotkova H, Hamani C, Sivanesan E, Le Beuffe MFE, Moon JY, Cohen SP, Huntoon MA. Neuromodulation for chronic pain. Lancet. 2021 May 29;397(10289):2111-2124. doi: 10.1016/S0140-6736(21)00794-7. PMID: 34062145. [3] Van Zyl J, Knotkova H, Kim P, Henderson CR Jr, Portenoy RK, Berman N, Frederic MW, Reid MC. Delivery of an at-home transcranial direct current stimulation intervention to mitigate pain in patients with end-stage kidney disease receiving hemodialysis (ESKD/HD). Front Pain Res (Lausanne). 2023 Apr 5;4:1132625. doi: 10.3389/fpain.2023.1132625. PMID: 37092011; PMCID: PMC10113462.

Acknowledgements: This project has been supported by the National Institute of Diabetes and Digestive and Kidney Diseases, study #1R01DK131050-01.

Learning Objectives: Upon completion of the presentation the attendees will be able to: 1) Critically review the evidence on tDCS efficacy in neuropathic pain; 2) Understand the criteria for patient selection for the tDCS procedure; 3) Discuss pros and cons of tDCS and its potential for management of neuropathic pain.

Financial Disclosures: Helena Knotkova, PhD receives funding from the National Institute on Aging, study #5R01AG068167-03 and by the National Institute of Diabetes and Digestive and Kidney Diseases, study #1R01DK131050-01.

Disclosure: No significant relationships.

IS060

Breakout Session
LOW ENERGY FOCUSED ULTRASOUND (LIFU)
15-05-2024 14:30 - 16:00

POTENTIAL MECHANISMS SUPPORTING LOW INTENSITY FOCUSED ULTRASOUND FOR NEUROMODULATION

Noah Philip, MD[1,2]
[1]Alpert Medical School of Brown University, Psychiatry And Human Behavior, Providence, United States of America, [2]VA Providence, Center For Neurorestoration And Neurotechnology, Providence, United States of America

Introduction and Discussion: Low intensity focused ultrasound (FUS) is poised to become a paradigm-shifting technology with the potential to deliver non-invasive, reversible, and focal deep brain stimulation (1). FUS uses acoustic energy to modulate regional brain activity, reaching deep and subcortical brain regions implicated in psychiatric disorders at millimeter precision. In contrast to high intensity focused ultrasound, which is thermally ablative and available as a lesion treatment for movement disorders and other indications, FUS uses energy at or below limits for diagnostic ultrasound and appears to reversibly modulate neural activity, presumably without injury (2,3). Other investigational uses of FUS include opening the blood brain barrier to deliver medications or other compounds to otherwise unreachable areas (4). As with any new field, there is no shortage of important questions. First and foremost, is FUS safe? Current ultrasound safety standards were developed before the current technology existed, underscoring the need to carefully establish safe use. Since FUS uses acoustic (i.e., mechanical) energy, and many deep brain regions are adjacent to important components of the cerebral vasculature (i.e., circle of Willis), careful implementation is warranted. Whether this technology can reliably modulate deep brain regions is an active area of inquiry; if successful, FUS will open a novel way to evaluate neurophysiological and clinical effects from direct target engagement. This session is designed for attendees to who wish to learn more about the use of FUS in humans and potential for future use in non-invasive and non-ablative neuromodulation. Potential mechanism(s) of action, including different use approaches (i.e., direct neuromodulation or in conjunction with acoustically-active contrast agents and nanoparticles) will be reviewed. Recent findings in human use will also be discussed (5,6). This presentation will include perspective from an investigator actively engaged in first-in-human applications of its technology and will touch upon other exciting and ongoing areas of research in this space.

Supplemental Data:

References: 1. Philip NS, & Arulpragasam AR (2023). Reaching for the unreachable: low intensity focused ultrasound for non-invasive deep brain stimulation. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology*, *48*(1), 251–252. https://doi.org/10.1038/s41386-022-01386-2 2. Dell'Italia, J., et al., Current State of Potential Mechanisms Supporting Low Intensity Focused Ultrasound for Neuromodulation. Front Hum Neurosci, 2022. 16: p. 872639. 3. Folloni D, Verhagen L, Mars RB, et al. Manipulation of Subcortical and Deep Cortical Activity in the Primate Brain Using Transcranial Focused Ultrasound Stimulation. Neuron. 2019;101(6):1109-16.e5. S. 4. Wang, J. B., Di Ianni, T., Vyas, D. B., Huang, Z., Park, S., Hosseini-Nassab, N., Aryal, M., & Airan, R. D. (2020). Focused Ultrasound for Noninvasive, Focal Pharmacologic Neurointervention. *Frontiers in neuroscience*, *14*, 675. https://doi.org/10.3389/fnins.2020.00675 5. Yaakub SN, White TA, Roberts J, et al., (2023). Transcranial focused ultrasound-mediated neurochemical and functional connectivity changes in deep cortical regions in humans. Nature communications, 14(1), 5318. 6. Kuhn T, Spivak NM, Dang BH, et al., (2023). Transcranial focused ultrasound selectively increases perfusion and modulates functional connectivity of deep brain regions in humans. Frontiers in neural circuits, 17, 1120410. https://doi.org/10.3389/fncir.2023.1120410

Acknowledgements: None

Learning Objectives: By the end of the presentation, participants should be able to: 1) Describe early data describing the use of FUS for neuromodulation 2) Discuss potential safety considerations for FUS neuromodulation 3) Describe potential mechanisms of action from recent human FUS neuromodulation studies

Financial Disclosures: No commercial conflicts of interest related to the content of this session. In the past three years, NSP has received clinical trial support (through US Dept of Veterans Affairs Contracts) from Wave Neuro and Neurolief; he is an advisor to Motif Neurotech and on the Scientific Advisory Board of Pulvinar Neuro.

Disclosure: No significant relationships.

IS061

Breakout Session
LOW ENERGY FOCUSED ULTRASOUND (LIFU)
15-05-2024 14:30 - 16:00

LOW INTENSITY FOCUSED ULTRASOUND FOR EPILEPSY

Emma Lescrauwaet, PhD student[1], Kristl Vonck, MD[1], Debby Klooster, PhD[1,2], Lara Hogeveen, PhD[1], Ann Mertens, MD[1], Dirk Buijvoets, MSc[2], Evelien Carrette, [1], Robrecht Raedt, PhD[1], Paul Boon, MD[1,2]
[1]Ghent University, 4brain, Department Head And Skin, Gent, Belgium, [2]Eindhoven Technical University, Eindhoven, Netherlands

Introduction and Discussion: Epilepsy affects about 1% of the population. Approximately one third of patients with epilepsy are drug-resistant (DRE) (Boon et al., 2018). Epilepsy surgery is an effective but invasive treatment for DRE, and only 1/3 of DRE patients are suitable surgery candidates. Transcranial focused ultrasound (TUS), a novel non-invasive neurointerventional method, is currently under investigation as a treatment alternative for DRE. By emitting one or more ultrasound waves, TUS can target cortical and subcortical structures in the brain at millimeter resolution (Bystritsky et al., 2011). High intensity focused ultrasound (HIFU) leads to ablation of tissue and could therefore potentially serve as a non-invasive alternative for resective surgery (Lescrauwaet et al., 2022). It is currently under investigation in clinical trials (NCT03417297) following the approval of HIFU for various neurological disorders, amongst others Parkinson's disease (Eisenberg et al., 2020). Low intensity focused ultrasound (LIFU) can modulate neuronal activity and could be used to lower cortical neuronal hyper-excitability in epilepsy patients in a non-invasive manner. The seizure-suppressive effect of LIFU-induced neuromodulation has been studied in several clinical and preclinical trials, showing promising results (Chen et al., 2020; Lee et al, 2022). In addition, TUS is under investigation as a strategy for opening up of the blood brain barrier (BBB). To this end LIFU is applied in combination with a microbubble injection to administer drugs directly to the brain (Baek et al, 2015; Burgess et al. 2015). To date, several clinical investigations are ongoing to fully demonstrate the effectiveness of these various applications of TUS in epileptic patients (NCT03868293, NCT02151175, NCT05947656, NCT03417297).

Supplemental Data: NA

References: Baek H, Lockwood D, Mason EJ, et al. Clinical Intervention Using Focused Ultrasound (FUS) Stimulation of the Brain in Diverse Neurological Disorders. Frontiers in Neurology. 2022;13. Accessed November 14, 2023. https://www.frontiersin.org/articles/10.3389/fneur.2022.880814 Boon, P., De Cock, E., Mertens, A., and Trinka, E. (2018). Neurostimulation for drug-resistant epilepsy. Curr. Opinion Neurol. 31, 198–210. Burgess A, Shah K, Hough O, Hynynen K. Focused ultrasound-mediated drug delivery through the blood-brain barrier. Expert Rev Neurother. 2015;15(5):477-491. doi:10.1586/14737175.2015.1028369 Bystritsky, A., Korb, A. S., Douglas, P. K., Cohen, M. S., Melega, W. P., Mulgaonkar, A. P., et al. (2011). A review of low-intensity focused ultrasound pulsation. Brain stimul. 4, 125–136. doi: 10.1016/j.brs.2011.03.007 Chen, S., Tsai, C., Lin, C., Cheng-Chia, L., Yu, H., Hsieh, T., et al. (2019). Transcranial focused ultrasound pulsation suppresses pentylenetetrazol induced epilepsy in vivo. Brain stimul. 13, 35–46. Eisenberg HM, Krishna V, Elias WJ, et al. MR-guided focused ultrasound pallidotomy for Parkinson's disease: safety and feasibility. Journal of Neurosurgery. 2020;135(3):792-798. doi:10.3171/2020.6.JNS192773 Lee, C., Chou, C., Hsiao, F., Chen, Y., Lin, C., Chen, C., et al. (2021). Pilot study of focused ultrasound for drug-resistant epilepsy. Epilepsia 62, 162–175. doi: 10.1111/epi.17105 Lescrauwaet E, Vonck K, Sprengers M, Raedt R, Klooster D, Carrette E and Boon P (2022) Recent Advances in the Use of Focused Ultrasound as a Treatment for Epilepsy. Front. Neurosci. 16:886584. doi: 10.3389/fnins.2022.886584 National Library of Medicine (2018). A Pilot Study: Focused Ultrasound Thalamotomy for the Prevention of Secondary Generalization in Focal Onset Epilepsy. Identifier NCT03417297. Available online at https://clinicaltrials.gov/ct2/show/NCT03417297. (accessed November 14, 2023). National Library of Medicine. (2019). Low Intensity Focused Ultrasound Treatment for Drug-Resistant Epilepsy: An Efficacy Trial (LIFUS). Identifier NCT03868293. Available online at https://clinicaltrials.gov/ct2/show/NCT03868293. (accessed February 16, 2022). National

Library of Medicine (2014). Low-intensity Focused Ultrasound Pulsation (LIFUP) for Treatment of Temporal Lobe Epilepsy. Identifier NCT02151175. Available online at https://clinicaltrials.gov/ct2/show/NCT02151175. (accessed November 14, 2023). National Library of Medicine (2023). Evaluation of the NaviFUS System in Drug Resistant Epilepsy. Identifier NCT05947656. Available online at https://classic.clinicaltrials.gov/ct2/show/NCT05947656. (accessed November 14, 2023).

Acknowledgements: Not applicable

Learning Objectives: Gain knowledge on the various applications and ongoing (pre) clinical trials with transcranial focused ultrasound: 1. Ablation 2. Neuromodulation 3. BBB opening Understand why these approaches have the potential to serve as a treatment option for epilepsy patients.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS062

Breakout Session
LOW ENERGY FOCUSED ULTRASOUND (LIFU)
15-05-2024 14:30 - 16:00

LOW ENERGY FOCUSED ULTRASOUND NEUROMODULATION OF THE SPINAL CORD

Julie Pilitsis, MD, PhD[1], Nicholas Kato, BS[2], Marisa Dimarzio, PhD[2], Deborah Morris, DPsych[2], Desmond Yeot, PhD[3], Clif Burdette, PhD[4]
[1]University of Arizona/Banner Health, Tucson, United States of America, [2]Florida Atlantic University, Boca Raton, United States of America, [3]GE Healthcare - Technology & Innovation Center, Wauwatosa, United States of America, [4]Acoustic Medsystems, Savoy, United States of America

Introduction and Discussion: Objective: Low intensity focused ultrasound (LIFU) has been used to neuromodulate both peripheral and central nervous system targets in preclinical models. LIFU may be particularly useful as a tool for chronic pain as it is a non-invasive alternative to invasive treatments such as spinal cord stimulation and/or peripheral nerve stimulation. Methods: We present a review of existing use of LIFU in modulating nervous tissues in preclinical models. We then describe our work with LIFU targeting occipital nervous tissue and the DRG. Results: We review the history of LIFU in situ and in vivo in nerve tissue and demonstrate the ability to slow nerve firings. We demonstrate our laboratory's work in rodent and swine models of pain including migraine, chemotherapy induced neuropathic pain and ligation injury models. We show that a single 3-minute treatment results in improvement in anti-nociceptive responses. Further, pilot mechanistic studies demonstrate changes in peripheral and central nervous tissues as a result.
Discussion: LIFU is an emerging means of neuromodulation and specifically could be valuable for the treatment of pain exacerbations. A handheld device offers promise for use in the existing workflow of pain providers in contrast to currently available MR guided FUS devices. However, there is great value of using MR FUS towards defining mechanism of action[JP1] . [JP1]Add CINTA grant number from current CV; authors me, Marisa, Debbie, you, Desmond, Clif

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1) Describe the potential of low-intensity focused ultrasound (LIFU) as a non-invasive treatment for chronic pain. 2) Summarize the evidence from preclinical models that supports the use of LIFU to modulate nervous tissues. 3) Discuss the advantages and disadvantages of LIFU for pain treatment, compared to other neuromodulation techniques.

Financial Disclosures: CINTA #5U54EB033650 Education/Research $5,001 - $20,000 USD

Disclosure: No significant relationships.

IS063

Breakout Session
NEUROMODULATION FOR GASTROINTESTINAL DISORDERS
15-05-2024 14:30 - 16:00

BIOELECTRIC NEUROMODULATION FOR GASTROINTESTINAL DISORDERS

Sophie Payne, PhD[1], James Fallon, PhD[1], Peter De Cruz, MD, PhD[2], John Furness, PhD[3]
[1]Bionics Institute, Melbourne, Australia, [2]Austin Health, Melbourne, Australia, [3]University of Melbourne, Anatomy And Physiology, Melbourne, Australia

Introduction and Discussion: Despite medical advancements, only 30% of patients with Crohn's Disease (CD) achieve long-term remission. Cervical vagus nerve stimulation (VNS) shows promising therapeutic effects in some patients with moderate-severe Crohn's disease. However, at the Bionics Institute we developed a medical device for implantation onto the abdominal vagus nerve for the benefits of: 1) being closer to the end organ; 2) avoiding off-target affects seen during cervical vagus nerve stimulation (VNS); 3) allowing a larger therapeutic window. **Current research**: Our abdominal vagus nerve stimulation (aVNS) array consists of 3-pairs of platinum electrodes that allow recording of electrically evoked neural responses and verification that stimulation is above threshold and activating appropriate fiber populations. We demonstrated that aVNS improved stool quality and reduced histopathological damage in the ileum in an experimental ileitis rat model (Payne et al., 2019). In sheep, the device was scaled up to human size and stimulated over 12 weeks (30 Hz, 2 mA, continuous). There were no changes to the animal's behavior, histopathology of the nerve was benign and no changes to evoked potential thresholds (Payne et al., 2018). The aVNS System is now in a first-in-human safety/efficacy clinical trial in patients with CD that are undergoing a bowel resection (NCT05469607, Austin Health, Melbourne, Australia). The trial (n=13 participants), led by A/Prof Peter De Cruz, will primarily investigate safety and prevention of inflammatory recurrence at the anastomosis site. Our first patient was successfully implanted and stimulation started (3 hrs/day; 10 Hz; 2 mA). After 5 months we report: no perception of stimulation at therapeutic levels (2 mA), no adverse side effects related to the device and no return of clinical symptoms. All electrodes have remained functional and recording of evoked potentials made. **Emerging research**: Although promising, the strategy of delivering 'fixed' (open loop) stimulation that fails to adapt to the rapidly changing conditions of Crohn's disease is potentially problematic in the long-term. As such, the next aim of our research program is to develop 'adaptive' (closed loop) aVNS technology that dynamically adjusts to each patient's evolving medical needs, providing optimal and personalized therapy. Here we describe pilot rat data that supports the use of an innovative recording system (PCT/AU2020/050570) that uses cross-correlation analysis (Payne et al., 2023) to extract vagal activity induced during intestinal inflammation. Recorded vagal activity correlates with indicators of intestinal inflammation and is highly promising as a feedback signal in a closed-loop system.

Supplemental Data:

References: Payne, S.C, Osborne P.B, Thomas A, Eiber C, Keast J.R, Fallon J.B (2023). Selective recording of physiologically evoked neural activity in a mixed autonomic nerve using a minimally invasive array. *APL Bioeng*. 7, 046110 (2023); doi:10.1063/5.0164951. Payne S.C, Burns O, Thomas R, Sedo A, Hyakumura T, Furness J.B, Shepherd R.K and Fallon J.B. 2019. Anti-inflammatory effects of abdominal vagus nerve stimulation on experimental intestinal inflammation. *Frontiers in Neuroscience.* 13; 418. DOI: 10.3389/fnins.2019.00418 Payne S.C, Burns O, Stebbing M.J, Thomas R, de Silva A, Sedo A, Weissenborn F, Hyakumura T, Huynh M, May C.N, Williams R.A, Furness J.B, Fallon J.B and Shepherd R.K. 2019. Vagus nerve stimulation to treat inflammatory bowel disease: A chronic, pre-clinical safety study in sheep. *Bioelectronics in Medicine.* 1:4. doi.org/10.2217/bem-2018-0011

Acknowledgements: The support of the Bionics Institute, the Florey Institute and Austin Health for this project is gratefully acknowledged. We acknowledge the following government funding bodies for financial support: Defense Advance Programs Agency (US) and National Institute of Medical Research (Aus).

Learning Objectives: 1. Understanding published preclinical data indicating safety and efficacy of the abdominal vagus nerve stimulation system 2. Understanding recent human safety and efficacy data from the first patient implanted with the abdominal vagus nerve stimulation system 3. Understanding the research program and pilot data supporting developing a feedback signal for closed loop control of Crohn's Disease.

Financial Disclosures: Nothing to disclose.

Disclosure: No significant relationships.

IS064

Breakout Session
NEUROMODULATION FOR GASTROINTESTINAL DISORDERS
15-05-2024 14:30 - 16:00

TRANSCUTANEOUS CERVICAL VAGAL NERVE STIMULATION FOR GASTRO-INTESTINAL ISSUES

Linda Anh Nguyen, Dr.
Stanford University, Medicine/gastroenterology, Redwood City, United States of America

Introduction and Discussion: Gastroparesis is a chronic digestive disorder that is associated with increased morbidity, mortality and healthcare utilization. Yet, in the US, metoclopramide remains the only FDA approved therapy for gastroparesis. Patients with gastroparesis often struggle with chronic overlapping pain conditions such that approximately 1/3 of patients with gastroparesis also have migraine headache. Transcutaneous cervical vagal nerve stimulation (nVNS) is FDA approved for treatment of migraine. Additionally, autonomic dysregulation has been described in patients with diabetic and idiopathic gastroparesis. Non-invasive vagal nerve stimulation was hypothesized to be effective in the treatment of gastroparesis. Three open-label studies of nVNS for treatment of gastroparesis have been published and will be discussed. The studies revealed promising results in reducing gastroparesis symptoms, including abdominal pain. Regular use of nVNS results in clinical meaningful reduction in gastroparesis symptoms in approximately 40% of patients with idiopathic gastroparesis. On demand use of nVNS can reduce gastroparesis symptom severity, medication utilization and autonomic symptoms. nVNS may also accelerate gastrointestinal motility and decrease mucosal inflammation. Discontinuation of nVNS does appear to result in recurrent symptoms. In conclusion, nVNS is a safe and promising therapy in the treatment of idiopathic gastroparesis. The ideal dosing and target population remains to be determined. Further, large, randomized sham-controlled studies are needed to confirm efficacy and determine optimal dosing.

Supplemental Data:

References: 1. Paulon E et al. Proof of concept: short-term non-invasive cervical vagus nerve stimulation in patients with drug-refractory gastroparesis. Frontline Gastroenterol 2017;8:325-330 2. Gottfried-Blackmore, A et al. Open-label pilot study: Non-invasive vagal nerve stimulation improves symptoms and gastric emptying in patients with idiopathic gastroparesis. Neurogastroenterol Motil 2020;32e13769. 3. Barahona G et al. Non-invasive vagal nerve stimulation reduces nausea rescue medication in patients with gastroparesis and related disorders, with additional benefits on multiple other associated symptoms. Am J Gastroenterol 2023;118(10S):p S1373-1374.

Acknowledgements:

Learning Objectives: 1. Understand the unmet need and burden of disease in gastroparesis. 2. Examine the impact of non-invasive vagal nerve stimulation on gastrointestinal symptoms and physiology. 3. Propose a framework for incorporating non-invasive vagal nerve stimulation in clinical practice.

Financial Disclosures: Disclosures: None

Disclosure: No significant relationships.

IS065

Breakout Session
NEUROMODULATION FOR GASTROINTESTINAL DISORDERS
15-05-2024 14:30 - 16:00

TRANSCUTANEOUS NEUROMODULATION FOR GASTROINTESTINAL DISORDERS

Jiande Chen, PhD
UNIVERSITY OF MICHIGAN, Internal Medicine - Gastroenterology, ANN ARBOR, United States of America

Introduction and Discussion: Several gastrointestinal disorders are attributed to inflammation and sympathetic overactivity. These include inflammatory bowel diseases and functional gastrointestinal diseases, such as gastroesophageal reflux disease, functional dyspepsia, irritable bowel syndrome and constipation. With appropriate selection of stimulation parameters and treatment regimens, electrical neuromodulation is capable of suppressing sympathetic activity and enhancing parasympathetic activity, resulting in an anti-inflammatory effect via the cholinergic anti-inflammatory pathways. In this presentation, several noninvasive neuromodulation methods will be introduced, including transcutaneous auricular vagal nerve stimulation (taVNS), percutaneous auricular vagal nerve stimulation (paVNS), transcutaneous cervical vagal nerve stimulation (tcVNS), transcutaneous electrical acustimulation (TEA), transabdominal interference stimulation, tibial nerve stimulation, and translumbosacral neuromodulation. Their clinical applications in the most common gastrointestinal diseases will be discussed, including gastroesophageal reflux disease, functional dyspepsia, constipation, irritable bowel syndrome and inflammatory bowel diseases. Numerous single-center placebo-controlled clinical trials have demonstrated the safety and effectiveness of several noninvasive neuromodulation methods for the treatment of functional gastrointestinal diseases. Multi-center randomized clinical trials are needed to demonstrate their clinical efficacies and refinement in device is also required.

Supplemental Data:

References: Chen JD. Parasympathetic control of gastrointestinal motility and cross-branch actions of parasympathetic neuromodulation. Chin Med J (Engl). 2023 Jan 5;136(1):53-55. doi: 10.1097/CM9.0000000000002568. PMID: 36878003; PMCID: PMC10106197. Song G, Trujillo S, Fu Y, Shibi F, Chen J, Fass R. Transcutaneous electrical stimulation for gastrointestinal motility disorders. Neurogastroenterol Motil. 2023 Nov;35(11):e14618. doi: 10.1111/nmo.14618. Epub 2023 Jun 8. PMID: 37288650. Chen JD, Yin J, Wei W. Electrical therapies for gastrointestinal motility disorders. Expert Rev Gastroenterol Hepatol. 2017 May;11(5):407-418. doi: 10.1080/17474124.2017.1298441. Epub 2017 Mar 21. PMID: 28277856.

Acknowledgements:

Learning Objectives: 1. Introduction of several commonly used noninvasive neuromdulation methods. 2. Clinical applications of noninvasive neruomodulation methods for treating gastrointestinal disorders. 3. Mechanisms of neuromodulation for gastrointestinal diseases.

Financial Disclosures: No signfiicant relationships

Disclosure: No significant relationships.

IS066

Breakout Session
NEUROMODULATION FOR GASTROINTESTINAL DISORDERS
15-05-2024 14:30 - 16:00

ELECTRONIC BYPASS FOR DIABETES: OPTIMIZATION OF STIMULATION PARAMETERS AND MECHANISMS OF GLUCAGON-LIKE PEPTIDE-1

Shiying Li, MBBS
University of Michigan, Ann Arbor, United States of America

Introduction and Discussion: Type 2 diabetes mellitus (T2DM) is one of leading epidemics in human history closely associated with obesity. Bariatric surgery remains the most effective strategy for the treatment of obesity and T2DM. The precise mechanisms responsible for improved glucose control after surgery remain uncertain. The reduction in postprandial blood glucose is believed to be largely attributed to the increased release of glucagon-like peptide-1 (GLP-1) from L-cells in the distal ileum resulted from a rapid delivery of nutrients to ileum(1,2). However, surgical treatment is limited since it is not only invasive but also irreversible and non-amendable. Developing strategies that physiologically mimic bariatric surgery but are less invasive is of great significance. Intestinal electrical stimulation (IES) mimics the effects of gastric bypass by decreasing gastric emptying rate, food intake, and nutrient absorption. Animal studies have shown that IES also promotes weight loss and enhances glucose tolerance, suggesting its potential as a treatment for Type 2 Diabetes. In a four-week study, rats equipped with one pair of electrodes at the duodenum were assigned to receive either a sham or IES of varied pulse widths ranging from 0.3ms to 3ms in a sequential way(3). The results demonstrated that IES with pulse widths of 1ms and 3ms, but not 0.3ms, reduced food intake and body weight, attributed to accelerated small bowel transit and enhanced GLP-1 secretion in a pulse width-dependent manner(4). A chronic two-month experiment of IES revealed significant improvements in glucose tolerance and insulin resistance in diet-induced obesity rats(5). Furthermore, a study involving pretreatment of atropine and M3 antagonist 4-DAMP inhibited the hypoglycemic effects of both 0.3 and 3ms as well as the increase in plasma GLP-1(4). GLP-1 functioned exclusively through GLP-1R, a G protein-coupled glucagon family protein. The activation of GLP-1R plays an important role in controlling glucose metabolism in T2D diabetes. In a chronic animal study, compared with sham-IES, chronic IES of two months elevated GLP-1R protein expression in the pancreas, small intestine, and nucleus tractus solitarius measured by protein expression and/or tissue immunofluorescence staining. In summary, acute IES reduces postprandial blood glucose by enhancing GLP-1 release mediated via the cholinergic mechanism. Chronic IES improves blood glucose metabolism and homeostasis through enhanced GLP-1 secretion and GLP-1R expression.

Supplemental Data:

References: 1. Thaler JP, Cummings DE. Minireview: Hormonal and metabolic mechanisms of diabetes remission after gastrointestinal surgery. *Endocrinology*. 2009;150(6):2518-2525. 2. Sandoval DA, Patti ME. Glucose metabolism after bariatric surgery: implications for T2DM remission and hypoglycaemia. *Nat Rev Endocrinol*. 2023;19(3):164-176. 3. Li S, Chen JD. Pulse Width-Dependent Effects of Intestinal Electrical Stimulation for Obesity: Role of Gastrointestinal Motility and Hormones. *Obes Surg*. 2017;27(1):70-77. 4. Dong Y, Zhang Y, Li S, Chen JDZ. Intestinal Electrical Stimulation Enhances Release of Postprandial Incretin Hormones Via Cholinergic Mechanisms. *Obes Surg*. 2021;31(5):1957-1966. 5. Li S, Zhu W, Zhang S, Chen JDZ. Chronic intestinal electrical stimulation improves glucose intolerance and insulin resistance in diet-induced obesity rats. *Obesity (Silver Spring)*. 2017;25(6):1061-1068.

Acknowledgements:

Learning Objectives: 1. Acute IES reduces postprandial blood glucose by enhancing GLP-1 release mediated via the cholinergic mechanism. 2. Chronic IES improves blood glucose metabolism and homeostasis through enhanced GLP-1 secretion and improved insulin sensitivity 3. The activation of GLP-1R plays an important role in controlling glucose metabolism in T2D diabetes.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

IS067

Breakout Session
NEUROMODULATION FOR GASTROINTESTINAL DISORDERS
15-05-2024 14:30 - 16:00

DEEP BRAIN STIMULATION (DBS) FOR OBESITY

Clement Hamani, MD
Sunnybrook Research Institute, Toronto, Canada

Introduction and Discussion: Obesity is a chronic and prevalent disorder defined as a body mass index (BMI) greater than 30 kg/m^2. First-line therapies include comprehensive lifestyle interventions, encompassing diet and physical activity, and different medical interventions. For patients with morbid obesity (BMI ≥ 40 or a BMI ≥ 35 with comorbidities), bariatric surgery is commonly offered with a high success rate. However, 20-40% of patients treated with bariatric procedures fail to achieve or sustain significant weight loss in the long term. In this patient population, deep brain stimulation (DBS) has been proposed to modulate functioning of neural elements involved in physiological aspects of food intake, hunger and/or satiety. We will review translational preclinical studies and clinical trials showing the safety of DBS in patients with obesity and its effects on food intake, metabolism, hunger, and satiety.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. Understand the translational basis for the development of recent clinical trials on DBS for obesity. 2. Characterize potential brain regions for the administration of DBS to treat obesity in recent clinical trials. 3. Describe the overall results of clinical trials on DBS for obesity.

Financial Disclosures: No significat relationships.

Disclosure: No significant relationships.

IS068

Breakout Session
PERIPHERAL NERVE STIMULATION + NON-EPILEPSY VAGUS NERVE STIMULATION
16-05-2024 08:00 - 10:00

SELECTIVE OPTOGENETIC STIMULATION OF EFFERENT FIBERS IN THE VAGUS NERVE

Lindsea Booth, PhD[1], Song Yao, BSc (Hons)[2], Sally Hood, BSc (Hons)[1], Angela Connelly, BSc (Hons)[2], Stuart McDougall, PhD[1], Andrew Allen, PhD[2], Clive May, PhD[1], Alexander Gourine, PhD[3]
[1]University of Melbourne, Florey Institute, Melbourne, Australia, [2]University of Melbourne, Anatomy And Physiology, Melbourne, Australia, [3]University College London, Npp, London, United Kingdom

Introduction and Discussion: Background: Electrical stimulation applied to individual organs, peripheral nerves, or specific brain regions has been used to treat a range of medical conditions. In cardiovascular disease, autonomic dysfunction contributes to the disease progression and electrical stimulation of the vagus nerve at the cervical level has been trialled as a treatment to restore autonomic balance. However, this approach lacks selectivity both in the fibre types activated and target organs effected. **Aim:** The aim of our study was to selectively stimulate vagal efferent fibres projecting from neurons in the dorsal motor nucleus of the vagus (DMV) using optogenetics in a large animal model. **Methods:** We used lentiviral vectors expressing the light-sensitive channel rhodopsin variant, oChIEF, under the control of the PRSx8 promoter, that selectively targets vagal preganglionic neurones. Vectors were injected in the caudal half of the left DMV in seven Merino ewes. Eight to twelve weeks later, channel expression and fibre conduction were assessed in anaesthetised sheep. **Results:** All sheep expressed optogenetic channels in a subset of efferent vagal fibres at the level of the cervical vagus, cardiac vagus and reaching beyond the level of the diaphragm. Blue laser or LED light (>10 mW/mm^2; 1 ms pulses) applied to the cervical vagus triggered precisely timed, strong bursts of efferent activity with evoked action potentials propagating at speeds of ~6 m/s. **Conclusions:** These findings show that in sheep, with large, multi-fascicled vagus nerves, it is possible to stimulate a specific sub-population of efferent fibres using light at a site remote from the vector delivery. This marks an important step forward for the use of optogenetic technology for autonomic neuromodulation.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1) Described is a method of selective efferent vagus nerve stimulation using light. 2) Vagal preganglionic neurons are targeted to express light-sensitive channels. 3) Specific efferent VNS by light delivery to the cervical vagus is achieved in a large animal model and this demonstrates feasibility of using optogenetic technology for autonomic neuromodulation.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS069

Breakout Session
PERIPHERAL NERVE STIMULATION + NON-EPILEPSY VAGUS NERVE STIMULATION
16-05-2024 08:00 - 10:00

MODULATION OF SYMPATHETIC NERVOUS SYSTEM FOR CARDIAC DISEASE

Olujimi Ajijola, MD, PhD
University of California Los Angeles, Medicine-cardiology/electrophysiology, Los Angeles, United States of America

Introduction and Discussion: The autonomic nervous system is central to homeostatic regulation of the heart across physiological states. In the setting of chronic cardiac injury, initially protective adaptive mechanisms orchestrated by the autonomic nervous system become deleterious. Structural and functional remodelling of neuronal and non-neuronal elements comprising reflex heart-brain circuits promote maladaptive processes that worsen cardiac function and enhance arrhythmias. Employing approaches ranging from in silico to mechanistic clinical studies, our work elucidates mechanisms governing adverse neural remodelling and develops interventions targeting nexus points within heart-brain reflex circuits to treat chronic heart disease

Supplemental Data:

References:

Acknowledgements: The support of the NIH/NHLBI and the Chan Zuckerberg Initiative is gratefully acknowledged.

Learning Objectives: 1. Understand role of the autonomic nervous system in regulating the heart in healthy and disease states. 2. Understand various targets within the peripheral nervous system for neuromodulation. 3. Understand various neuromodulation approaches used for the heart.

Financial Disclosures: Dr. Ajijola reports ownership of NeuCures LLC; Anumana; and nFerence. OAA has filed a patent for intellectual property owned by University of California Regents in the areas of catheter ablation and neuromodulation. OAA reports honoraria from Biosense Webster Inc., Abbott, Biotronik, Boston Scientific, Medtronic, AltaThera, and Atricure.

Disclosure: No significant relationships.

IS070

Breakout Session
PERIPHERAL NERVE STIMULATION + NON-EPILEPSY VAGUS NERVE STIMULATION
16-05-2024 08:00 - 10:00

DOES NEUROMODULATION HAVE A ROLE IN THE MANAGEMENT OF HEAD & FACIAL PAIN?

Jean-Pierre Van Buyten, MD, PhD
VITAZ Hospitals, The Multidisciplinary Pain Management Centre, Sint-Niklaas, Belgium

Introduction and Discussion: In terms of neuromodulation for pain management, the head is the forgotten part of the body and in my opinion not the unimportant one. Neuromodulation for pain management focuses mainly on pain of spinal origin and most of the neurostimulators are implanted for neuropathic pain due to PSPS II. Fortunately, new indications and other targets are in the pipeline (DRG stimulation for CRPS and Chronic Post-Surgical Pain, SCS for non-operated low back pain and diabetic polyneuropathy). However, headaches and facial pain are very frequent complaints for which patients could consult a pain center. Little attention is paid to this pathology by Neuromodulation centers and by the industry. 1) chronic refractory cluster headache and Chronic Migraine If pharmacotherapy has insufficient effect, there are options for these patients by using neuromodulation techniques. For the treatment of chronic refractory cluster headache, The European Headache Federation recognizes this therapy in a consensus paper published in The Journal of Headache and Pain 2013 14:86 Meanwhile, there is Level I evidence, and the Icon Study published in the Lancet Neurology marked a milestone in the scientific evidence of ONS. Meanwhile, long-term results (2–8-year extension of the Icon study) on efficacy and safety have been recently published in The Lancet (Dec. 2023) In case of insufficient result of ONS, additional implantation of an electrode (off label) at the level of the sphenopalatine ganglion can be a rescue therapy. Stimulation of the SPG has already been scientifically proven to abort CH attacks with a RF system connected to an electrode on the SPG with which we could not stimulate continuously. A review article on Managing Cluster headache with SPG stimulation was already published in the J Pain Res in2018. 2)Facial Pain (Trigeminal Neuropathy) According to the classification published by Kim Burchiel in Neurosurgery 2003, a clear distinction should be made between Trigeminal neuralgia and Trigeminal neuropathy usually iatrogenic. These patients can be helped with neuromodulation techniques. Peripheral nerve stimulation and or stimulation of Gasserian ganglion may be a good alternative for these patients. Minimal invasive approach to Gasser's ganglion for electrode placement (custom made and off label) using EM neuronavigation is discussed. Some large case series have been published in the last decennium. We would argue that the industry should pay more attention to the development of specific devices considering the unmet medical need to be able to treat this underestimated number of patients with chronic neuropathic pain with neuromodulation techniques.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1) paying attention to many head & Facial pain problems that could be treated by neuromodulation techniques 2) show the different techniques supported by the literature 3) by showing many cases by imaging, go through the actual applied therapies

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS071

Breakout Session
PERIPHERAL NERVE STIMULATION + NON-EPILEPSY VAGUS NERVE STIMULATION
16-05-2024 08:00 - 10:00

VAGUS NERVE STIMULATION (VNS) IN POST TRAUMATIC STRESS DISORDER (PTSD)

Doug Bremner, MD
Emory University, Department Of Psychiatry & Behavioral Sciences, Atlanta, United States of America

Introduction and Discussion: Non-invasive Vagal Nerve Stimulation (nVNS) is a promising new approach for stress-related psychiatric disorders. Posttraumatic stress disorder (PTSD) is associated with increased sympathetic responses to stress, alterations in brain areas mediating the stress response, including the insula, and deficits in declarative memory encoding and consolidation. In a study of 56 individuals with a history of exposure to psychological trauma with and without the diagnosis of PTSD, we assessed brain, inflammatory biomarkers, vascular and peripheral cardiac and autonomic responses to exposure to traumatic reminders in the form of personalized scripts of traumatic events, as well as “neutral” mental arithmetic stressors (public speaking, mental arithmetic). Stress exposures were paired with transcranial cervical VNS (tcVNS) or sham stimulation. A subgroup of PTSD patients underwent twice daily tcVNS or sham stimulation at home for three months followed by monthly assessment of PTSD symptoms and declarative memory (paragraph encoding paired with stimulation) followed by repeat assessments. tcVNS (but not sham) was associated with a blocking of response to stress including, sympathetic response measured with pre-ejection period (PEP) and peripheral vasoconstriction, insula response measured with brain imaging, the immune biomarker interleukin-6 (IL-6), and stress-related neuropeptides Pituitary Adenylate Cyclase Activating Peptide (PACAP) and ghrelin in blood (in PTSD patients). Daily tcVNS in PTSD led to a 91% enhancement of paragraph recall when encoding and consolidation were paired with tcVNS (versus 0% for sham) and a 31% reduction in PTSD symptoms compared to sham stimulation after three months as measured with the PTSD Checklist (PCL). These findings show blocked sympathetic, immune, stress-related neuropeptide and insula responses to traumatic reminders, reduced PTSD symptoms, and enhanced declarative memory function in PTSD patients with tcVNS.

Supplemental Data: None

References: 1. 1. **Bremner JD**, Rapaport MH: Vagal nerve stimulation: Back to the future. *Am J Psychiatry.* 2017; 147(7): 609-610. doi: 10.1176/appi.ajp.2017.17040422. PMC8136752. 2. Gurel NZ, Shandhi MH, **Bremner JD**, Vaccarino V, Ladd SL, Shallenberger LH, Shah A, Inan OT: Toward Closed-Loop Transcutaneous Vagus nerve stimulation using peripheral cardiovascular physiological biomarkers: A proof-of-concept study. *IEEE International Conference on Wearable and Implantable Body Sensor Networks (BSN)*. Las Vegas NV. 2018, 78-81. doi: 10.1109/BSN.2018.8329663. 3. Adair D, Truong D, Esmaeilpour Z, Gebodh N, Borges H, Ho L, **Bremner JD**, Badran BW, Napadow V, Clark VP, Bikson M: Electrical stimulation of cranial nerves in cognition and disease. *Brain Stimul.* 2020; 13; (3):717-750, May 01, 2020. Epub February 23, 2020. doi:10.1016/j.brs.2020.02.019. PMC7196013. 4. Gurel NZ, Gazi AH, Scott KL, Wittbrodt MT, Shah AJ, Vaccarino V, **Bremner JD**, Inan OT. Timing considerations for noninvasive Vagal Nerve Stimulation in clinical studies. *AMIA Ann Symp Proc*. 2020; 2019:1061-1070. Epub 2020 Apr 1l. doi: 10.1016/j.jpsychores.2020.110110. PMC7153149. 5. Gurel NZ, Huang M, Wittbrodt MT, Jung H, Ladd SL, Shandhi MH, Ko Y-A, Shallenberger L, Nye JA, Pearce B, Vaccarino V, Shah AJ, **Bremner JD**, Inan OT: Quantifying acute physiological biomarkers of transcutaneous vagal nerve stimulation in the context of psychological stress. *Brain Stimul.* 2020; 13(1): 47-59. Jan-Feb 2020. Epub 2019 Aug 6. doi: 10.1016/j.brs.2019.08.002. PMC8252146 6. **Bremner JD**, Wittbrodt MT. Stress, the brain, and trauma spectrum disorders. *Int Rev Neurobiol*. 2020; 152:1-22. Epub 2020 Feb 19. doi: 10.1016/bs.irn.2020.01.004. PMC8214870. 7. Gurel NZ, Wittbrodt WT, Jung H, Ladd, SL, Shah AJ, Vaccarino V, **Bremner JD**, Inan OT: Automatic detection of target engagement in transcutaneous cervical Vagal Nerve Stimulation for traumatic stress triggers. *IEEE J Biomed Health Inform.* 2020: 24(7):1917-1925. Jul 2020. Epub 2020 Mar 16. doi:10.1109/JBHI.2020.2981116. PMC7393996. 8. Wittbrodt MT, Gurel NZ, Nye JA, Ladd S, Shandhi MMH, Huang M, Shah AJ, Pearce BD, Alam ZS, Rapaport MH, Murrah N, Ko Y-A, Haffer AA, Shallenberger LH, Vaccarino V, Inan OT, **Bremner JD**:

Non-invasive vagal nerve stimulation decreases brain activity during trauma scripts. *Brain Stimul* 2020; 13(5):1333-1348. Sep-Oct 2020. Epub 2020 Jul 10. 2020 Sep-Oct. doi: 10.1016/j.brs.2020.07.002. PMC8214872. 9. Gazi AH, Gurel NZ, Richardson KLS, Wittbrodt MT, Shah AJ, Vaccarino V, **Bremner JD**, Inan OT: Digital cardiovascular biomarker responses to transcutaneous cervical vagus nerve stimulation: State-space modeling, prediction, and simulation. *JMIR mHealth and uHealth*. 2020; 8(9):e20488. 2020 Sep. Epub 22 JSep 2020. doi: 10.2196/20488. PMC7539162. 10. **Bremner JD**, Gurel NZ, Wittbrodt MT, Shandhi MH, Rapaport MH, Nye JA, Pearce BD, Vaccarino V, Shah AJ, Park J, Bikson M, Inan OT. Application of non-invasive vagal nerve stimulation to stress-related psychiatric disorders. *J Pers Med*. 2020; 10(119):1-25. Epub 2020 Sep 9. doi: 10.3390/jpm10030119. PMC7563188. 11. **Bremner JD**, Gurel NZ, Jiao Y, Wittbrodt MT, Levantsevych OM, Huang M, Jung H, Shandhi MH, Beckwith J, Herring I, Rapaport MH, Murrah M, Driggers E, Ko Y-K, Alkhalaf ML, Soudan M, Song J, Ku BS, Shallenberger L, Hankus AN, Nye JA, Park J, Vaccarino V, Shah AJ, Inan OT and Pearce BD. Transcutaneous vagal nerve stimulation blocks stress-induced activation of interleukin-6 and interferon-γ in posttraumatic stress disorder: A double-blind, randomized, sham-controlled trial. *Brain Behav Immun Health* 2020; 9:100138. 2020 Dec. Epub 11 Sep 2020. doi: 10.1016/j.bbih.2020.100138. PMC8474180 12. Gurel NZ, Jiao Y, Wittbrodt MT, Ko Y-A, Hankus A, Driggers EG, Shallenberger L, Murrah N, Huang M, Haffar A, Alkhalaf M, Levantsevych O, Nye JA, Vaccarino V, Shah AJ, **Bremner JD**, Inan OT, Pearce BD: Effect of transcutaneous vagus nerve stimulation on the Pituitary Adenylate Cyclase-Activating Polypeptide (PACAP) response to stress: A randomized, sham controlled, double blind pilot study. *Comp Psychoneuroendocrinol.* 2020; 4:100012. Epub 27 Oct 2020. doi: 10.1016/j.cpnec.2020.100012. PMC9216713 13. Gurel NZ, Wittbrodt MT, Jung H, Shandhi MH, Driggers EG, Ladd SL, Huang M, Ko Y-A, Shallenberger L, Beckwith J, Nye JA, Pearce BD, Vaccarino V, Shah AJ, Inan OT, **Bremner JD**, Inan OT: Transcutaneous vagal nerve stimulation reduces sympathetic responses to stress in posttraumatic stress disorder: A double-blind, randomized, sham controlled trial. *Neurobiol Stress.* 2020; 13:e100264. 2020 Nov. Epub 2020 Oct 20. doi: 10.1016/j.ynstr.2020.100264. PMC7739181. 14. **Bremner JD**, Wittbrodt MT, Gurel NZ, Shandhi MH, Gazi AH, Jiao Y, Levantsevych OM, Huang M, Beckwith J, Herring I, Murrah N, Driggers EG, Ko Y-A, Alkhalaf ML, Soudan M, Shallenberger L, Hankus AN, Nye JA, Park J, Woodbury A, Mehta PK, Rapaport MH, Vaccarino V, Shah AJ, Pearce BD, Inan OT. Transcutaneous cervical vagal nerve stimulation in patients with posttraumatic stress disorder (PTSD): A pilot study of effects on PTSD symptoms and interleukin-6 response to stress. *J Affect Disord Rep*. 2021; 6:100190. Dec 2021. Epub 2021 Jun 10. doi: 10.1016/j.jadr.2021.100190. PMC8580056. 15. Wittbrodt MT, Gurel NZ, Nye JA, Shandhi MH, Gazi AH, Shah AJ, Pearce BD, Murrah N, Ko Y-A, Shallenberger L, Inan OT, **Bremner JD**. Non-invasive cervical vagal nerve stimulation alters brain activity during traumatic stress in individuals with posttraumatic stress disorder. *Psychosom Med* 2021; 83(9):969-977. 2021 Nov-Dec 01. Epub 2021 Jul 21. doi: 10.1097/PSY.0000000000000987. PMC8578349. 16. Gazi AH, Sundararaj S, Harrison AB, Gurel NZ, Wittbrodt MT, Shah AJ, Vaccarino V, **Bremner JD**, Inan OT. Transcutaneous cervical vagus nerve stimulation lengthens exhalation in the context of traumatic stress. *IEEE EMBS International Conference on Biomedical and Health Informatics (BHI)* 2021; 1-4. Epub 2021 Aug 10. doi: 10.1109/BHI50953.2021.9508534. PMC10114770. 17. Gazi AH, Sundararaj S, Harrison AB, Gurel NZ, Wittbrodt MT, Alkhalaf M, Soudan M, Levantsevych O, Haffar A, Shah AJ, Vaccarino V, **Bremner JD**, Inan OT. Transcutaneous cervical vagus nerve stimulation inhibits the reciprocal of the pulse transit time's responses to traumatic stress in posttraumatic stress disorder. *Annu Int Conf IEEE Eng Med Biol Soc*. 2021:1444-1447. Nov 2021. doi: 10.1109/EMBC46164.2021.9630415. PMID: 34891557. PMC10114282. 18. Gazi AH, Wittbrodt MT, Harrison AB, Sundararaj S, Gurel NZ, Nye JA, Shah AJ, Vaccarino V, **Bremner JD**, Inan OT. Robust estimation of respiratory variability uncovers correlates of limbic brain activity and transcutaneous cervical vagus nerve stimulation in the context of traumatic stress. *IEEE Trans Biomed Eng* 2022; 69(2):849-859. 2022 Feb. Epub 2021 Aug 27; doi: 10.1109/TBME.2021.3108135. PMC8853700. 19. Choudhary T, Elliott M, Euliano NR, et al. Effect of transcutaneous cervical vagus nerve stimulation on declarative and working memory in patients with Posttraumatic Stress Disorder (PTSD): A pilot study. *J Affect Disord*. 2023; 339:418-425. 2023 Oct 15. Epub 2023 Jul 12. doi: 10.1016/j.jad.2023.07.025. PMID 37442455. 20. Moazzami K, Pearce BD, Gurel NZ, Wittbrodt MT, Levantsevych OM, Huang M, Shandhi MH, Herring I, Murrah N, Driggers E, Alkhalaf MJL, Soudan M, Shallenberger L, Hankus AN, Nye JA, Vaccarino V, Shah AJ, Inan OT and **Bremner JD**: Transcutaneous vagal nerve stimulation modulates stress-induced plasma ghrelin levels: A double-blind, randomized, sham-controlled trial. *J Affect Disord* 2023; 342:85-90. doi: 10.1016/j.jad.2023.09.015.

Acknowledgements: This work was sponsored by the Department of Defense Small Business Technology Transfer (DOD STTR) Program Army A21c-t024, Defense Advanced Research Projects Agency (DARPA) Biological Technologies Office (BTO) Targeted Neuroplasticity Training (TNT) program through the Naval Information Warfare Center (NIWC) Cooperative Agreement No. N66001-16-4054 and investigator-initiated grant awards from ElectroCore LLC and the Brain and Behavior Foundation. Stimulation devices were provided for some studies by ElectroCore free of charge.

Learning Objectives: At the conclusion of this presentation the participant should be able to: 1. List key research findings related to neurobiology in PTSD 2. Understand the effects of vagal nerve stimulation on sympathetic and immune function 3. Describe effects of vagal nerve stimulation on memory in PTSD patients.

Financial Disclosures: Free stimulation devices were provided by electroCore for some of the studies in this presentation. The presentor is on the scientific advisory board for Evren.

Disclosure: No significant relationships.

IS072

Breakout Session
PERIPHERAL NERVE STIMULATION + NON-EPILEPSY VAGUS NERVE STIMULATION
16-05-2024 08:00 - 10:00

NEUROMODULATORY MECHANISMS OF VAGUS NERVE STIMULATION (VNS)-ENHANCED REHABILITATION

Catherine Thorn, PhD
The University of Texas at Dallas, Dept. Of Neuroscience, Richardson, United States of America

Introduction and Discussion: Vagus nerve stimulation (VNS) has been shown to induce neuroplasticity in the motor system and to improve functional recovery following neural injuries such as stroke. VNS activates key visceral sensory pathways that regulate autonomic function and support food-seeking behaviors that are necessary for survival. Activation of these pathways is thought to enhance motor learning, in part through upregulation of broadly projecting neuromodulatory systems in the CNS. This talk will focus on recent work examining the extent to which VNS-driven noradrenergic and dopaminergic signaling contribute to experience-dependent plasticity in the motor cortex and reinforcement of learned behaviors.

Supplemental Data:

References: None

Acknowledgements: This work was supported by NIH grants R01 NS123074, R21 DA055166, and R01 NS126816.

Learning Objectives: Objective 1: Participants will learn about the cortical catecholaminergic mechanisms that likely contribute to VNS-enhanced recovery of motor function. Desired Result 1: Participants will have an increased understanding of the complex mechanisms underlying VNS therapy and how it can be used to enhance recovery of function after neurological damage. Objective 2: Participants will learn about the preclinical and clinical studies supporting the use of VNS paired with rehabilitative training to enhance neuroplasticity and improve recovery of function after neurological damage. Desired Result 2: Participants will be able to describe preclinical and clinical evidence supporting the use of VNS paired with rehabilitative training, and understand the potential of this approach to improve recovery of function in neurological disorders. Objective 3: Participants will learn how basic research into VNS mechanisms can inform the development of bioelectronic therapies and future research in the field of neuroplasticity and neurological rehabilitation. Desired Result 3: Participants will recognize how an enhanced understanding of the mechanisms and functional effects of VNS can inform the development of new bioelectronic therapies and to guide future research in the field of neuroplasticity and neurological rehabilitation.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

IS073

Breakout Session
ARTIFICIAL INTELLIGENCE
16-05-2024 08:00 - 10:00

PRACTICAL ARTIFICIAL INTELLIGENCE (AI) ALGORITHM TO OPTIMIZE DEEP BRAIN STIMULATION (DBS) PLANNING AND PROGRAMMING

Nevair Gallani, MD
Clinica Neuro Logica, Functional Neurosurgery, São Paulo, Brazil

Introduction and Discussion: Despite many sophisticated computational tools and neuroimaging information available for neurosurgeons, accurate targeting remains mostly an intuitive human task with inter-surgeon and intra-surgeon variabilities. Deep brain stimulation (DBS) programming also, remains an essay-error paradigm. Due to those uncertainty, there is still a need to perform clinical testing and neurophysiological monitoring during DBS surgery. Thus, this is the discription of a simple yet original mathematical solution - GACPC Algorithm© - to standardize nuclei targeting and DBS programming. To build this contruct, the volumes of a computationally reconstructed subthalamic nucleus (STN) and of a simulated volume of tissue activated (VTA) were measured according to the LPBA40 average brain template and Anne Morel's Atlas of basal ganglia, with MNPS© software. The intersection volume between the two volumes was calculated, and several different parameters of stimulation were simulated. Three indices of comparison between volumes were calculated at each VTA: Paddick conformity index, Jaccard and Sorensen similarity indexes. All indexes exhibit a slope of variation as VTA increases; the maximum value corresponds mathematically to the best match possible between STN and VTA. The best possible DBS stimulation parameter can eventually be determined. At LPBA40, at 50% the distance of STN center of mass and its posterior limit: (x,y,z) - 11.161, -1.465, -3.639; for the whole STN; with 1.000Ω impedance, 90µs, 130Hz, was at 2.0V, 2.0mA. For targeting, given a certain VTA, the best possible coordinate to stimulate can be also computationally determined, since it is at the site of maximum value of the indexes. The algorithm can be used for any target or any region of interest, determined by the neurosurgeon. Furthermore, there is not even necessary the existance of cognitive human physician to visually search for visual clues based on lead localization upon target nuclei anatomy, and infer for the best lead contact or the best shape of simulated VTA, since the best match is computationally and mathematically determined, autonomously, individually for a given target. The described algorithm has the property of pushing DBS targeting and programming to a new paradigm. The GACPC algorithm© allow neurosurgeons to determine the best target coordinate for each patient and facilitate programming sessions for the best clinical results for individual patients.

Supplemental Data:

References: None

Acknowledgements: Dr Armando Alaminos-Bouza, Dr Sylvine Carrondo-Cottin, Dr Michel Prudhomme, Dr Leo Cantin.

Learning Objectives: 1-Understand three dimentional aspects of targets and of the stimulated region by DBS treatment. 2-Acknowledge the goal of the best possible matching between the anatomy volume of the target and of the volume of stimulated tissue by the lead DBS. 3-Apply this paradigm for individual patients in real world.

Financial Disclosures: No significant relationships.

Disclosure: No significant relationships.

IS074

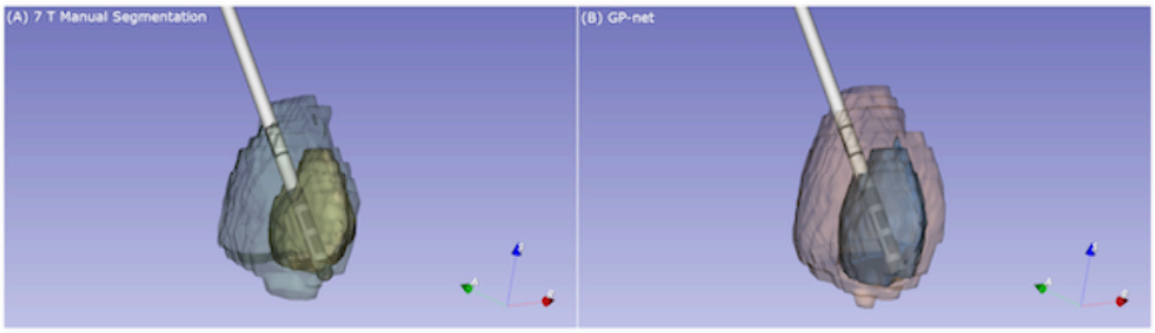
Breakout Session
ARTIFICIAL INTELLIGENCE
16-05-2024 08:00 - 10:00

ARTIFICIAL INTELLIGENCE (AI) BRAIN IMAGING FOR SURGICAL TARGETING

Noam Harel, PhD
University of Minnesota, Radiology, Minneapolis, United States of America

Introduction and Discussion: Artificial Intelligence (AI) has revolutionized medical imaging, particularly in the context of deep brain stimulation (DBS) procedures. In recent years, there has been an exponential growth in studies using AI for medical imaging across three main categories: 1) Image analysis and segmentation, 2) image reconstruction, and more recently, 3) artifact correction and denoising methods. These capabilities are driven by several factors, including the maturation of deep learning algorithms, increased localized computing power, accessible labeled datasets, and the growing awareness of the potential benefits of deep learning in medical imaging. Focusing on DBS surgery, the impact of AI is profound. A fully automated segmentation process offers several clear advantages, including accuracy (unbiased) and speed (seconds) of inference. It enables improved target localization precision by accounting for patient-specific anatomical differences and reducing electrode placement variability, thereby leading to better outcomes. AI's impact on medical imaging extends to expanded access to care. AI technology could alleviate the scarcity of specialized neurosurgeons by enabling less experienced practitioners to perform DBS procedures. It also enables tailoring of treatment plans to individual patients. Although significant advances have been made, there are still challenges to overcome in achieving optimal accuracy and precision. These challenges are related to the quality and diversity of training data, which can vary in terms of imaging protocols, data quality, and anatomical differences. Overall, AI's transformative potential in medical imaging for DBS surgery promises enhanced accuracy, safety, accessibility, and efficiency.

Supplemental Data:



(a) 3D reconstruction of a DBS electrode placement with respect to the manually delineated GPe (green)/GPi (yellow) for a specific PD patient. (b) 3D reconstruction of the same DBS electrode with respect to AI-generated GP segmentation of the GPe (orange)/ GPi (blue). Adopted from Solomon et al., 2021.

References: Selected References: Solomon et al., Deep-learning based fully automatic segmentation of the globus pallidus interna and externa using ultra-high 7 Tesla MRI. *Hum Brain Mapp. 2021 Jun 15;42(9):2862-2879. doi: 10.1002/hbm.25409. Epub 2021 Mar 18. PMID: 33738898.* Duchin et al., Patient-specific anatomical model for deep brain stimulation based on 7 Tesla MRI. *PLoS ONE 2018 Aug 22;13(8):e0201469.* Kim et al., Automatic Localization of the Subthalamic Nucleus on Patient-Specific Clinical MRI by Incorporating 7T MRI and Machine Learning: Application in Deep Brain Stimulation. *Hum Brain Mapp. 2018;1–20. https://doi.org/10.1002/hbm.24404.*

Acknowledgements: National Institution of Health, Award Numbers: S10 OD025256, P41 EB027061, P50 NS098753, R01 NS081118, R01 NS113746.

Learning Objectives: I will review the recent advantages of using AI in deep brain stimulation surgical procedures.

Financial Disclosures: Dr. Harel is a co-founder of Surgical Information Sciences, Inc.

Disclosure: No significant relationships.

IS075

Breakout Session
ARTIFICIAL INTELLIGENCE
16-05-2024 08:00 - 10:00

MAPPING FUNCTIONAL CONNECTOME OF THE DEFAULT MODE NETWORK FOR TARGETED NEUROMODULATION

Dirk De Ridder, MD
University of Otago, Surgical Sciences (neurosurgery), Dunedin, New Zealand

Introduction and Discussion: The Default mode network (DMN) was described in 2001 by Raichle consisting of a constellation of cortical brain areas that are active at rest, i.e. when the brain is not performing stimulus dependent tasks. It is involved in stimulus independent cognition, self-referential processing and mind wandering. It is made up of spatially widely distributed brain areas divided in a medial and lateral component: the medial subnetwork relates to 'self' processing, the lateral component to 'non-self' processing. The cortical building blocks include the ventromedial prefrontal cortex (inhibition), dorsomedial prefrontal cortex (intention), posterior cingulate cortex (environment), temporoparietal junction (multisensory integration), and anterior midtemporal area (unknown function). Some authors also include the hippocampal area. The DMN is part of the triple network model that proposes that abnormal interactions within and between 3 canonical brain networks underlie brain disorders. These 3 networks include the self-representational default mode network, the behavioural relevance encoding salience network and the goal oriented central executive network. The default mode network is involved in many mental disorders, either by hypo-, hyper-or dysconnectivity and abnormal activity, leading to disorganized cognition. This includes Alzheimer's disease, depression, schizophrenia, ADHD, autism, PTSD, OCD, TBI, and personality disorders

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. understand the anatomy of the default mode network 2. understand the function of the default mode network 3. understand the pathology associated with the default mode network

Financial Disclosures: Dirk De Ridder, Abbott, speakers' bureau, consultant

Disclosure: No significant relationships.

IS076

Breakout Session
ARTIFICIAL INTELLIGENCE
16-05-2024 08:00 - 10:00

MACHINE LEARNING STN BIOMARKERS FOR PD PATIENT

Hagai Bergman, MD, D.Sc
Hebrew U, Elsc, Jerusalem, Israel

Introduction and Discussion: The subthalamic nucleus (STN) is a driving force of basal ganglia physiology and pathophysiology. Thus, understanding its input-output dynamics is vital for improving therapies for Parkinson's disease. Here, we analyzed micro-electrode recordings from Parkinson's disease (PD) patients undergoing deep brain stimulation (DBS) procedures, distinguishing between local field potential (LFP) for input and spike discharge rate (SPK) for output. Natural systems often exhibit power-law dynamics characterized by the exponent α. We, therefore, used the Fitting Oscillations & One Over F (FOOOF) tool to dissect data from 146 patients and 25,000 recording sites into their aperiodic (power law) and superimposed periodic components. Subthalamic LFP had significantly higher values of aperiodic exponents ($\alpha = 2.2 \pm 0.4$) than SPK ($\alpha = 0.1 \pm 0.2$). Population LFP showed predominant high beta (>20 Hz) periodic oscillations, while SPK exhibited low and high beta oscillations. The frequency distribution of oscillations for SPK and LFP individual sites is tightly narrow. A downward shift in the center frequencies of SPK beta oscillations, compared to concurrently recorded LFP, likely contributes to the distinct distribution of SPK/LFP population oscillatory patterns. Regression models revealed that the subthalamic aperiodic parameters and spiking activity explained a significant fraction of the variance of the burden of Parkinson’s disease and the efficacy of its treatment. The unique subthalamic input-output dynamics may explain its role in Parkinson's disease physiology and the success of subthalamic DBS. Closed-loop DBS therapy may use subthalamic input-output aperiodic and periodic LFP and SPK components to optimize treatment in the spatial and temporal domains.

Supplemental Data: None

References: None

Acknowledgements: This study is supported by the grants of the ISF Breakthrough Research program (Grant 1738/22), Collaborative research center TRR295, Germany (Project number 424778381), Israel-China bi-national scientific foundation (with Prof. Mingsha Zhang, Beijing Normal University, Beijing, China, Grant 3380/20), The Silverstein foundation (to Hagai Bergman) and the scholarship from China Scholarship Council (to Dr. Xiaowei Liu).

Learning Objectives: 1. Aperiodic behavior of STN LFP and spiking activity in PD patients. 2. Comparison of STN LFP and spiking activity in PD patients. 3. STN physiological biomarkers for the burden of Parkinson’s disease and the efficacy of its treatment.

Financial Disclosures: Hagai Bergman is a consultant of Alpha Omega, Israel. He received travel honoraria for lectures, presentations, and speaker’s bureaus from Medtronic, Boston Scientific, and Alpha-Omega. He has several patents with Alpha Omega. These financial disclosures are not related to this study.

Disclosure: No significant relationships.

IS077

Breakout Session
ARTIFICIAL INTELLIGENCE
16-05-2024 08:00 - 10:00

APPLYING AI DATA SCIENCE IN BRAIN NEUROMODULATION FOR EPILEPSY

Martha Morrell, PhD[1,2]
[1]NeuroPace, Mountain View, United States of America, [2]Stanford, Neurology, Palo Alto, United States of America

Introduction and Discussion: Many neurologic disorders are temporally, anatomically, and electrophysiologically discrete. Examples include tremor, migraine, and epilepsy. Continuous and duty cycle neuromodulation therapies are available for each of these conditions. Responsive neuromodulation offers the potential advantage to treat only when and where needed, and to modify treatment according to electrophysiological changes that correlate with clinical symptoms. An FDA approved responsive neuromodulation device for drug resistant focal epilepsy responds to specific intracranial electrophysiological patterns identified by the physician as significant, and provides physician specified stimulation in response. The device also collects chronic ambulatory intracranial EEG data for physician review. The size of this database offers opportunities to understand epileptic networks within and across patients, and an opportunity to identify quantitative biomarkers to inform treatment decisions, including detection and stimulation approaches, and to predict the clinical response. However, it is not possible for a physician to extract all relevant information from this rich brain data repository because of its sheer size and because important features may not be apparent to the human user. Ultimately, AI can be applied to improve patient outcomes by increasing the efficiency and effectiveness of care. AI provides an opportunity to learn from complex and large datasets, and to apply those learnings to suggest promising neuromodulation approaches. However, the benefits of AI cannot be realized without a physician guide. First, the clinical problem must be clearly defined, and relevant data sets identified. Then, ML and generative models can be developed to identify and validate meaningful biomarker proxies for disease expression. If the physician's clinical assessment can incorporate information obtained from AI identified biomarkers with the patient's subjective experience, then AI will have delivered meaningful clinical value. An example of physician and AI fueled biomarker discovery, and application of these biomarkers to patient care, will be provided using the experience of a responsive neuromodulation device for treatment of epilepsy.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: Using an example of a responsive direct brain neurostimulator for epilepsy: 1. Appreciate the potential for devices to collect brain data of sufficient size to utlize AI 2. Understand the potential opportunities for AI to provide information relevant to treatment of brain disorders 3. Recognize the criticality of physicians to define clinical problems and apply AI to achieve meaningful clinical outcomes

Financial Disclosures: Name of company: NeuroPace Role: Chief Medical Officer; Stockholder Company level of compensation: > 100,000

Disclosure: No significant relationships.

IS078

Breakout Session
NEUROMODULATION FOR GENITOURINARY DISORDERS
16-05-2024 08:00 - 10:00

NEW IN SACRAL NEUROMODULATION FOR GU INDICATIONS

Stefan De Wachter, PhD
Antwerp University, Urology, Wilrijk, Belgium

Introduction and Discussion: Sacral neuromodulation has been a standard treatment for GU indications since the early '90s. Long term clinical efficacy has been reported around 75% on per protocol analysis and 55-60% on an intention to treat analyse. Furthermore, large variability in efficacies have been reported. The past years the technique has been standardized and tailored to the patients. Also neurophysiological methods have revealed new insights in its mechanism of action. This presentation will present the latest data on techniques and indications for sacral neuromodulation for GU indications.

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1) make correct interpretation on published data 2) learn the theoretical background of the standardized technique 3) update your knowledge with recent efficacy rates along the different GU indications

Financial Disclosures: Stefan De Wachter is cofounder, shareholder and CSO in Amber Therapeutics, a company developing bioelectrical therapies.

Disclosure: No significant relationships.

IS079

Breakout Session
NEUROMODULATION FOR GENITOURINARY DISORDERS
16-05-2024 08:00 - 10:00

HIGH-DENSITY SPINAL CORD STIMULATION (SCS): SELECTIVE ACTIVATION OF LOWER URINARY TRACT NERVES

Robert Gaunt, Associate Professor[1], Maria Jantz, BSc[2], Chaitanya Gopinath, PhD[1], Xiaoqi Fang, MSc[1], Lucy Liang, MSc[2], Arianna Damiani, MSc[2], Alessandro Fasse, MSc[3], Taylor Newton, PhD[3], Esra Neufeld, PhD[3], T Kevin Hitchens, PhD[4], Bryan McLaughlin, PhD[5], Marco Capogrosso, PhD[6], Elvira Pirondini, PhD[1], Lee Fisher, PhD[1]
[1]University of Pittsburgh, Physical Medicine And Rehabilitation, Pittsburgh, United States of America, [2]University of Pittsburgh, Department Of Bioengineering, Pittsburgh, United States of America, [3]Z43, It'is Foundation, Zurich, Switzerland, [4]University of Pittsburgh, Department Of Neurobiology, Pittsburgh, United States of America, [5]Micro-Leads Inc, Somerville, United States of America, [6]University of Pittsburgh, Department Of Neurosurgery, Pittsburgh, United States of America

Introduction and Discussion: Losing control of bladder function is one of the most significant ongoing consequences of spinal cord injury (SCI) and improving bladder function is a major rehabilitation priority for people living with SCI. Unfortunately, there are no devices available today that address this critical need. Electrical stimulation of the epidural surface of the spinal cord may provide a method to change this. Spinal cord stimulation (SCS) with implanted epidural leads is widely used to treat pain, and multiple studies have demonstrated its potential effectiveness to improve locomotion after SCI. In several studies, SCS has even improved bladder function. However, these outcomes are highly variable and the mechanisms behind these observations are unclear. To establish the scientific rationale for SCS as a viable neuromodulation technique to control bladder function, we conducted experiments in both anesthetized and awake cats with high-resolution SCS electrode arrays placed over the sacral spinal cord[1]. These electrodes directly activated both pudendal and pelvic nerve afferents, which are the primary sensory innervation of the bladder and urethral. There was considerable variability in the specific nerves recruited through individual electrodes; some electrodes were selective for pudendal or pelvic afferents, while others recruited mixed populations, including the sciatic nerve. To test the functional relevance of this electrophysiological recruitment, we conducted further experiments in both anesthetized and awake animals. Stimulation both evoked and inhibited bladder contractions, depending on the stimulation frequency, suggesting that sacral SCS activates reflex mechanisms similar to those driven by peripheral nerve stimulation. Next, we built computational models of the feline sacral cord to interrogate how SCS activates populations of afferents distributed throughout the complex anatomy of the sacral spinal cord[2,3]. Finally, we extended this model to the human cord and identified regions of the spinal cord that may be particularly beneficial for evoking changes in bladder function after SCI. This combination of experimental and modelling work establishes a clear anatomical and mechanistic rationale for pursuing SCS as an intervention to improve bladder function after SCI. Future work must ask whether these results can be replicated in animals with clinically relevant spinal injuries. Given the general clinical acceptability of SCS, short term clinical trials should be performed to evaluate these ideas in people with SCI.

Supplemental Data:

References: 1. Jantz MK, Gopinath C, Kumar R, Chin C, Wong L, Ogren JI, Fisher LE, McLaughlin BL, Gaunt RA. High-density spinal cord stimulation selectively activates lower urinary tract nerves. J Neural Eng. 2022 Nov 22;19(6). PMID: 36343359 2. Jantz MK, Liang L, Damiani A, Fisher LE, Newton T, Neufeld E, Hitchens TK, Pirondini E, Capogrosso M, Gaunt RA. A Computational Study of Lower Urinary Tract Nerve Recruitment with Epidural Stimulation of the Lumbosacral Spinal Cord. 2022 44th Annu Int Conf Ieee Eng Medicine Biology Soc Embc. 2022;00:744–747. PMID: 36086335 3. Fang X, Collins S, Nanivadekar AC, Jantz M, Gaunt RA, Capogrosso M. An Open-source Computational Model of Neurostimulation of the Spinal Pudendo-Vesical Reflex for the Recovery of Bladder Control After Spinal Cord Injury. 2022 44th Annu Int Conf Ieee Eng Medicine Biology Soc Embc. 2022;00:1607–1610. PMID: 36086204

Acknowledgements: This research was supported by the Office Of The Director at the NIH under awards OT2OD030537 and OT2OD024908.

Learning Objectives: 1. Understand sacral spinal anatomy relevant for lower urinary tract control. 2. Understand how spinal cord stimulation activates sensory afferents and can modulate lower urinary tract function. 3. Appreciate the contributions of computational modeling to understanding physiological function.

Financial Disclosures: Robert Gaunt, Blackrock Neurotech, Consultant, $20,001-$100,000 Robert Gaunt, Neurowired, Scientific Advisory Board, $501-$5,000 Marco Capogrosso, Reach Neuro, Stockholder Stock Value >5, $501-$5,000 Bryan McLaughlin, Micro-Leads Medical, Stockholder Stock Value >5, >$100,000

Disclosure: No significant relationships.

IS080

Breakout Session
NEUROMODULATION FOR GENITOURINARY DISORDERS
16-05-2024 08:00 - 10:00

MECHANISM OF ACTIONS FOR SACRAL, TIBIAL AND PUDENDAL NERVE STIMULATION – LOOKING FOR SIMILARITIES AND DIFFERENCES

Magdy Hassouna, MD, PhD
UHN, Surgery, Toronto, Canada

Introduction and Discussion: Sacral neuromodulation (SNM), posterior tibial nerve stimulation (PTNS), and pudendal neuromodulation (PNM) have emerged as effective modalities for managing individuals with several disorders of the lower urinary tract and pelvic floor dysfunctions. Despite their shared goal of neuromodulation, each technique operates through distinct anatomical pathways and mechanisms. Understanding the shared mechanisms and unique characteristics of SNM, PTNS, and PNM is crucial for optimizing patient selection and treatment outcomes. Moreover, exploring potential synergies between these modalities may pave the way for novel therapeutic approaches in pelvic floor dysfunction and neurological disorders. In this review, we aim to elucidate the similarities and differences in the mechanisms of action underlying these three nerve stimulation modalities.

Supplemental Data:

References:

Acknowledgements: No disclosures Acknowledge the input of Dr Waha Alqahtani MD

Learning Objectives: 1. The role of pelvic neuromulation through SNM, PTNS and PNS 2. The mechanism of action implicated in all 3 modalities 3. Similarity in the 3 modalities of treatment

Financial Disclosures: No financial disclosures

Disclosure: No significant relationships.

IS081

Breakout Session
NEUROMODULATION FOR GENITOURINARY DISORDERS
16-05-2024 08:00 - 10:00

CLOSED LOOP NEUROMODULATION IN GU DYSFUNCTION

Tim Denison, PhD
Oxford University, Institute Of Biomedical Engineering, Department Of Engineering Science, Oxford, United Kingdom

Introduction and Discussion: As the medical field increasingly adopts automated technologies, it becomes imperative to explore how engineers and clinicians can collaborate to deploy intelligent systems through system design and risk management. This presentation offers an overview of the considerations surrounding the design of physiological control loops controllers for semi-to-fully automated operation in Gastro- and Urological applications. Beginning with an examination of physiologic control in neuromodulation, this presentation provides a framework for the design of closed-loop controllers while emphasizing safety considerations. Specific risk areas and potential mitigation strategies are then discussed, drawing from historical examples in medical device development to illustrate key concepts. I will focus on closed-loop systems for gastrointestinal (GI) and incontinence management. Case studies will be drawn from spinal cord injury, stress incontinence, and gastroparesis. These systems could offer personalized therapy by dynamically adjusting to physiological changes and providing real-time, patient-specific stimulation while minimizing side effects. For robust design, this presentation also presents a comprehensive design checklist framed by recent regulatory guidance in the area of closed-loop control. By systematically addressing risk factors and incorporating adaptive capabilities into the design process, engineers and clinicians can enhance the safety and efficacy of closed-loop bioelectronic systems for a wide range of medical applications, including GI and incontinence management. By leveraging lessons learned from both successes and challenges in other domains, engineers and clinicians can collaborate to develop innovative solutions that prioritize patient safety while harnessing the transformative potential of smart technologies in healthcare.

Supplemental Data:

References: Majerus S, et al. Wireless Bladder Pressure Monitor for Closed-Loop Bladder Neuromodulation. Proc IEEE Sens. 2016 Peterken F, et al. Adapting the Finetech-Brindley Sacral Anterior Root Stimulator for Bioelectronic Medicine. Annu Int Conf IEEE Eng Med Biol Soc. 2021 Nissenkorn I, et al. Patient-adjusted intermittent electrostimulation for treating stress and urge urinary incontinence. BJU Int. 2004 doi: 10.1111/j.1464-410x.2004.04856.x. Luman Wang et al, A novel approach for model-based design of gastric pacemakers, Computers in Biology and Medicine, 2020.

Acknowledgements: Denison is sponsored by a Royal Academy of Engineering Chair in Emerging Technology.

Learning Objectives: 1) Provide a framework and common language for physiologic closed-loop controllers (PCLCs) as they apply to GU applications 2) Use examples from sensing-based domains to provide intuition for PCLC operation, and the problems they help solve, as template for any system using adaptive technology 3) Reinforce key terms and concepts for safe sensing-based systems from FDA guidance documents and PCLC standards (e.g. risk, 60601-1-10) for robust design and safe use – design template

Financial Disclosures: Denison is a co-founder and director at Amber Therapeutics, which is developing bioelectronic therapies for incontinence.

Disclosure: No significant relationships.

IS082

Breakout Session
NEUROMODULATION FOR GENITOURINARY DISORDERS
16-05-2024 08:00 - 10:00

TRANSCUTANEOUS ELECTRICAL STIMULATION OR NEUROGENIC BLADDER FOLLOWING SCI

Evgeniy Kreydin, MD
UNIVERSITY OF SOUTHERN CALIFORNIA, Urology, Los Angeles, United States of America

Introduction and Discussion: In addition to affecting somatic sensorimotor function, spinal cord injury has a significant impact on the function of the lower urinary tract. Most patients with SCI develop urinary incontinence because of bladder overactivity. However, because of discoordination with the urethral sphincter, these overactive contractions are not sufficient to empty the bladder completely. As a result, patients with SCI are faced with both socially embarrassing urinary incontinence and urinary retention that results in recurrent urinary tract infections, poses risk to renal function and usually relegates SCI individuals to a lifetime of relying on catheters to empty the bladder. Current treatments for bladder dysfunction after SCI focus on managing these complications without addressing the underlying neurological dysfunction. And while we can successfully make patients dry, eliminate the risk to the kidneys and decrease the rate of urinary tract infections, there are no treatments that can restore normal bladder sensation and enable volitional voiding. On the other hand, neuromodulation is a therapy whose goal is to alter the behavior of neural networks and it has been used extensively to treat lower urinary tract disorders in patients with idiopathic conditions like overactive bladder. Spinal cord stimulation specifically has been studied as a neuromodulation technique to improve function in patients with SCI. Implantable spinal cord stimulators have shown great promise for restoring function even after severe injuries [1]. However, implantable stimulators come with significant risks and morbidity. As a result, transcutaneous spinal cord stimulation may offer a noninvasive option to achieve goals that are still missing in bladder care of SCI individuals. In our preliminary studies, we have demonstrated that transcutaneous spinal cord stimulation can promote both urinary voiding and storage in patients with SCI [2]. This technique appears to improve coordination between the bladder and urethral sphincter and mitigate sensation of bladder fullness, giving patients more time to avoid an incontinence episode. The mechanism of these changes remains to be demonstrated. However, we hypothesize that spinal neuromodulation takes advantage of remnant uninjured fibers to effect changes across the entire neuraxis, including the brain. We have previously demonstrated that transcutaneous spinal cord stimulation changes bladder-associated brain activity in incontinent stroke survivors [3]. Future work will focus on assessing whether the same phenomenon occurs in patients with SCI.

Supplemental Data:

References: 1. Rowald, A., et al., Activity-dependent spinal cord neuromodulation rapidly restores trunk and leg motor functions after complete paralysis. Nat Med, 2022. 28(2): p. 260-271. 2. Gad, P.N., et al., Non-invasive Neuromodulation of Spinal Cord Restores Lower Urinary Tract Function After Paralysis. Front Neurosci, 2018. 12: p. 432. 3. Kreydin, E.I., et al., A Pilot Study of the Effect of Transcutaneous Spinal Cord Stimulation on Micturition-Related Brain Activity and Lower Urinary Tract Symptoms After Stroke. J Urol, 2024. 211(2): p. 294-304.

Acknowledgements: 1. American Urological Association/Urology Care Foundation

Learning Objectives: 1) Understand the normal function of the lower urinary tract 2) Understand the effect of spinal cord injury on the function of the lower urinary tract 3) Understand current evidence supporting the use of transcutaneous spinal cord stimulation to improve lower urinary tract function and future directions in its development

Financial Disclosures: a) SpineX Inc. b) Stock Value >5% c) Level of Compensation - none

Disclosure: No significant relationships.

IS083

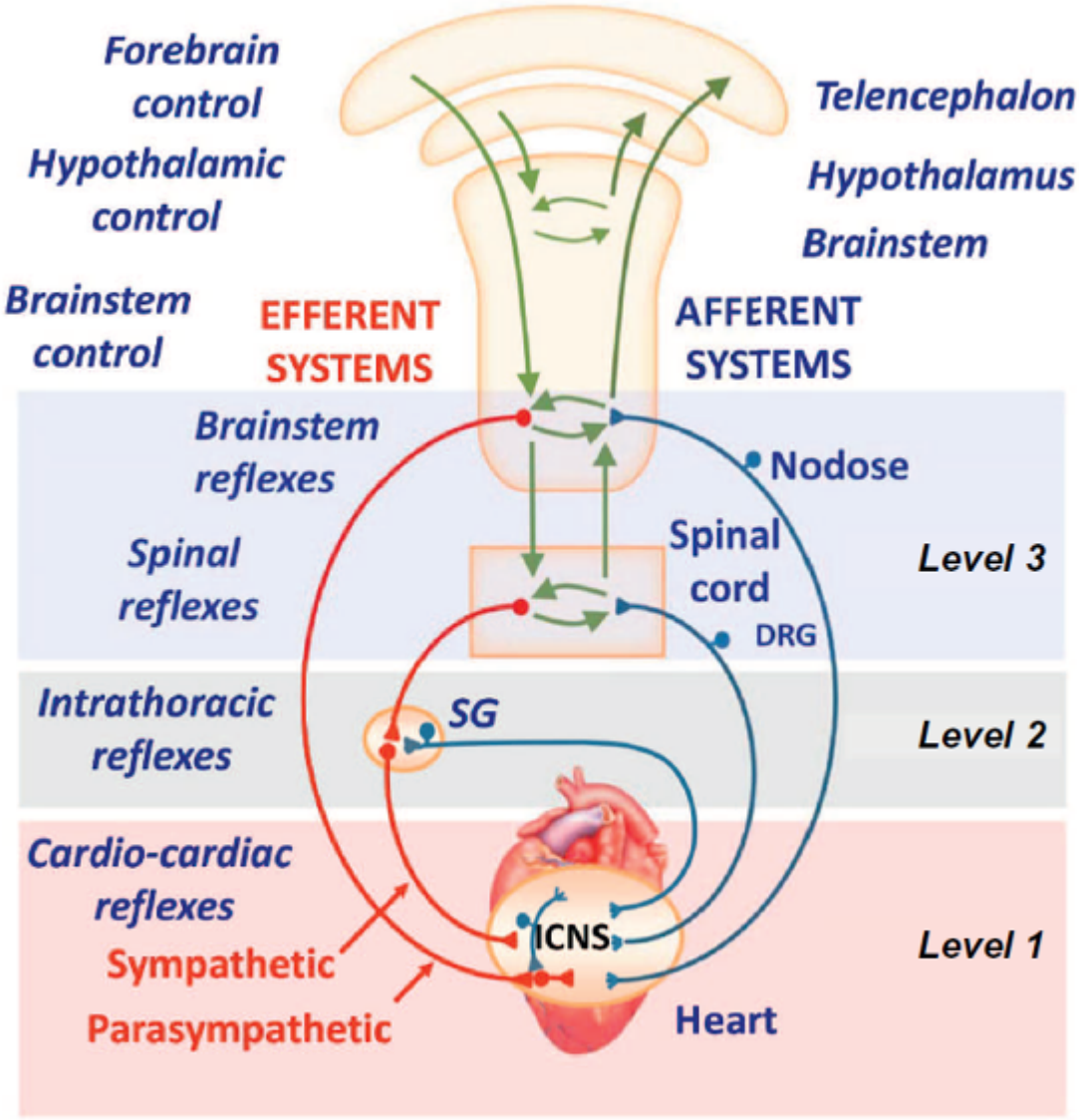
Breakout Session
NEUROMODULATION FOR NEUROCARDIOLOGY
16-05-2024 08:00 - 10:00

MYOCARDIAL ISCHEMIC CHALLENGES AND NEURAL CONTROL STRATEGIES

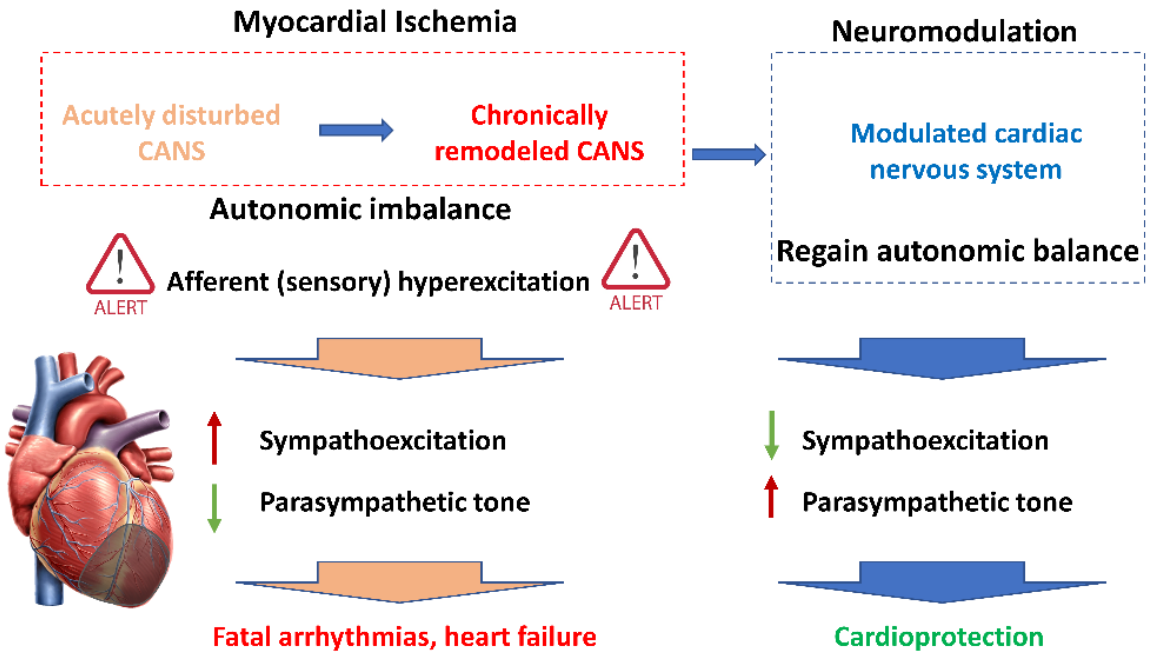
Siamak Salavatian, MEng. PhD
University of Pittsburgh, Anesthesiology, Pittsburgh, United States of America

Introduction and Discussion: Myocardial ischemia occurs when the blood flow to the heart muscle is reduced due to partial or complete blockage of the coronary arteries. Myocardial ischemia can lead to serious complications including myocardial infarction (heart attack), heart failure, and fatal ventricular tachyarrhythmias (VTs).[1,2] VTs are the leading cause of sudden cardiac death, yet there are no effective preventive therapies.[3-6] Patients with ischemic heart disease are particularly at risk for VTs due to cardiac sympathoexcitation and autonomic imbalances.[7,8]
The cardiac injury caused by myocardial ischemia activates the cardiac sensory (afferent) neurons in both the dorsal root and nodose sensory ganglia.[9,10] This afferent information is processed at different levels of the cardiac autonomic nervous system (CANS), and results in the sympathetic tone augmentation and suppression of the parasympathetic tone.[11,12] This initial sympathoexcitatory response is to help the injured heart to pump enough blood to the body by increasing the cardiac output. However, when this sympathoexcitatory and parasympathetic inhibitory response becomes persistent, it causes adverse remodeling in the CANS which can lead to a failing heart and fatal complications.[13,14]
Cardiac neuromodulation therapies aim to restore the CANS balance by either 1) blocking or modulating the initial afferent neurotransmission, 2) decreasing the sympathetic tone, or 3) increasing the parasympathetic tone.[15] In this talk, we will briefly discuss some of these neuromodulation therapies including device-based, surgical, and pharmacological neuromodulation techniques. In the device-based category, we will discuss spinal cord stimulation (SCS) and dorsal root ganglion stimulation (DRGS) which suppress sympathoexcitation, and vagus nerve stimulation (VNS) which provides cardioprotective effect by increasing the parasympathetic tone. Baroreceptor activation therapy (BAT) is another form of device-based neuromodulation that provides beneficial effects by restoring the autonomic balance. In pharmacological-based neuromodulation therapies, we will discuss thoracic epidural anesthesia (TEA) and stellate ganglion block (SGB) which suppress the activity of preganglionic and postganglionic sympathetic neurons to reduce sympathoexcitation. In the surgical category, we will discuss cardiac sympathetic denervation, renal denervation, and cardiac ganglionated plexus
ablation.

Autonomic control of the heart



Hanna, Peter, et al. "Cardiac neuroanatomy-Imaging nerves to define functional control." *Autonomic Neuroscience* 207 (2017): 48-58.



Supplemental Data:

References: 1 Reimer, K. A. & Ideker, R. E. Myocardial ischemia and infarction: anatomic and biochemical substrates for ischemic cell death and ventricular arrhythmias. *Hum Pathol* **18**, 462-475, doi:10.1016/s0046-8177(87)80031-x (1987). 2 Russell, D. C., Lawrie, J. S., Riemersma, R. A. & Oliver, M. F. Mechanisms of phase 1a and 1b early ventricular arrhythmias during acute myocardial ischemia in the dog. *Am J Cardiol* **53**, 307-312, doi:10.1016/0002-9149(84)90444-2 (1984). 3 Zucker, I. H., Kp, P. & Schultz, H. D. Neurohumoral stimulation. *Heart Fail Clin* **8**, 87-99 (2012). 4 Chugh, S. S. *et al.* Epidemiology of sudden cardiac death: clinical and research implications. *Progress in Cardiovascular Diseases* **51**, 213-228, doi:10.1016/j.pcad.2008.06.003 (2008). 5 Fukuda, K., Kanazawa, H., Aizawa, Y., Ardell, J. L. & Shivkumar, K. Cardiac innervation and sudden cardiac death. *Circ Res* **116**, 2005-2019, doi:10.1161/CIRCRESAHA.116.304679 (2015). 6 Khan, I. M. *et al.* Elimination of rat spinal substance P receptor bearing neurons dissociates cardiovascular and nocifensive responses to nicotinic agonists. *Neuropharmacology* **54**, 269-279, doi:10.1016/j.neuropharm.2007.09.014 (2008). 7 Borovac, J. A., D'Amario, D., Bozic, J. & Glavas, D. Sympathetic nervous system activation and heart failure: Current state of evidence and the pathophysiology in the light of novel biomarkers. *World J Cardiol* **12**, 373-408, doi:10.4330/wjc.v12.i8.373 (2020). 8 Alenazy, B. *et al.* In-hospital ventricular arrhythmia in heart failure patients: 7 year follow-up of the multi-centric HEARTS registry. *ESC Heart Fail* **6**, 1283-1290, doi:10.1002/ehf2.12525 (2019). 9 Salavatian, S. *et al.* Thoracic spinal cord neuromodulation obtunds dorsal root ganglion afferent neuronal transduction of the ischemic ventricle. *Am J Physiol Heart Circ Physiol* **317**, H1134-H1141, doi:10.1152/ajpheart.00257.2019 (2019). 10 Salavatian, S. *et al.* Thoracic spinal cord and cervical vagosympathetic neuromodulation obtund nodose sensory transduction of myocardial ischemia. *Auton Neurosci* **208**, 57-65, doi:10.1016/j.autneu.2017.08.005 (2017). 11 Salavatian, S. *et al.* Spinal neuromodulation mitigates myocardial ischemia-induced sympathoexcitation by suppressing the intermediolateral nucleus hyperactivity and spinal neural synchrony. *Front Neurosci* **17**, 1180294, doi:10.3389/fnins.2023.1180294 (2023). 12 Vaseghi, M. *et al.* Parasympathetic dysfunction and antiarrhythmic effect of vagal nerve stimulation following myocardial infarction. *JCI Insight* **2**, doi:10.1172/jci.insight.86715 (2017). 13 Elia, A. & Fossati, S. Autonomic nervous system and cardiac neuro-signaling pathway modulation in cardiovascular disorders and Alzheimer's disease. *Front Physiol* **14**, 1060666, doi:10.3389/fphys.2023.1060666 (2023). 14 Hadaya, J. & Ardell, J. L. Autonomic Modulation for Cardiovascular Disease. *Front Physiol* **11**, 617459, doi:10.3389/fphys.2020.617459 (2020). 15 Salavatian, S. & Ardell, J. L. in *Neuromodulation* 1519-1530 (Elsevier, 2018).

Acknowledgements: The support of the University of Pittsburgh for this project is greatfully acknowledged.

Learning Objectives: 1-Understanding the neural control of the heart: Participants will learn about different levels of the cardiac autonomic nervous system that control the heart function. 2-Pathophysiology of Myocardial Ischemia and Autonomic Imbalances: Participants will gain comprehensive knowledge of the mechanisms underlying myocardial ischemia and its association with cardiac sympathoexcitation and autonomic imbalances, leading to adverse cardiovascular remodeling and fatal complications. 3-Exploring Neuromodulation Therapies for Restoring Autonomic Balance: Attendees will learn about various neuromodulation techniques, including device-based interventions such as spinal cord stimulation (SCS), dorsal root ganglion stimulation (DRGS), vagus nerve stimulation (VNS), and baroreceptor activation therapy (BAT), as well as pharmacological and surgical approaches. The objective is to understand how these therapies aim to restore autonomic balance by modulating sympathetic and parasympathetic tone, offering potential cardioprotective effects and preventing fatal ventricular tachyarrhythmias.

Financial Disclosures: Owner of the NeuroCardio LLC that provides consulting services in the cardiac autonomic nervous system and cardiac neuromodulation fields.

Disclosure: No significant relationships.

IS084

Breakout Session
NEUROMODULATION FOR NEUROCARDIOLOGY
16-05-2024 08:00 - 10:00

OVERVIEW NEUROMODULATION IN PATIENTS WITH REFRACTORY ANGINA PECTORIS

Fabienne Vervaat, MD
Catharina Hospital, Cardiology, Eindhoven, Netherlands

Introduction and Discussion: There is a growing number of patients with coronary artery disease (CAD) with persisting angina pectoris despite optimal medical therapy, known as refractory angina pectoris (RAP). The term RAP was first formulated in 2002 and was defined as a chronic disease (more than three months) characterized by diffuse CAD in the presence of proven ischemia with no interventional treatment options (percutaneous coronary intervention and/or coronary artery bypass grafting) and optimal medical therapy. Current estimates indicate that 5 to 10% of patients with stable CAD have RAP. There are currently few treatment modalities for patients with RAP. One such treatment modality is spinal cord stimulation (SCS) with a Class of recommendation IIB, level of evidence B, in the 2019 European Society of Cardiology guidelines for the diagnosis and management of chronic coronary syndromes. This presentation will give an overview of neuromodulation as a treatment modality for patients with RAP. A comprehensive overview will be given on the history, proposed mechanism of action, safety, efficacy and current use of SCS.

Supplemental Data: N/A

References: Vervaat FE, van der Gaag A, Teeuwen K, van Suijlekom H & Wijnbergen I. Neuromodulation in patients with refractory angina pectoris: a review. Eur Heart J Open 2023;3(1):oeac083

Acknowledgements: N/A

Learning Objectives: - Give an overview of the proposed mechanism of action of spinal cord stimulation in patients with RAP - Show a method of screening to ensure uniformity in patient selection for SCS - Look at current use of SCS in patients with RAP and the future perspectives

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS086

Breakout Session
NEUROMODULATION FOR NEUROCARDIOLOGY
16-05-2024 08:00 - 10:00

DORSAL ROOT GANGLION (DRG) STIMULATION FOR MANAGEMENT OF CARDIOVASCULAR DISEASE

Alexander Green, PhD FRCS(SN)
University of Oxford, Nuffield Department Of Surgical Sciences, Oxford, United Kingdom

Introduction and Discussion: DRG stimulation is used routinely to treat chronic neuropathic pain. In addition to C fibres, the DRG contains autonomic fibres that connect, via rami communicantes to the sympathetic chain. In a human study of 14 patients with DRG stimulation we have shown that DRG stimulation significantly reduces muscle sympathetic nerve activity (MSNA) as measured using microneurography. The reduction in MSNA does not correlate well with reduction in pain. Further studies looking at left T2 DRG stimulation in porcine models (our preliminary data and those of other groups) shows that in non-pain models, similar reductions in sympathetic efferent activity is seen, in terms of cardiac sympathetic efferent activity. We have found that low frequency (6-8Hz) DRG stimulation has the most profound effect on this activity, completely obliterating the sympathetic increases seen in a sleep apnoea model. Studies of spinal cord stimulation also show changes in autonomic activity but results are mixed and in spinal cord injury, many studies show increases in sympathetic activity with stimulation. Furthermore, the effects of DRG stimulation are an order of magnitude greater. Further studies are required to determine whether DRG stimulation can be used as a viable treatment for cardiovascular disorders. However, it is likely that left T2 stimulation can be used to treat cardiac rhythm disease and other levels (possibly T12-L3) may be used to control blood pressure. The mechanisms likely relate to organs affected e.g. cardiac at T2 and splanchnic or renal at the lower levels. These mechanisms require further investigations, as do the clinical effects of DRG stimulation

Supplemental Data:

References: None

Acknowledgements:

Learning Objectives: 1. To understand the role of the Dorsal Root Ganglion in the autonomic nervous system 2. To understand the effects of DRG stimulation on sympathetic activity 3. To appreciate the potential for DRG stimulation to treat cardiovascular disease

Financial Disclosures: Alexander L Green, Amber Therapeutics, Founder (3.5% stake) Alexander L. Green, Abbot inc., Paid Faculty Neuromodulation Fellowship Course (includes DRG stimulation), £2000 per day (up to £30,000 per year) Alexander L Green, InBrain, Consultant, 200 Euros per hour (10-20 per year)

Disclosure: No significant relationships.

IS087

Breakout Session
NEUROMODULATION FOR NEUROCARDIOLOGY
16-05-2024 08:00 - 10:00

A FUTURE PERSPECTIVE ON NEUROMODULATION FOR CARDIOVASCULAR DISEASES

Mike Jl Dejongste, MD, PhD[1,2]
[1]UMCG, Metc, Groningen, Netherlands, [2]University Medical Center Groningen, Metc, Groningen, Netherlands

Introduction and Discussion: A Future Perspective on Neuromodulation for Cardiovascular Diseases The growing number of survivors from cardiovascular diseases results in an increasing number of patients with chronic symptoms becoming more and more resistant to standard therapies. And so there is an unmet need for new therapies. In the wake of beneficial effects of Spinal Cord Stimulation, for among others angina, newer neuromodulation techniques are introduced, such as dorsal root ganglion stimulation, vagal nerve stimulation for a variety of indications, such as heart failure and arrhythmias. In addition, research developments have provided better mechanistic insights into the brain-heart interface. The latest developments in neuromodulation are discussed, such as chemical vagal stimulation (*Ripplinger CM, Cardiovasc Res. 2017;113:1270-2),* optical neural stimulation *(Emilini V, Nature reviews methods primers, 2022;2:55),*and the neuro-immune cardiac interface *(Clyburn C, Nature, 2022;605:32-34.* Beneficial effects on ventricular remodeling were observed, following *chemical stimulation* of efferent vagal neurons, using excitatory Designer Receptors Exclusively Activated by Designer Drugs (DREADDs). DREADDs are chemogenetically reprogrammed G protein-coupled receptors, able to respond to specific neutral molecules (i.e. ligands) only. Following activation by means of DREADD, neuron excitability is altered. However, irrespective of the ligand chosen, no drug is capable to bind to one receptor. To affect the activity of photosensitive neuronal receptors optical neural stimulation can be executed through *optogenetic neuromodulation*. The latter technique requires genetic modification of neurons, followed by the application of light to induce expression of (light-sensitive made) structures, such as channels and proteins, and so allow control over the activity of cell(membrane)s and pathways. In the future progression of atherosclerosis is thought to be beneficially tempered through neuromodulation of the so-called *neuro-immune cardiac interface* (NICI). The NICI involves the nervous, the immune, and the cardiovascular system. Within the NICI complex interactions take place, inducing among others innervation of the adventitia by the axons of the peripheral nervous system. Finally, the observation that NICIs are part of the artery-brain circuit (ABC), implies a circuit from adventitia nociceptive afferents to higher brain centers and sympathetic efferent neurons, projecting from hypothalamic neurons to the adventitia. Activation of ABC increases vagal nerve activity and disease progression. In contrast, ganglionectomy induces degeneration of NICIs in adventitia of arteries, reduces atherosclerotic progression and enhanced plaque stability.

Supplemental Data:

References: Ripplinger CM *et al.* From drugs to devices and back again: chemical vagal nerve stimulation for treatment of heart failure. *Cardiovasc Res. 2017;113:1270-2 and* Garrott K *et al.* Chronic activation of hypothalamic oxytocin neurons improves cardiac function during left ventricular hypertrophy-induced heart failure *Cardiovasc Res,* 2017;113:1318-28 Technical review: Jiang S *et al.* Shedding light on neurons: optical approaches for neuromodulation. Natl Sci Rev, 2022;9:nwac007. Doi 10.1093/nsr/nwac007 Clinical Review: Emilini V *et al.* Optogenetics for light control of biological systems. Nature reviews methods primers, 2022;2:55 Review: Mohanta SK *et al.* Adventitia Neuro-Immune Cardiac Interface (NICI). Frontiers in Cell Dev Biol, 2023 Clyburn C and Birren SJ. Crosstalk between *nerves, immune cells and plaques* drives atherosclerosis. Nature, 2022 May;605:32-34

Acknowledgements: No acknowledments

Learning Objectives: 1. Discuss neuromodulation technics for a variety of potential cardiovascular indications and so 2. offer insight into emerging neuromodulation strategies for cardiovascular diseases. 3. Provide a future perspective on neuromodulation for cardiovascular diseases.

Financial Disclosures: No financial disclosures

Disclosure: No significant relationships.

IS088

Plenary
CLOSING PLENARY
16-05-2024 11:30 - 13:40

SOCIOECONOMIC IMPACT OF SPINAL CORD STIMULATION: BEST PRACTICES FOR ASSESSMENT AND MEASURING WHAT MATTERS - ANYWHERE

Rod Taylor, PhD
University of Glasgow, Mrc/cso Social And Public Health Sciences Unit & Robertson Centre For Biostatistics, School Of Health And Well Being, College Of Medical, Veterinary And Life Sciences, Glasgow, United Kingdom

Introduction and Discussion: Neuropathic pain has a major burden in terms of loss of health-related quality and both high direct and indirect (loss employment) costs to patients, clinicians, healthcare regulators and payors. Multiple randomised controlled trials have shown spinal cord stimulation (SCS) to be a safe and effective treatment for chronic conditions including failed back surgery syndrome (FBSS), complex regional pain syndrome, and painful diabetic polyneuropathy. Trial- and model-based economic evaluations have also shown SCS to be a highly cost-effective therapy. This plenary presentation will focus on the importance of the cotemporary assessment of SCS value that considers both the quantification of a holistic patient-related outcome approach and the wider societal economic perspective.

Supplemental Data: None

References: Zhou M, Zhong H, Xing C, Li H, Liu S, Wang L, Ma H, Ning G. Comparison of clinical outcomes associated with spinal cord stimulation (SCS) or conventional medical management (CMM) for chronic pain: a systematic review and meta-analysis. Eur Spine J. 2023;32:2029-2041. Niyomsri S, Duarte RV, Eldabe S, Fiore G, Kopell BH, McNicol E, Taylor RS. A systematic review of economic evaluations reporting the cost-effectiveness of spinal cord stimulation. Value Health. 2020;23:656-665. Levy RM, Mekhail N, Abd-Elsayed A, Abejón D, Anitescu M, Deer TR, Eldabe S, Goudman L, Kallewaard JW, Moens M, Petersen EA, Pilitsis JG, Pope JE, Poree L, Raslan AM, Russo M, Sayed D, Staats PS, Taylor RS, Thomson S, Verrills P, Duarte RV. Holistic treatment response: An international expert panel definition and criteria for a new paradigm in the assessment of clinical outcomes of spinal cord stimulation. Neuromodulation. 2023;26:1015-1022.

Acknowledgements: None

Learning Objectives: 1. To be familiar with the current clinical and cost-effectiveness evidence supporting SCS. 2. To understand the importance of a wider holistic approach to the assessment of patient-related outcomes receiving SCS. 3. To appraise the current evidence-base for the wider socioeconomic benefits of SCS.

Financial Disclosures: Prof Rod Taylor has received personal funding support from Medtronic, Nevro and Saluda.

Disclosure: No significant relationships.

IS089

Plenary
CLOSING PLENARY
16-05-2024 11:30 - 13:40

ADVANCES IN OUR CLINICAL UNDERSTANDING OF AUTONOMIC REGULATION THERAPY USING VAGAL NERVE STIMULATION IN PATIENTS WITH HEART FAILURE

Jeffrey Ardell, PhD
University of California, Los Angeles, Ucla Cardiac Arrhythmia Center And Ucla Neurocardiology Research Program Of Excellence, Los Angeles, United States of America

Introduction and Discussion: Dysfunction of the autonomic nervous system has been implicated in the pathogenesis of cardiovascular disease, including congestive heart failure and cardiac arrhythmias. Despite advances in the medical and surgical management of these entities, progression of disease persists. Heart failure with reduced ejection fraction (HFrEF) is associated with reflex increases in sympathetic activity with a corresponding decrease in parasympathetic tone. With greater knowledge of the dynamic relationships between the nervous system and heart, neuromodulatory techniques, such as cardiac vagal nerve stimulation (VNS), have emerged as possible therapeutic approaches for the management of HFrEF. Three clinical trials have recently explored the therapeutic potential for reactive VNS to mitigate progression of congestive heart failure; INOVATE-HF, NECTAR-HF and ANTHEM-HFrEF. Each utilized substantially different bioelectric approaches with respect to stimulation protocols (e.g. duty cycle, pulse width, frequency, intensity) and not all realized their pre-specified stimulation levels during the treatment phases. Ultimately, the efficacy of targeted autonomic regulation therapy depends on patient status, location and temporal aspects of the stimulation protocol and consideration of the effects of bioelectric interventions on integrated reflex control of the diseased heart. This presentation will discuss our understanding of the VNS for HFrEF as derived from the recent clinical and preclinical studies and against the background of future rational neurocardiology-based optimization for neuromodulatory treatment of cardiac disease.

Supplemental Data:

References:

Acknowledgements:

Learning Objectives: 1. To understand the basic principles of autonomic - heart interactions during progression of heart failure 2. To define the rationale for targeted neuromodulation as a therapeurtic option for heart failure 3. To discuss the state of the field of autonomic regulation therapy for cardiac disease in light of recent preclinical and clinical studies.

Financial Disclosures: Consultant for Liva Nova co-Founder and shareholder - NeuCures

Disclosure: No significant relationships.

IS090

Plenary
CLOSING PLENARY
16-05-2024 11:30 - 13:40

DECIPHERING VAGAL ANATOMY AND BRAIN-BODY SIGNALING TO OPTIMIZE NEUROMODULATION THERAPIES

Theodoros Zanos, PhD
Feinstein Institutes for Medical Research, Division Of Health Ai, Manhasset, United States of America

Introduction and Discussion: Our bodies have built-in neural reflexes that continuously monitor organ function and maintain physiological homeostasis, with many of the control signals responsible for the afferent and efferent arcs of these reflexes transmitted through the vagus nerve (VN), the tenth cranial nerve. Whereas the field of neuromodulation has mainly focused on the stimulation of neural circuits to treat various conditions, recent studies have started to investigate the possibility of leveraging the sensory arm of these reflexes to diagnose disease states. To accomplish this, a deeper understanding of the anatomical organization of the nerve and its projections is required, coupled with decoding efforts of the neural signals emanating from the body's built-in biosensors and propagating through the vagus, and physiological recordings of autonomic responses, to identify the presence or levels of relevant biomarkers of disease. In this talk, we will discuss our efforts on leveraging artificial intelligence on multi-modal and multi-scale data sources (micro-CT, immunohistochemistry/microscopy images, neural and physiological recordings) to enable a deeper understanding of both the anatomical and the physiological substrate or these neural reflexes. Understanding vagal anatomy, decoding nerve activity and physiological responses related to disease states will not only enable the development of real-time diagnostic devices, but also help advancing truly closed-loop neuromodulation technologies.

Supplemental Data:

References:

Acknowledgements: Part of the results presented is funded by a NIH SPARC grant (Reconstructing Vagal Anatomy). The support of the Feinstein Institutes for Medical Research at Northwell Health for this project is gratefully acknowledged.

Learning Objectives: 1. Participants will gain a comprehensive understanding of the effort required / carried out to examine the anatomical organization of the vagus nerve and its projections. At the end of the talk, participants should be able to describe the anatomical features of the vagus nerve and some of its projections and demonstrate a comprehension of the challenges and ways to reconstruct vagal anatomy. 2. Participants will learn about the different methods used to decode neural signals emanating from the body's built-in biosensors and propagating through the vagus nerve, emphasizing the importance of these signals in diagnosing disease states. By the conclusion of the talk, participants should be able to explain the decoding efforts involved in understanding neural signals transmitted through the vagus nerve, showcasing an appreciation for the role of biosensor-derived signals in the diagnosis of disease states. 3. Participants will understand the significance of physiological recordings of autonomic responses in identifying relevant biomarkers of disease and appreciate the potential of leveraging artificial intelligence on multi-modal and multi-scale data for advancing diagnostic technologies. Upon completion of the talk, participants should be able to articulate the importance of physiological recordings in identifying disease biomarkers and recognize the potential of artificial intelligence in integrating diverse data sources (micro-CT, immunohistochemistry/microscopy images, neural and physiological recordings) for the development of real-time diagnostic devices and closed-loop neuromodulation technologies.

Financial Disclosures: No significant relationships

Disclosure: No significant relationships.

IS091

Plenary
CLOSING PLENARY
16-05-2024 11:30 - 13:40

INS RESEARCH AWARD WINNER LECTURE

Dominic Siler, MD, PhD[1], Ahmed Raslan, MD[2], Eric Mittra, MD, PhD[2], Chris Madden, PhD[2], Kim Burchiel, MD[3]
[1]Oregon Health & Science University, Neurological Surgery, Portland, United States of America, [2]Oregon Health & Science University, Portland, United States of America, [3]Oregon Health and Science University, Neurological Surgery, Portland, United States of America

Introduction and Discussion: Obesity is a worldwide epidemic that contributes to significant morbidity and mortality. Metabolic alterations associated with obesity include diabetes, hyperlipidemia, and hypercholesterolemia. Brown adipose tissue has been recently discovered as a potential therapeutic target to combat obesity. Preclinical studies have demonstrated that increasing BAT activation restores insulin sensitivity and promotes weight loss in obesity. However, all efforts to activate BAT in clinical trials have fallen short due to off-target effects. We have successfully induced BAT activation through spinal cord stimulation (SCS) in a preclinical model with minimal off-target effects. In this first-in-human pilot study, patients undergoing routine trial placement of a percutaneous SCS electrode for chronic pain will undergo placement of an additional electrode in the high thoracic region; the area associated with BAT activation in our pre-clinical work. After successful implantation, subjects are randomized to either an SCS ON group, or SCS OFF group, and undergo PET/CT with 18F-FDG for quantification of BAT activation. Subjects will then undergo a 48hr washout and cross over to the opposite group for a second PET/CT study. The PET results of SCS ON and OFF will be the basis for a determination of whether SCS can activate BAT in humans. Here we present the science behind BAT activation with SCS and cover preliminary findings from our study.

Supplemental Data:

References: none

Acknowledgements: The support of the International Neuromodulation Society Innovative Research Grant for this project is gratefully acknowledged.

Learning Objectives: 1. To understand the current trends and secondary complications associated with the worldwide obesity epidemic 2. To gain an understanding of the mechanisms of brown adipose tissues activation in adult humans 3. Understand current theories in spinal cord stimulation activation of autonomic homeostatic pathways

Financial Disclosures: No significant disclosures

Disclosure: No significant relationships.

Author Index

Author Index	
Aarsman, Ralph	O086
Abad, Cristina	284, 314, 334
Abboud, Jacques	229
Abd-Elsayed, Al	O132
Abejón, David	284, 314, 334, 354
Abellaneda, Killian Amadeus	O139
Absoch, Aviva	207
A Davis, Rachel	IS045
Adeel, Muhammad	327
Ader, Leonie	263
Adler, Alexandra	342
Afonso, Thiago	274, 355
Ahmadi, Rezvan	262, 263, O012
Ahmed, Mariam	345
Ahmed, Sharmin	O148
Ahsan, Aamna	232, 248
Aidarov, Seitzhan	210
Ajakwe, Reginald	O113
Ajijola, Olujimi A.	IS069, O002
Al-Abed, Yousef	O015
Albanese, Alberto	O021
Aldred, Jason	216, 217
Al-Kaisy, Adnan	264, 359, 360
Allam, Anthony	O028
Allegri, Massimo	322
Allen, Andrew	IS068
Alm, John	O058
Almac, Emre	O090
Almonte, Wilson	311, O132, O133
Alsaqabi, Eman	O070

Hofsté, Willem-Jan	291, O086, O090
Hogeveen, Lara	IS061
Holder, David	O002
Hollunder, Barbara	IS020
Holt-Becker, Abbey	207, 208, O023
Hood, Sally	IS068
Hosokawa, Patrick	IS045
Hosseini, Golkoo	186
Hu, Michele	203, O026
Huertas, Ismael	243, 244, 293, O053
Huh, Ryoong	O021
Humphrey, Jessica	O074
Hung, Galen Chin Lun	O034
Hungerford, Lars	IS058
Hunter, Corey W.	266, 267, O088
Hussain, Namath	O060
Hutchison, William	189
Huttunen, Jukka	356, O045
Huygen, Frank	250, 333, IS008, O090, O094, O095, O120
Iacoviello, Francesco	O002
Ibrahim, George M.	IS039
Ibrahim, Mohab	199
Ikäheimo, Tiina-Mari	356, O045
Illes, Judy	IS033
Im, Chang-Hwan	227, O076, O142
Ince, Nuri F.	190
Infante, Nazaret	O139
Ismail, Mostafa	O126
Ispierto González, Lourdes	215
Iyassu, Yohannes	O077
Izquierdo, Rosa	243, 244
Jaasma, Michael	294, O050, O056

Zhang, Yuhuan	O019
Zhao, Cong Z.	217
Zhao, Kun	O080
Zhou, Samuel	O081
Zhu, Meixuan	O136
Zub, David	267
Zuidema, Xander	O137