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Invited Faculty Abstracts from the International Neuromodulation Society's 14th World Congress

*Pages 1-93: Invited Faculty Abstracts from the International Neuromodulation Society's 14th World Congress

(*not peer reviewed content)

Saturday, May 25, 2019
Pre-Conference
Pre-Conference Noninvasive Brain Stimulation (NIBS)

1. INS19-0467

NONINVASIVE DEEP BRAIN STIMULATION VIA TEMPORALLY INTERFERING ELECTRIC FIELDS

N. Grossman PhD[1]

[1]*Imperial College London & UK Dementia Research Institute, Medicine, London, United Kingdom*

Electrical brain stimulation is a key technique in research and clinical neuroscience studies, and also is in increasingly widespread use from a therapeutic standpoint. However, to date all methods of electrical stimulation of the brain either require surgery to implant an electrode at a defined site, or involve the application of non-focal electric fields to large fractions of the brain. We report a noninvasive strategy for electrically stimulating neurons at depth. By delivering to the brain multiple electric fields at frequencies too high to recruit neural firing, but which differ by a frequency within the dynamic range of neural firing, we can electrically stimulate neurons throughout a region where interference between the multiple fields results in a prominent electric field envelope modulated at the difference frequency. We validated this temporal interference (TI) concept via modeling and physics experiments, and verified that neurons in the living mouse brain could follow the electric field envelope. We demonstrate the utility of TI stimulation by stimulating neurons in the hippocampus of living mice without recruiting neurons of the overlying cortex. Finally, we show that by altering the currents delivered to a set of immobile electrodes, we can steerably evoke different motor patterns in living mice.

Saturday, May 25, 2019
Pre-Conference
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2. INS19-0443

INDIVIDUALIZED AND NOVEL APPROACHES IN BRAIN STIMULATION FOR POSTTRAUMATIC STRESS DISORDER

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Posttraumatic Stress Disorder (PTSD) is a prevalent, chronic psychiatric disorder associated with marked occupational and social dysfunction. PTSD is characterized by pervasive intrusive thoughts and recollections, avoidance of trauma-related stimuli, hyperarousal, and mood/cognitive impairment. PTSD also has substantial psychiatric and medical comorbidity. Unfortunately, although treatments exist for PTSD, a majority of patients remain symptomatic despite evidence-based interventions. Thus, new interventions are sorely needed for PTSD. To this end, the use of non-invasive neuromodulation is developing rapidly across neuropsychiatry. There is an established body of literature that supports its use in depression and other areas, although excitement for brain stimulation in PTSD has been tempered by questions about whether lessons learned in depression studies are applicable to PTSD. Although the two disorders overlap in symptomatology and neural network profiles, they also exhibit important differences that are likely relevant for target engagement. Thus, critical questions remain about how to develop and identify the optimal neuromodulatory approaches best suited to modify the underlying neurobiological underlying this disorder. Therefore, this session will describe a programmatic series of studies to reduce symptoms of PTSD using noninvasive brain stimulation. Using individualized, neural network-based and advanced technical approaches, we will demonstrate modified uses of standard transcranial magnetic and direct current stimulation approaches for PTSD, and highlight how these interventions can leverage neural circuits to identify those most likely to respond and also modify underlying network-based pathology. In summary, the data presented will demonstrate the near-term potential for brain stimulation in PTSD. This session will prompt further discussion about new methods to engage targets of interest, and how to leverage new technologies in clinically meaningful applications.

Saturday, May 25, 2019
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3. INS19-0514

CAN OSCILLATORY SYNCHRONY BE USED TO GUIDE RTMS TREATMENT?

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Repetitive Transcranial Magnetic Stimulation (rTMS) is an effective treatment for Major Depressive Disorder (MDD), but results are variable. Variability in pretreatment resting-state functional connectivity as well as treatment-emergent changes are related to these differences in treatment outcome. These findings suggest that changes in functional connectivity may be related to the mechanism of action (MOA) of rTMS and may serve as biomarkers of outcome. We examined changes in electroencephalographic (EEG) functional connectivity during the first rTMS treatment in 109 subjects treated with 10 Hz rTMS stimulation to left dorsolateral prefrontal cortex (DLPFC). All subjects subsequently received 30 treatments and clinical response was defined as >40% improvement in the Inventory of Depressive Symptomatology (IDS-30 SR) score at treatment 30. Connectivity change was assessed with coherence, envelope correlation, and a novel measure, the spectral correlation coefficient (SCC). Machine learning was used to develop predictive models of outcome for each connectivity measure, which were compared with prediction based upon early clinical improvement. Machine learning models based on SCC yielded the most accurate prediction (area under the curve, AUC = 0.83), and performance improved when combined with early clinical improvement measures (AUC = 0.91). In subsequent experiments, we examined changes in SCC following a series of brief "frequency interrogations" between 3-20 Hz. The degree of increase in SCC following a brief 10 Hz frequency interrogation was related to the degree of improvement following a full course of 10 Hz rTMS treatment. Subjects who failed to show increases in SCC with 10 Hz interrogation showed on average little improvement with 10 Hz treatment. These subjects did, however, show SCC increases associated with interrogation in other frequency bands. These findings suggest that it may be possible to perform a frequency interrogation procedure to detect SCC changes across the frequency spectrum to identify a stimulation frequency that maximizes immediate increases in functional connectivity. It may be possible to use such a procedure to identify an optimal rTMS treatment frequency for each patient that could enhance treatment outcomes.

Saturday, May 25, 2019
Pre-Conference
Pre-Conference Noninvasive Brain Stimulation (NIBS)

4. INS19-0462

PRECLINICAL STUDIES OF BRAIN STIMULATION: CAN WE LEARN FROM ANIMAL MODELS?

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Repetitive transcranial magnetic stimulation (rTMS), a non-invasive form of brain stimulation, is used in the clinic to promote healthy brain function. Although the mechanisms of rTMS remain unclear, many years of research and treatment in human volunteers and patients suggest it works by harnessing endogenous mechanisms of plasticity to alter connectivity and function. However, a significant challenge in the field is that outcomes are variable both within and between individuals, suggesting that treatment protocols remain suboptimal. This is underpinned by a lack of fundamental mechanistic understanding of rTMS, and very little systematic preclinical evaluation of protocols.

My lab has developed custom rTMS devices for stimulation of the rodent brain in order to better understand the cellular and molecular mechanisms of rTMS. We have demonstrated frequency-dependent changes in intracellular calcium levels in neurons and glial cells during stimulation. These calcium changes are associated with changes in gene expression and in neuronal excitability, which likely contribute to the large-scale circuit reorganisation and improvement in behavioural function we report in some, but not all, disease models. We have also found evidence for interactions between rTMS and endogenous brain activity that may contribute to the individual variability described in humans. Our recent work using resting state fMRI in rodents indicates analogous changes in rodents and humans following rTMS, suggesting that despite significant differences in brain size and morphology, preclinical studies have translational relevance and may play a useful role in the development of brain stimulation protocols tailored to the disorder and/or patient.

Saturday, May 25, 2019
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5. INS19-0474

TARGETING LEARNING NETWORKS WITH TRANSCRANIAL MAGNETIC STIMULATION

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[1]*National Institute of Neurological Disorders and Stroke, Clinical Neurosciences Program, Bethesda, USA*

The brain systems involved in learning and memory have been targets for interventional and experimental modulation with TMS for decades. The dominant paradigm has been to disrupt or facilitate processing in a cortical region to find evidence of its participation in a particular cognitive process or advance a cognitive enhancement concept. While we knew from functional imaging that these cortical targets were nodes in distributed processing networks, they were considered mainly in isolation. Moreover, in the absence of accepted method for measuring the biological effect of TMS on the target, we resorted to concepts borrowed uncritically from the corticospinal motor system, where these issues had been partially worked out. Recently, however, functional imaging has shown unambiguously that TMS alters connections from the stimulation site to downstream areas and produces lasting changes in these pathways and networks and the cognitive functions they serve. Moreover, it has allowed us to adopt the model of synaptic modulation to explain and predict the effects of TMS and provided mechanistic biomarkers for use in therapeutic development. This talk will give a brief historical overview and then describe how TMS has and can been used to target networks of cortical and deep structures to produce changes in learning and memory.

Saturday, May 25, 2019
Pre-Conference
Pre-Conference Noninvasive Brain Stimulation (NIBS)

6. INS19-0471

ADVANCING NONINVASIVE BRAIN STIMULATION FOR DEPRESSION WITH PERSONALISED TREATMENT APPROACHES

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[1]*Director- Therapeutic Brain Stimulation MAPrc Monash University Central Clinical School and The Alfred, Epworth Centre for Innovation in Mental Health, Melbourne, Australia*

Introduction: There is currently rapidly expanding interest in the use of novel brain stimulation treatments in psychiatry. Repetitive transcranial magnetic stimulation (rTMS) has been at the forefront of this and is now a well-established new treatment modality for patients with depressive disorders. It has been evaluated across a large range of controlled studies. However, limited research has explored the basic parameters used in the design of rTMS treatment protocols especially in regards to variables determining the dose of treatment. There has also been a dearth of studies exploring methods of personalisation of therapeutic parameters as a way of enhancing therapeutic outcomes.

Methods: We have conducted several studies designed to address these issues. First, we conducted a functional imaging study and a quantitative meta-analysis to explore the region within the dorsal prefrontal cortex most implicated in the aetiology of depression. In addition, we conducted a randomised controlled trial evaluating the relative efficacy of neuro-navigationally targeted rTMS. Finally, we will present data describing the use of near infrared spectroscopy to explore the optimisation of coil placement in prefrontal cortex.

Results: Functional imaging studies in patients with depression do not provide a clear and well defined target for rTMS treatment. However, neuro-navigationally localising treatment based on dorsolateral prefrontal cortex structure does produce a greater antidepressant response than standard methods of rTMS application. Finally, NIRS methods appear to be able to be used to improve aspects of prefrontal coil placement.

Conclusions: Improvements in the application of rTMS treatment are possible using a range of neuroscientific tools that can enhance coil placement and localisation. Improvements in rTMS application are likely to arise from individualisation of treatment site based on individual patient brain characteristics.

Saturday, May 25, 2019
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7. INS19-0447

CIRCUIT THERAPEUTICS FOR THE TREATMENT OF DEMENTIA: A RANDOMISED CONTROLLED TRIAL OF THETA BURST STIMULATION FOR MILD TO MODERATE ALZHHEIMER'S DISEASE

K. Hoy BBNSc(Hons) DPsych (Clin Neuro)[1]

[1]*Monash University, Therapeutic Brain Stimulation- Central Clinical School, Melbourne, Australia*

In Australia there are currently over 420,000 people suffering from dementia and, with no significant treatment breakthroughs, this number is predicted to rise to over 1.1 million by 2056. Between 2002 and 2012 there were 413 clinical drug trials for Alzheimer's with an overall failure rate of 99.6%, and of the 244 drugs trialled in this time only one received FDA approval (in 2003). While there are a number of new drugs currently under development, early findings have been largely disappointing. In light of this, the inherent challenges and costs of drug development, and the recent withdrawal of drug companies from Alzheimer's research (i.e. Pfizer announced in January 2018 that it will be ending its research into drug development for Alzheimer's) alternative treatment approaches must be considered. Non-invasive brain stimulation techniques hold considerable promise as novel treatment approaches for dementia.

Recent findings regarding the pathophysiology of dementia have indeed suggested an alternative treatment approach, with studies showing damage to specific large-scale, distributed, function-critical neural networks. Whereby it may be these **pathophysiological consequences** of identified neuropathology (i.e. abnormal neuronal firing patterns throughout specific circuits) which are most related to dementia symptoms. Such pathophysiological processes are ideally suited to modulation with brain stimulation techniques that can induce both local and global changes in brain activity (i.e., Transcranial Magnetic Stimulation [TMS], Theta Burst Stimulation [TBS], transcranial Direct and Alternating Current Stimulation [tDCS, tACS]). This 'circuit therapeutics' approach represents a novel way to approach dementia treatment. We are currently conducting three such RCTs, and I will be presenting initial data analysis from the most progressed of these trials. Namely, a randomised controlled trial of TBS in mild to moderate Alzheimer's disease.

In this sham controlled double-blind trial patients are randomly allocated to receive a treatment course of either active or sham TBS. Patients undergo a total of 21 TBS sessions over 6 weeks. TBS is applied to four brain sites sequentially at each treatment (i.e. lDPFC. rDLPFC, lPPC, lPPC). Comprehensive cognitive and clinical assessment tailored for the patient group is conducted at baseline, week 3 and 6, and at 3, and 6 month follow ups to assess duration of effects. We are also using resting EEG and TMS-EEG to examine changes in cortical activity throughout the brain networks of interest.

Sunday, May 26, 2019
Special Session
Public Education Program

8. INS19-0518

WELCOME AND INTRODUCTION

N. Christelis[1]

[1]*Pain Specialist, Pain Specialists Australia, Richmond, Australia*

A welcome and introduction to the neuromodulation public education event.

Sunday, May 26, 2019
Special Session
Public Education Program

9. INS19-0519

NEUROMODULATION IS PROVEN, COST-EFFECTIVEAND REVERSIBLE: THE THERAPY'S HISTORY AND DEVELOPMENT, AND THE USE OF SPINAL CORD STIMULATION IN MEDICAL PRACTICE

N. Christelis[1]

[1]*Pain Specialist, Pain Specialists Australia, Richmond, Australia*

We'll run you through neuromodulation, what it is, how it works and what it is used for.

Sunday, May 26, 2019
Special Session
Public Education Program

10. INS19-0520

OPIOID CRISIS AND NEUROMODULATION

L. Poree MD PhD[1]

[1]*University of California- San Francisco UCSF, Anesthesia and Pain Management, San Francisco, USA*

The recent escalation in opioid related deaths is a reflection of multiple medical, social, political, and economic pressures that converge to exponentially expand the harmful toll opioid toxicity can have. Throughout the millennium, humans have struggled with balancing the beneficial and harmful impacts of opioid use. In the past 200 years the response by our respective societies has primarily focused on tackling the social, political, and economic determinants that contribute to the rise in opioid misuse. However, in light of the observation that the GDP for illicit drug trafficking is now estimated to be approximately 300 billion dollars per year, 10 times greater that the GDP of any nation, it is no wonder that relying solely on a political and law enforcement approach has failed. In fact, the past Secretary General of the United Nation, Kofi Annan, characterized the war on drugs as a war on the individuals that use drugs. In addition, with the financial resources of the illicit drug trafficking industry dedicated to the neurobiology of addiction by producing more potent and in turn more lethal drugs, it is only rational that the international response to this epidemic should also be based on understanding and addressing the opioid crisis as the medical crisis that it is. In 2004 The World Health Organization and the International Association of for the Study of Pain declared that relief of pain should be a fundamental human right. While this has been translated by some to suggest greater access to opioid therapy, recent events reveal that it is critical to balance the care of patients in pain with the complex biopsychosocial factors that contribute to addiction. Thus, the opportunity has arisen for the international medical community to address the opioid epidemic as the medical problem that it is by balancing these two competing medical disorders. For the neuromodulation community in particular the challenge is to provide alternatives to opioids for the treatment of pain, investigate the pathophysiology of addiction and provide neuromodulation therapies to modulate the neurobiology determinants of addiction. Recent clinical trials show promise on both of these fronts. Only by combining the medical strategies with the political, social, and legal approaches can we hope to turn the tide on this current epidemic and provide a sustainable solution to opioid and other chemical addictions in the future.

Sunday, May 26, 2019
Special Session
Public Education Program

11. INS19-0508

PATIENT TESTIMONY ON EFFICACY AND QUALITY OF LIFE CHANGES AFTER DEEP BRAIN STIMULATION FOR PARKINSON'S DISEASE, DEEP BRAIN STIMULATION FOR MOVEMENT DISORDER: INDICATION, EFFECTIVENESS AND COST EFFICACY, DISCUSSION AND QUESTIONS

T. Coyne MD[1]

[1]*Queensland Brain Institute- BrizBrain & Spine, Neurosurgeon, Brisbane, Australia*

This public education presentation on neuromodulation for movement disorders will focus on deep brain stimulation (DBS) for Parkinson's Disease (PD).

DBS for PD and other movement disorders is still often perceived as "new therapy", despite having been in successful clinical use for >30 years. It has been estimated that only approximately 15% of patients who might benefit from this therapy receive it.

In this presentation, the time and place for considering DBS in PD will be explained. The evidence of clinical benefit will be outlined, including discussion of high quality randomised trials demonstrating superiority of DBS over best medical therapy alone for PD motor symptoms such as "on-off" fluctuations, dyskinesia, and drug resistant tremor. Evidence of economic cost/benefit will be presented. The limitations and risks of DBS will also be discussed.

It is hoped that educational presentations such as this might assist in DBS becoming better known to the general public and the wider medical profession, such that more patients who might benefit from this therapy have access to it.

Monday, May 27, 2019
Plenary
Opening Plenary Session

12. INS19-0468

NON-SURGICAL DEEP BRAIN STIMULATION

N. Grossman PhD [1]

[1]*Imperial College London & UK Dementia Research Institute, Medicine, London, United Kingdom*

Electrical brain stimulation is a key technique in research and clinical neuroscience studies, and also is in increasingly widespread use from a therapeutic standpoint. However, to date all methods of electrical stimulation of the brain either require surgery to implant an electrode at a defined site, or involve the application of non-focal electric fields to large fractions of the brain. We report a noninvasive strategy for electrically stimulating neurons at depth. By delivering to the brain multiple electric fields at frequencies too high to recruit neural firing, but which differ by a frequency within the dynamic range of neural firing, we can electrically stimulate neurons throughout a region where interference between the multiple fields results in a prominent electric field envelope modulated at the difference frequency. We validated this temporal interference (TI) concept via modeling and physics experiments, and verified that neurons in the living mouse brain could follow the electric field envelope. We demonstrate the utility of TI stimulation by stimulating neurons in the hippocampus of living mice without recruiting neurons of the overlying cortex. Finally, we show that by altering the currents delivered to a set of immobile electrodes, we can steerably evoke different motor patterns in living mice

Monday, May 27, 2019
Plenary
Opening Plenary Session

13. INS19-0521

CLOSED-LOOP SPINAL CORD STIMULATION: EVOKE STUDY *RESULTS*

L. Poree MD PhD[1]

[1]*University of California- San Francisco UCSF, Anesthesia and Pain Management, San Francisco, USA*

Title: Randomized, Double-Blind Trial Comparing Evoked Compound Action Potential (ECAP)-Controlled Closed-Loop Spinal Cord Stimulation (SCS) to Conventional, Open-Loop SCS

Lawrence Poree, MD, PhD; for the members of the Evoke study group *University of California San Francisco, San Francisco, CA*

Background and Aims: Spinal cord stimulation (SCS) is a well-established treatment for chronic pain. Advancements in SCS systems have focused on eliminating paresthesias, but long-term success rates remain suboptimal. Variability in spinal cord (SC) activation with open-loop systems results in unpredictable inhibition of pain processing pathways, and may limit the efficacy of SCS. We report the first randomized, double-blind, pivotal study of SCS and the first therapy to measure real-time in-vivo SC neurophysiology using **E**voked **C**ompound **A**ction **P**otentials (ECAPs). This study provides comparative efficacy and safety of closed-loop (CL) feedback stimulation compared to open-loop (OL) stimulation.

Methods: 134 subjects were randomized into OL or CL. Subjects and the clinical staff were blinded to the treatment assignment. A pain assessment and other patient reported outcome measures per IMMPACT were collected. ECAPs were also collected in both groups to compare the magnitude of SC activation and the percentage of time within the therapeutic window.

Results: The primary composite endpoint demonstrated superior results in overall pain responders (P=0.005) for CL-SCS (82.3%) compared to OL-SCS (60.3%). In addition, all pre-specified hierarchical endpoints demonstrated better outcomes in the CL group, with both back pain reduction (P=0.015) and back pain responders (P=0.003) demonstrating superiority. The magnitude of SC activation was 7 times greater for CL-SCS and CL subjects spend 50% more time within the therapeutic window. In both groups, subjects showed improvements across secondary outcomes.

Conclusions: ECAP-controlled closed-loop SCS has demonstrated superior overall pain relief compared to open-loop SCS. The study has just completed the primary outcome data analysis

Monday, May 27, 2019
Plenary
Opening Plenary Session

14. INS19-0486

BLINDED RANDOMIZED CONTROLLED TRIAL ON WAVEFORMS: THE SURF STUDY

R. Bolash[1]

[1]*Cleveland Clinic, Pain Management and Evidence Based Pain Research, Cleveland, USA*

We herein provide the results of a multicenter randomized controlled trial comparing 10 kHz SCS with heterogeneous paresthesia and non-paresthesia programming paradigms.

Monday, May 27, 2019
Plenary
Opening Plenary Session

15. INS19-0523

MULTIFIDIS PERIPHERAL NERVE STIMULATION RANDOMIZED CONTROLLED TRIAL

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Restorative Neurostimulation for Chronic Low Back Pain – Randomized Controlled Trial

Chris Gilligan[1], on behalf of the ReActiv8-B study investigators

[1]*Brigham and Women's Healthcare, Harvard Medical School, Boston, Massachusetts, USA*

Introduction: ReActiv8-B is an international, multicenter, prospective, randomized, sham-controlled, blinded clinical trial with one-way crossover, conducted under an IDE from the FDA (clinicaltrials.gov/show/NCT02577354). The study, performed at 26 investigational sites in the United States, Australia and Europe, is intended to evaluate safety and efficacy of a novel implantable neurostimulator for adults with Chronic Low Back Pain (CLBP) and no prior spine surgery.

The therapeutic target is the multifidus muscle which normally provides functional stability to the lumbar spine. Fundamental to the therapeutic effect is arthrogenic multifidus inhibition, and the associated segmental instability and possible atrophy.

Bilateral electrical stimulation of the L2 dorsal ramus medial branch elicits episodic contractions of the deep multifidi, thus overriding underlying inhibition. Reactivation of motor control and restoration of functional stability is the hypothesized mechanism of action.

Materials and Methods: Key eligibility criteria included debilitating CLBP despite medical management with at least pain medications and physical therapy in patients who were not candidates for spine surgery. Subjects were implanted and randomized to 'Treatment' (stimulation eliciting multifidus contractions) or 'Sham-Control' (subthreshold stimulation). All subjects were blinded and self-administered two 30-minute "stimulation" sessions daily. After primary endpoint assessment, subjects in the 'Sham-Control' group crossed-over to 'Treatment'.

The primary endpoint was a comparison of responder rates at 120 days post-randomization. A 'Responder' is a subject with ≥30% reduction from baseline in Average LBP VAS (VAS), without any increase in pain medication or muscle relaxants in the two weeks prior to primary outcome assessment.

Results: At baseline (N=204), LBP duration was 14±11 years, age 47±9 years, VAS 7.3±0.7 and Oswestry Disability Index (ODI) 39±10. Most subjects (80%) were regularly using back pain medications, including opioids (37%).

In the intent-to-treat cohort, the difference in responder rates was not significant at 120 days (56% vs. 47%). After exclusion of the 6 subjects who increased pain medication for reasons unrelated to back pain (prespecified analysis), 'Treatment' was superior to 'Sham-Control' (61% vs. 47%).

Secondary endpoints and supporting analyses also showed statistically significant differences.

Matched one-year data was available for 116 subjects. VAS improved from 7.3±0.8 to 3.0±2.5 and ODI from 38±10 to 19±14.

- § 64% reported ≥50% VAS improvement
- § 52% remitters (VAS≤2.5)
- § 44% (22/50) eliminated (28%) or reduced (16%) opioid use
- § 70% reported ≥15-point improvement on ODI

The safety profile is favorable compared to other neurostimulation modalities.

Conclusion: The totality of data supports the validation of ReActiv8 as a viable therapy.

Monday, May 27, 2019
Plenary
Opening Plenary Session

16. INS19-0131

ANATOMICAL LEAD PLACEMENT IS A VIABLE ALTERNATIVE TO TARGETED LEAD PLACEMENT FOR SPINAL CORD STIMULATION: RESULTS FROM A PROSPECTIVE, RANDOMIZED, SINGLE-BLINDED, MULTI-CENTER, INTERNATIONAL, STUDY

J.E. Pope MD[1], S. Schu MD[2], D. Sayed MD[3], A. Raslan MD[4], G. Baranidharan MD[5], T.R. Deer MD[6]

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[3]*Kansas University Medical Center, Kansas City, KS, USA*
[4]*Oregon Health and Science University, Portland, OR, USA*
[5]*Leeds Teaching Hospital NHS Trust, Leeds, UK*
[6]*The Spine and Nerve Center of the Virginias, Charleston, West Virginia*

Introduction: Epidural lead placement for spinal cord stimulation (SCS) has been traditionally determined by paresthesia mapping. With the advent of paresthesia-free waveforms, use of paresthesia mapping to determine lead placement has been brought into question. Anatomic placement of leads may provide broader therapeutic coverage but the effect of this procedural variation on the qualification for a SCS permanent implant is not currently known. The purpose of this study was to compare the qualification rate for permanent implant between anatomic and targeted lead placement techniques using a novel paresthesia-free waveform.

Materials and Methods: Eligible patients with back and/or leg pain, NRS score ≥ 6, and no previous exposure to SCS were included. After enrollment, subjects were randomized to anatomic or targeted lead placement in a 1:1 ratio. In the anatomic group, one lead tip was placed at the rostral end of T8, and the other at the rostral end of T9. Leads in the targeted group were placed using paresthesia mapping. Subjects underwent a trial evaluation period for 3-5 days. The qualification rate for permanent implant was a composite of: ≥ 50 % patient-reported pain relief at the end of the minimum 3-day trial period, physician's recommendation, and the subject's interest in placement of a permanent implant. The primary endpoint of this study was the qualification rate for permanent implant after the trial period.

Results: Of the 270 subjects who were randomized, 126 subjects completed the trial for the anatomic group and 122 subjects completed the trial for the targeted group. The qualification rate was similar between groups: 84.4% anatomic, 82.3% targeted. The overall procedure time was significantly shorter for anatomic compared to targeted placement for two trial leads: 40 $\pm$ 12.4 min, 45 $\pm$ 13.7 min, respectively, ($p < 0.01$). The trial implant procedure time (needle-in to needle-out) was also significantly shorter between the two groups: 14 $\pm$ 8.2 min, 19.9 $\pm$ 10 min, respectively, ($p < 0.01$). No difference in intra-operative fluoroscopy time was observed. Additionally, physicians preferred anatomic placement technique (66.7% v 33.3%).

Conclusions: The qualification rate for permanent implant for anatomic lead placement was comparable to the targeted lead placement, and could therefore be a viable alternative during SCS trial procedure. Anatomic placement of leads saved, on average, 5 minutes of procedure time when placing two trial leads.

***Learning Objectives*:** To understand the effectiveness of SCS during anatomic lead placement versus paresthesia-guided placement, using a paresthesia-free waveform.

Monday, May 27, 2019
Breakout Session
Improving Delivery of Neuromodulation for Pain

17. INS19-0442

ADDING OBJECTIVE MARKERS TO SPINAL CORD STIMULATION ASSESSMENTS

J. Pilitsis MD PhD[1]

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Spinal cord stimulation (SCS) has become a widely accepted treatment option for a several chronic refractory pain conditions. However, there are a significant subset of patients with sub-optimal response to the therapy. Current assessment of response relies on subjective patient reported responses, with unilateral dimensions similar to the Visual Analog Scale and multidimensions such as the McGill Pain Questionnaire. Such measures are plagued by limited validity. Alternative measure such as functional outcomes assess day to day impact of outcomes, but may be biased by secondary gains. Similarly, reduction in opioid usage may be confounded by opioid misuse/prescribing patterns. Objective biomarkers of pain would aid in assessment of SCS outcomes. Many options have been suggested though all remain research tools to date. Electrophysiologically, these include Quantitative sensory testing (QST), objectively assesses detection of sensory stimuli in a clinic setting, and somatosensory evoked potentials, which help to identify accurate SCS placement intraoperatively. We and others propose that electroencephalography (EEG) and magnetic encephalography (MEG) may aid additional value. Other potential markers include: functional magnetic resonance imaging (fMRI) shows differential responses in chronic pain patients and serum markers. The addition of objective biomarkers is essential for pain management of the future. They would have profound implications for improving SCS treatment and our understanding of its mechanism of action.

Monday, May 27, 2019
Breakout Session
Improving Delivery of Neuromodulation for Pain

18. INS19-0516

SYSTEMATIC TROUBLESHOOTING INTRATHECAL DELIVERY SYSTEMS: EMERGING TOOLS

M. Saulino MD PhD[1]

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Intrathecal delivery of medications is a well-established technique for the management of chronic pain and spasticity. The treatment approach can be a highly effective therapy for these syndromes. A suboptimal response to therapy warrants investigation of the system. A variety of Troubleshooting procedures that vary from routine to sophisticated undertakings.

This presentation will describe four relatively novel approaches to troubleshooting these systems.

1: Utility of bedside ultrasonography for the management of intrathecal delivery systems. Potential uses for this technique include utilization guidance of reservoir refill, diagnosis of inadvertent subcutaneous drug injection (pocket fill) and detection of a flipped pump. Examples of these techniques will be reviewed

2: Safe execution of computed tomography (CT) myelography despite prior negative side port aspiration. Traditionally, diagnostic injections through the catheter access port require removal of the drug contents prior to myelogram dye infusion so as to not immediately expose the patient to accident overdose. An approach to circumvent this difficulty will be described.

3: Analysis of cerebrospinal fluid (CSF) pressure wave detection. Certain pressure signatures (cardiac pulsations and respiratory pressure modulation) present only in the intrathecal space may be useful for the detection of catheter malfunction. These signatures provide evidence that the tip of the catheter is located in the intrathecal space, and the catheter is intact, unobstructed, and can deliver drug into the CSF. Results of pilot study will be described.

4: Analysis of Beta 2 transferrin testing of side port aspirate. Beta 2 transferrin is a carbohydrate-free isoform of transferrin, which is almost exclusively found almost exclusively in the CSF. Detection of this substance during a side port aspiration suggests catheter continuity. Similarly, discovery of this protein in a seroma could imply a catheter break. Results of pilot study will be described.

Monday, May 27, 2019
Breakout Session
Improving Delivery of Neuromodulation for Pain

19. INS19-0507

ANIMAL MODELS OF PARESTHESIA BASED-SCS AND SUB-PERCEPTION-SCS AND CLINICAL CORRELATES

G. Franken MS[1], B. Joosten[1]

[1]*Maastricht University Medical Centre+, Anesthesiology, Maastricht, The Netherlands*

Today, various Spinal Cord Stimulation (SCS) paradigms are applied for the treatment of chronic neuropathic pain disorders. In this lecture the status of Dorsal Column stimulation and the mechanisms underlying Conventional (or Tonic) and Burst-SCS, but also the status and mechanisms of action of Dorsal Root Ganglion Stimulation (DRGS) will be discussed. The different paradigms and locations are hypothesized to exert their analgesic effects through different stimulation-induced mechanisms.

Animal studies have shown that with Burst-SCS supraspinal brain areas involved in cognitive-motivational aspects of pain show increased activation as compared to Tonic-SCS. These findings are further substantiated by behavioral studies using escape latency in the mechanical conflict avoidance test (MCAS). The MCAS allowed discriminating between Burst- and Tonic-SCS behavioral effects on pain relief which were not detectable with use of the reflex based von Frey paw withdrawal response.

Additionally, this lecture will highlight the use of novel stimulation paradigms of DRGS, like Burst-DRGS, in the treatment of chronic neuropathic pain. Interestingly, in the first study to test Burst-DRGS for chronic neuropathic pain, Burst-DRGS was found to have a prolonged effect after stimulation cessation over Tonic-DRGS. Also, the effect of individual stimulation parameters (e.g. intensity, frequency) within a single stimulation paradigm, like tonic and burst-DRGS, will be discussed. Lastly, the involvement of the GABAergic system will be highlighted, as early data suggests that DRGS is not dependent on GABA release in the dorsal horn of the spinal cord in the way SCS is.

Future research is necessary for optimization and analysis of SCS and DRGS driven by insights into the underlying mechanisms of the various stimulation paradigms.

Monday, May 27, 2019
Breakout Session
Brain Neuromodulation

20. INS19-0465

ADAPTIVE STIMULATION IN DEEP BRAIN STIMULATION

T. Coyne MD[1]

[1]*Australia*

DBS is established therapy for a number of medically refractory movement disorders, including Parkinson's Disease (PD), essential tremor (ET), and dystonia. While beneficial, DBS is far from perfect, and while there have been advances in patient selection, target identification, and electrode and pulse generator technology, the stimulation paradigm of continuous high frequency current has not changed substantially since Benabid's landmark paper of 1987, which is generally regarded as the commencement of the modern era of DBS. Adaptive DBS (aDBS), also referred to as closed-loop stimulation, refers to stimulation dynamically controlled by biomarkers of pathological brain activity. These biomarkers can be central, such as local field potentials (LFP's), or peripheral, such as EMG recordings of tremor activity. aDBS has theoretical advantages over conventional DBS, including being more physiological, less battery energy consumption, and automatic rather than manual stimulation adjustments, both acutely and in the long term as the underlying condition progresses. Current evidence is restricted to animal studies and limited clinical studies in humans, which have generally been intra-operative or short term post-operative studies. This evidence has been promising, but clinical application awaits refinement of biomarkers and advances in device technology allowing recording and analysis of these biomarkers, along with the capacity to make appropriate programming adjustments.

Monday, May 27, 2019
Breakout Session
Brain Neuromodulation

21. INS19-0509

RHYTHMS OF THE BRAIN

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Many observations have established that human brain networks overlap.

These networks can be thought of as requiring interacting sources connectivities and sinks.

And has provided frameworks for studying and modifying normal and abnormal rhythms in the brain.

Furthermore, it has enabled the development of platforms for understanding why diverse brain diseases can have the identical structural brain target, and conversely that diverse brain targets can modulate a single brain disease phenotype.

A system for studying online deep brain single neuron recordings and oscillations will be shown; And this has allowed direct study of awake human brain neurophysiology.

Some clinical examples of modifying involuntary brain dysfunctions will demonstrated.

These applications to various human brain disorders will be discussed.

Monday, May 27, 2019
Breakout Session
Brain Neuromodulation

22. INS19-0479

DEEP BRAIN STIMULATION FOR OBESITY

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Loss of control eating (LOC) is pervasive in obese binge eaters and is related to hypersensitization of the reward processing circuit. Dysregulation of the mesolimbic dopamine system in the nucleus accumbens shell (NAcSh) has specifically been implicated in this intractable disorder, contributing to treatment-resistance in obesity. We have previously demonstrated the ability of deep brain stimulation (DBS) of the NAcSh to block LOC eating in mice and found that dopamine signaling partly mediates this effect. Moreover, we found that NAcSh DBS acutely reduces binge eating and induces weight loss in obese mice, however, this effect was not sustained. Field potentials recorded from the NAc of mice and a human anticipating conventional rewards identified increased power in 1- to 4-Hz oscillations immediately before receipt. A clinically available closed-loop DBS system adapted to mice was capable of automatically sensing and therapeutically responding to this signal by triggering neurostimulation. This closed-loop approach reduced binge-eating behavior in mice more robustly and durably than traditional DBS and did so without blocking normal feeding and social behavior.

To translate our preclinical findings to a first-in-human trial, we need to be able to detect this subregion in human MRI. We have found that the NAc can be divided into presumed core (dorsolateral) and shell (i.e. NAcSh, ventromedial) subregions based on connectivity profiles using Human Connectome Project (HCP), as well as clinical diffusion MRI data. This subdivision was confirmed by functional neuroimaging and dissociable acute effects evoked by direct stimulation of these subregions in a human subject. The NAcSh has monosynaptic connections to the lateral hypothalamus (LH), Brodmann's area 25 (BA25), insula, hippocampus, and amygdala, which are critically involved. Notably, our tractography-defined NAcSh was found to be the NAc subregion with the higher streamline probability to these chief nodes of the mesolimbic reward processing pathway. Finally, we used tractography in subjects with LOC eating and identified a decreased number of tractography-defined NAc-BA25 streamlines in higher BMI subjects. This finding justifies our plan to utilize this targeting methodology in our imminent first-in-human trial of closed-loop DBS for loss of control eating in treatment-refractory obesity.

Monday, May 27, 2019
Breakout Session
Brain Neuromodulation

23. INS19-0480

DEEP BRAIN STIMULATION FOR ADDICTION

C. Zhang MD,PhD[1], V. Voon[2], T. Li[3], B. Sun[1], X. Wang[4], L. Lu[5], G. Gao[4]

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[5]*Institute of Mental Health- National Clinical Research Center for Mental Disorders- Key Laboratory of Mental Health and Sixth Affiliated Hospital of Peking University, Psychiatry, Beijing, China*

Deep brain stimulation (DBS) is currently used to treat addiction. DBS of the nucleus accumbens (NAc) or combined with the anterior limb of the internal capsule (ALIC) appears to be safe, with acceptable side effects and may prevent long-term heroin relapse in certain opioid addiction patients. However, large scale randomized controlled trial is lacking. Here we present the preliminary data of an ongoing multi-center randomized controlled trial in China which aimed for 60 patients using parallel active vs. sham group design. Five patients (3 males; age:28-48) were followed for 2-11 months, and four patients were abstinent in the follow-up, one patient had multiple urine tests positive record in the first month after DBS. The DBS parameters optimization were consistent in all patients for 25 weeks but those impulse generators in the sham group were not responded (double-blind). There is also a noticeable improvement in mood and sleep. Despite these promising results, the placebo effect needs to be investigated in further progress.

Monday, May 27, 2019
Breakout Session
Cardiovascular Neuromodulation

24. INS19-0472

WHAT'S HOT AND WHAT'S NOT IN NEUROMODULATION FOR CARDIAC DISEASES

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What's hot and what's not in neuromodulation for cardiac diseases

Mike JL DeJongste, MD, PhD, FESC, Department of Cardiology and University of Groningen, The Netherlands

Since the sixties, mortality from cardiovascular diseases decreased by > 70%. The subsequently improved life expectancy mainly took place through improved prevention measures (treatment of risk factors [for instance diabetes, hypertension, dyslipidemia], opposing unhealthy habits [smoking; sedentary life style]) and better understanding and recognition of underlying mechanisms. These preventive actions have been developed in conjunction with successive advancements in treatment approaches (medication; percutaneous coronary intervention during a myocardial infarction).

As a result of the upgraded strategies, the average age of dying increased by a decade, in the Western World. Hence, more and more subjects live longer with their chronic (cardiovascular) diseases, such as ischemic heart diseases, heart failure and arrhythmias. In addition, a predicament of the increasing cardiovascular morbidity, is that an increasing number of standard therapies often fail to relieve the symptoms, ultimately. Therefore, electrical neuromodulation (EN), as an additional therapy for patients with chronic cardiovascular diseases, refractory to standard treatment, is worth to take into consideration.

There is sufficient and convincing basic and clinical literature available, consistently demonstrating that the use of neuromodulation to treat patients with chronic refractory angina is effective and beneficial. Albeit that the results of EN therapy in basic, often mechanistic, studies making use of EN to treat systolic heart failure show convincing and beneficial outcomes, the clinical studies frequently have conflicting outcomes. Since the clinical design (randomized versus observational) of the clinical studies and the methods (vagal nerve versus spinal cord stimulation) are not easily comparable, the outcomes of clinical EN studies as an additional therapy for systolic heart failure are debatable. Studies on baroreceptor modulation are awaiting. The use of neuromodulation to treat arrhythmias is still in statu nascendi.

In conclusion, EN is an effective and safe method for relief of severe angina in patients with refractory angina. Though in general, basic EN studies often provide favorable outcomes, clinical studies frequently fail to validate the initial enthusiasm generated by basic studies and thus, it might be a long way from bench to bedside, before EN is generally accepted for heart failure. Finally, it is too early to jump into conclusion on the effectiveness of EN on the treatment of (a variety of) arrhythmias.

In the current session the different EN methods for treatment of refractory cardiovascular conditions will be discussed extensively.

Monday, May 27, 2019
Breakout Session
Cardiovascular Neuromodulation

25. INS19-0463

BASIC MECHANISMS OF VAGAL MODULATION IN CARDIAC DISEASES

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Heart disease remains the primary cause of morbidity and mortality. The fundamental premise of neurocardiology is that it is the dynamic interactions between autonomic control and the heart that ultimately determines how closed-loop control of cardiac function evolves in response to cardiovascular stressors including those leading to cardiac disease. In the worst case scenario, imbalances in autonomic control coupled with regional variations in cardiac electrical/mechanical function set the stage for arrhythmias leading to sudden cardiac death or heart failure. Through a mechanistic understanding of neurohumoral-cardiac processes, a rationale for therapies designed to maintain cardiovascular homeostasis can be defined.

Vagus nerve stimulation (VNS) is an emerging therapy for treatment of chronic heart failure and cardiac arrhythmias. VNS, when delivered to the cervical vagosympathetic trunk activates both ascending (afferent) and descending (parasympathetic efferent) projections. The cardiac nervous system works in a "push push-back" fashion. Functional cardiac responses to afferent activation are engaged at lower stimulus intensities leading to withdrawal of centrally-derived parasympathetic tone with the potential to modify sympathetic activity. As stimulus intensity is increased, parasympathetic efferents are engaged with expected decreases in regional cardiac function. When ascending and descending projections within the cervical vagus are activated in a "balanced" fashion, multiple levels of the cardiac neuraxis are engaged with little or no change in basal cardiac function – we refer to this as the neural fulcrum. The major effects of VNS delivered at this operating point are placing restraints on aberrant reflex processing within the peripheral neural networks of the intrinsic cardiac nervous system, rendering myocytes stress-resistant and exerting anti-adrenergic effects on the heart itself.

Cardiac disease is a dynamic process; neuromodulation is too. As a patient's sympathovagal balance shifts during the course of the disease process, changes in stimulation parameters may be warranted. It is much more than set and forget. Future studies should also consider relevant biomarkers in assessing engagement of the neural elements and the effects on end-organ function. With such biomarkers, the potential for effective closed-loop systems can become a reality.

Monday, May 27, 2019
Breakout Session
Cardiovascular Neuromodulation

26. INS19-0477

BASIC MECHANISMS OF SPINAL CORD STIMULATION IN CARDIAC DISEASES

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Cardiac diseases such as angina pectoris, and their treatment, depend on the neural hierarchy of the brain, spinal cord and the heart to modulate complex mechanisms. This presentation will provide insights about mechanisms of spinal cord stimulation (SCS) that contribute to pain relief of angina pectoris and improve cardiac function resulting from the progression of cardiac pathology. Myocardial ischemia activates nociceptive sensory afferent fibers in the C7-T5 spinal segments that transmit information to excite cells of the spinothalamic tract that also receive primarily muscle and to a less extent cutaneous input from overlying somatic structures such as the chest and upper arm, and contribute to pain perception. Animal studies have shown that SCS of the C8-T1 dorsal column reduces the number of action potentials of spinothalamic tract neurons that are evoked by administrating intracardiac injections of bradykinin, a mediator of inflammation. The reduced activity of these cells most likely occurs because SCS antidromically activates dorsal column collaterals in the gray matter of the T3-T4 segments that release the k-opioid, dynorphin, which may suppress spinal neuronal activity directly and/or indirectly. This neurotransmitter may also reduce the quantity of substance P that is released in spinal neuronal circuits during myocardial ischemia. This presentation will also suggest how SCS of the dorsal column at the upper thoracic segments or upper cervical segments reduces the frequency and severity of angina attacks, reduces the use of short-acting nitrate intake, and increases exercise tolerance. Experimental studies have also shown that SCS induces myocardial protection by stabilizing the intrinsic cardiac nervous system, reducing local efferent sympathoexcitaion, redistributing blood flow, and reducing infarct size. Additionally, SCS lowers the incidence of ventricular fibrillation, ventricular arrhythmias, and atrial arrhythmias. It should also be noted that SCS decreases sympathetic nerve activation regionally in the ischemic myocardium but does not affect neural activity on the normal myocardium. In summary, basic research has shown that SCS may directly diminish pain. This may also occur because SCS improves the function of organs. Basic and clinical studies indicate that neuromodulation therapies maintain effectiveness over time, evoke minimal adverse autonomic or somatic consequences, and provide the added benefit of reducing angina and arrhythmias in patients with ischemic heart disease.

Monday, May 27, 2019
Breakout Session
Cardiovascular Neuromodulation

27. INS19-0484

ANESTHETIC CONSIDERATIONS AND PERIOPERATIVE MANAGEMENT OF SCS

M. Harned MD[1]

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Perioperative Management of Neurostimulators and Cardiovascular Implanted Electronic Devices

Michael E. Harned

University of Kentucky, Lexington, Kentucky, USA

Neurostimulation including deep brain stimulators (DBS) and spinal cord stimulators (SCS) are accepted as standard treatment for many chronic and otherwise difficult to manage disease states. Concurrently, the population is aging, with more heart disease and need for cardiovascular implanted electronic devices (CIEDs). These neurostimulation devices pose a potential risk to patients who have coexisting CIEDs. CIEDs including internal cardiac defibrillators (ICD) and permanent pacemakers (PPM) deliver lifesaving therapy by sensing when the heart rate is either too slow, irregular, or in a lethal arrhythmia. Because CIEDs rely on sensing the electrical activity of the heart, there is a concern that emitted electrical activity from the SCS could cause a malfunction in the CIED. In the case of a PPM, interpretation of the SCS signal as cardiac activity could result in failure of the needed pacing therapy. With ICD, the SCS signal, read as a lethal arrhythmia, could results in an inappropriate shock to the patient or result in complete reprograming of the neurostimulator.

Currently, implantation of a neuromodulation device in a patient with a CIED is a relative contraindication due to the perceived risk of device-to-device interaction. While the literature does report a case of PPM inhibition with increasing amplitudes in a SCS and complete reset of a DBS after ICD discharge, the vast majority of reports document no interaction between the devices. Despite this, if combination therapy is utilized, myriad precautions should be exercised including a frank conversation with the patient detailing the potential risks.

Monday, May 27, 2019
Breakout Session
Cardiovascular Neuromodulation

28. INS19-0492

CLINICAL OUTCOMES OF NEUROMODULATION FOR ANGINA

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In recent decades, evolution of medical therapy, coronary artery bypass grafting (CABG) and percutaneous coronary interventions (PCI) significantly reduced the morbidity and mortality in patients presenting with coronary artery disease (CAD). Despite all treatment innovations, 5 – 10% of patients with stable CAD remain symptomatic despite optimal therapy referred to as "refractory angina pectoris (RAP)". This condition is defined as a "chronic condition (> three months) characterized by diffuse coronary artery disease in the presence of proven ischemia, which is not amendable to a combination of medical therapy, angioplasty or coronary bypass surgery. Patients with RAP are severely restricted in performing daily life activities, by debilitating angina complaints, leading to decreased quality of life.

Spinal cord stimulation (SCS) is a treatment option that has been developed for patients with RAP to improve quality of life and reduce angina pectoris episodes.

The aim of our prospective observational study was to assess the efficacy of spinal cord stimulation (SCS) on severity of angina symptoms and quality of life in patients with refractory angina pectoris in a large, real-life patient cohort from a single centre.

From July 2010 through to March 2017, 127 patients with RAP were referred to our hospital (Catharina Hospital, Eindhoven, Netherlands). Patients were included if the criteria for definition of RAP were met: 1. Stable angina pectoris (AP) Canadian Cardiovascular Society (CCS) class 3 or 4 for at least three months. 2. Significant CAD with no options for revascularization (CABG and/or PCI). 3. Optimal medical anti-angina therapy. 4. Test for ischemia (MIBI-SPECT, stress echo and/or ergometry) positive.

Quality of life and frequency of angina symptoms were the primary endpoints in this study. Data were collected using generic (SF- 36) and disease specific (Seattle Angina Questionnaire, SAQ) questionnaires.

Our study showed a significant improvement in quality of life and reduction of angina pectoris severity after one-year follow-up in patients treated with spinal cord stimulation for refractory angina pectoris.

Tuesday, May 28, 2019
Plenary
Plenary Session 2

29. INS19-0502

NEUROMODULATION CENTERS OF EXCELLENCE

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There is a growing public awareness of neuromodulation, both for its broad range of potential benefits as well as its limitations and complications. To improve the safety, efficacy and cost effectiveness of neuromodulation therapies, we suggest that Centers of Excellence in Neuromodulation be established. The author of Genius, Malcolm Gladwell, and neuroscience researcher Dr. Daniel Levitan both emphasize that excellence in any given venture requires a great deal of practice. Their research has demonstrated that it takes roughly 10,000 hours (or about 10 years) of good practice to become an expert, whether it be in music, computer science or sports. This seems to apply to medical disciplines as well; the effect of experience on outcomes has been demonstrated in several disciplines including cardiac, vascular and bariatric surgery. Centers of Excellence have been established, for example, in Bariatric Surgery, Stroke Management and Pain Medicine.

The early data on neuromodulation therapies seems to closely parallel that obtained from other medical specialties: the greater the experience of the practitioner and facility, the greater the outcomes and the lower the complication rates for such procedures are. In light of the highly variable complication and outcomes rates in our field, we believe that it is time to establish certification programs for neuromodulation and develop International Centers of Excellence for neuromodulation therapies. Several additional benefits accrue from such a program including improved training and education, improved cost effectiveness of neuromodulation therapies and more efficient use of both government and non-governmental financial support. One drawback could be the distance patients are required to travel to access such a center. The devil, of course, is in the details. What exactly are the criteria necessary to become and maintain a Centers of Excellence designation? Are these criteria the same regionally, nationally and internationally? The INS has convened a Centers of Excellence committee to tackle these challenging issues and the results of their deliberations thus far will be addressed during this presentation.

Tuesday, May 28, 2019
Plenary
Plenary Session 2

30. INS19-0525

PROGRESS IN BRAIN MACHINE INTERFACE

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For people with spinal cord injury, pontine stroke, neuromuscular disease including amyotrophic lateral sclerosis, and other neurologic illnesses, currently available assistive and rehabilitation technologies are inadequate. In severe brainstem stroke and advanced ALS, patients may suddenly or progressively enter a locked-in state of being awake and alert but unable to move or communicate. Clinical translation based on decades of fundamental neuroscience research have yielded intracortical "brain-computer interfaces" (iBCIs) which are poised to revolutionize our ability to restore lost function. Over the past 20 years, neurotechnologies to record the individual and simultaneous activities (action potentials, multi-unit activity, and local field potentials) of dozens to hundreds of cortical neurons have yielded new understandings of cortical function in movement, vision, cognition, and memory. The first, ongoing pilot clinical trials (IDE) of an iBCI system - BrainGate - seek to determine the feasibility of persons with tetraplegia controlling a computer cursor, other external devices, or (via functional electrical stimulation) their own limb simply by 'intending' the movement of their own hand. Through the ongoing multi-institutional BrainGate collaboration, a variety of methods for decoding brain signals are being tested with the hope of not only restoring communication with ubiquitous communication technologies, but also providing a robust, intuitive signal for the long-term control of assistive robotic and prosthetic arms and hands, as well as the reanimation of paralyzed limbs. The platform approach of decoding high resolution neuronal ensemble activity and acting on that information in real-time now supports a wide range of research, particularly toward closed-loop neuromodulation for better and highly personalized management of both neurologic and neuropsychiatric disorders.

Tuesday, May 28, 2019
Plenary
Plenary Session 2

31. INS19-0487

PERSPECTIVES OF GASTROINTESTINAL NEUROMODULATION

J. Chen PhD[1]

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The gastrointestinal (GI) tract is the largest organ in the human body and GI disorders, such as gastroesophageal reflux, abdominal pain, functional dyspepsia, irritable bowel syndrome and constipation. In addition, a few major chronic diseases, such as obesity and diabetes are closely associated with the functions of the gut. Accordingly, there are great potentials for neuromodulation to play an important role in the treatment of the disorders of the gut. Gastrointestinal (GI) neuromodulation can be classified as modulation of the nervous systems for GI diseases and modulation of the gut for GI and GI-related diseases.

Modulation of the nervous system for GI diseases includes 1) emerging method of vagal nerve stimulation for inflammatory bowel diseases, 2) emerging method of spinal cord stimulation for gastroparesis and postoperative ileus; 3) spinal cord stimulation for visceral pain; 4) established method of sacral nerve stimulation for fecal incontinence; 5) potential of sacral nerve stimulation for GI motility disorders, constipation and inflammatory bowel diseases.

Modulation of the GI tract for GI and GI-related disorders includes 1) electrical stimulation of the lower esophageal sphincter for gastroesophageal reflux, 2) gastric electrical stimulation for nausea and vomiting in patients with gastroparesis; 3) gastric electrical stimulation for obesity; 4) potential of intestinal electrical stimulation for obesity and diabetes; 4) colonic electrical stimulation for constipation.

Perspectives of GI neuromodulation will be presented and discussed in this presentation, focusing on emerging therapies. Pros, cons and challenges associated with a few major neuromodulation methods will be discussed. Such as GI stimulation for obesity and diabetes, and sacral nerve stimulation for constipation. For a few potentially novel therapies, mechanisms and clinical perspectives will be highlighted, such as vagal nerve stimulation/sacral nerve stimulation for inflammation and spinal cord stimulation for gastroparesis.

Tuesday, May 28, 2019
Breakout Session
Allied Health Workshop on Neuromodulation - Nurses, Psychologists, Physiotherapists

32. INS19-0500

OUTCOMES FROM THE IMPLEMENTATION OF A POST-IMPLANT REHAB PROGRAM

K. Stone AEP AES ESSAM[1]

[1]*Workplace Physiotherapy, Exercise Physiology, Newcastle, Australia*

This presentation will cover aspects which have influenced the development of a nerve stimulator implant rehabilitation program including education, guidance and exercise/ activity application. Compliance to the protocol, prevalence of complications, alternate approaches to physical upgrading, use of telehealth with remote patients and patient feedback will also be discussed.

Tuesday, May 28, 2019
Breakout Session
Basal or Non-Basal: Intrathecal Regimens for 2019

33. INS19-0377

TAILORING INTRATHECAL THERAPY TO MATCH YOUR PATIENT'S NEEDS

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Intrathecal analgesics were historically administered by continuous basal infusion using an implantable pump to treat refractory pain states. While doses, and the choice of medications were variable, these analgesics were exclusively administered by basal infusion due to non-programmable hardware constraints. Contemporary intrathecal drug delivery systems now permit timed administration and patient controlled bolus delivery with or without basal infusions. In parallel with these intrathecal drug delivery hardware advancements, a body of clinical evidence is emerging in support of clinical outcomes observed when minimizing reliance on basal dosing and tailoring therapy to each patients' pain patterns. During this session, we will challenge the audience's basal dosing paradigms by presenting evidence in support of bolus only administration, and present alternative dosing strategies including combined basal and on-demand bolus dosing, as well as timed bolus administration with or without a basal infusion. Efficacy and outcome data in support of each novel dosing strategy will be presented along with clinical vignettes demonstrating patients who are most likely to succeed with each method of administration. Upon completion of this session, the learner will return to their practice with a broadened skillset and the immediate ability to utilize heterogeneous dosing strategies to treat their patients.

Tuesday, May 28, 2019
Breakout Session
Basal or Non-Basal: Intrathecal Regimens for 2019

34. INS19-0457

FUNCTIONAL IMPROVEMENT WITH CONTINUOUS INTRATHECAL MORPHINE INFUSION IN CHRONIC NON-CANCER PAIN

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Aim of the study: to investigate the long-term (till 48 months FU) results of continuous intrathecal morphine infusion on functional abilities and quality of life in patients suffering from chronic low back and leg non-cancer pain.

Materials and Methods: 44 patients, with chronic non-cancer pain, unresponsive to multimodal analgesic therapy, were selected after a three week trial period with epidural infusion of morphine*. During the trial period, all the drugs taken have been discontinued in order to detect the efficacy of the infusion treatment. The sample size has been defined by ethics committee because of a prospective observational study. After informed consent and positive trial period, patients underwent to implantation of a pump for intrathecal morphine infusion. Pain intensity (VAS: 0-100), functional abilities (Oswestry Disability Index, ODI), and quality of life (Short Form 36 Health Survey, SF-36) were assessed at baseline, 12, 24 and 48 months after the implantation. We also recorded the adverse side effects and complications in order to investigate the safety of the therapy.

Results: Back and leg pain significantly decreased from baseline to 12 months FU visits ($p<0.001$). Performance Functional Status, evaluated with ODI, significantly improved from baseline to each FU visit ($p<0.001$). For what concerns Quality of Life analysed with SF-36 questionnaire, at 12 months a significant improvement was obtained in Physical Component and Mental Component Scores ($p<0.001$) and other significant scores we can see at 24 months ($p<0.001$) and in the following months.

Conclusions: continuous intrathecal morphine infusion, using an implantable programmable pump, is helpful for pain control. It could also improve functional activity, patients' health status and quality of life for a long time.

Tuesday, May 28, 2019
Breakout Session
Basal or Non-Basal: Intrathecal Regimens for 2019

35. INS19-0504

ARE SIDE EFFECTS ASSOCIATED WITH THE LONG-TERM USAGE OF INTRATHECAL DRUG DELIVERY SO FRIGHTFUL?

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Before discussing side effects related to Intrathecal Drug Delivery (IDD), it is important to consider the dose, the type of infusion, the drug(s) used and how these factors can affect side effects. Similar to systemic administration of a medication, side effects with intrathecal administration will be associated with the overall dose and how quickly the dosage is increased. Some patients may be more sensitive to one medication compared to another medication. A lower effective dose should be required when placing medication directly at the site of action. A lower dose should have a lower incidence of side effects. Furthermore, low dose or "micro-dosing" is becoming more common and these very small intrathecal opioid doses will likely have a lower side effect profile than higher traditional doses. Utilizing intrathecal mono-therapy with on-label medications may also decrease the risk of side effects and adverse events. The literature for low dose intrathecal drug delivery will be reviewed specifically looking at the incidence of side effects with a low dose technique. An animal model of CSF flow dynamics will explain why lipophilic and hydrophilic medications may have a similar side effect profile. Intrathecal opioids can still rarely cause respiratory depression and death, especially when utilized with other CNS depressants. One must be vigilant when managing patients with intrathecal drug delivery systems and monitor patients closely according to current standards of care. Side effects and adverse events related to specific medications, the implant procedure, and those attributable to the delivery system itself will be explored. Side effects and adverse events related to intrathecal drug delivery from a large prospective registry will be discussed.

Tuesday, May 28, 2019
Breakout Session
Basal or Non-Basal: Intrathecal Regimens for 2019

36. INS19-0490

THE ECONOMICS OF CANCER RELATED PAIN: NEW DATA TO SUPPORT USE OF TARGETED DRUG DELIVERY FOR BOTH SHORT TERM AND LONG TERM SURVIVORS

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Targeted drug delivery (TDD) is an alternative to systemic opioid treatment that has demonstrated improved pain control, reduced opioid toxicity[1][2], and cost savings when compared to conventional medical management (CMM) yet remains underutilized to treat cancer pain[3]. Healthcare utilization and costs were analyzed in a retrospective claims analysis, as were patient safety and outcomes in prospective surveillance registry. At the onset of the registry in 2003, data was collected to monitor device performance. The protocol was expanded in 2012 to also collect data including adverse events related to the therapy, the device, and implant or revision procedures, and quality of life measures. Patients are enrolled in the registry prior to device implant or replacement and are followed prospectively until death, device explant, or until the patients are no longer able to be followed (i.e. transferred care to another physician).

TDD demonstrates both significant cost savings to U.S. payers when compared to patients treated with CMM and adequate or improved pain control, even as disease progresses. Both long-term and short-term survivors with cancer related are candidates for TDD, especially when systemic opioids do not sufficiently control pain or result in intolerable side effects. Safety outcomes and adverse events are in line with other therapies commonly employed in patients with cancer-related pain[4]. The registry demonstrated statistically-significantly improvements in pain scores at 6 and 12 months and EQ-5D scores showing significant improvement at 6 months. Considering the current opioid epidemic and the high risks associated with high dose opioid use, long-term cancer survivors may also benefit from improved safety with TDD.

[1] Brogan SE et al. A cost utilization analysis of intrathecal therapy for refractory cancer pain: identifying factors associated with cost benefit. Pain Med. 2013;14(4):478-486.

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Tuesday, May 28, 2019
Breakout Session
Deep Brain Stimulation for Pain

37. INS19-0489

STIMULATION OF THE ACCUMBENS REGION

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Patients presenting with persistent and medically-refractory post-stroke hemibody pain and anesthesia dolorosa due to contralateral lesion(s) of thalamic areas and somatosensory pathways can be challenging to treat and suffer significant pain related disability. We enrolled 10 patients with post-stroke pain syndrome in a prospective, double-blind, randomized, placebo-controlled, double-arm crossover trial over 24 months. Patients had had severe pain for more than six months and had failed treatment with at least one antidepressant, one anticonvulsant and one opioid. A quadripolar lead was implanted along the ALIC into the VS bilaterally, with the tip ~3-5 mm ventral to the junction between the ALIC and the anterior commissure.

A total of nine patients completed the trial and primary and secondary clinical outcome measures were prospectively acquired in each study phase. Active DBS versus sham stimulation was associated with an increased probability of response (i.e. ≥ 50% improvement) in the Montgomery-Åsberg Depression Rating Scale (44% DBS ON v. 19% DBS OFF, p=0.02), Beck's Depression Inventory (45% DBS ON v. 27% DBS OFF, p=0.004), and the Affective Pain Rating Index (39% DBS ON v. 18% DBS OFF, p=0.002) and Present Pain Intensity (10% DBS ON v. 3% DBS OFF, p=0.002) in the Short-form McGill Pain Questionnaire. Individual patients showed changes in the following measures but we did not observe significant group effects: Visual Analog Scale, Pain Disability Index and the Sensory Pain Rating Index in the Short-form McGill Pain Questionnaire.

Our results suggest that DBS of the ventral capsule and ventral striatal area is safe and feasible. DBS can effectively modulate the affective sphere of chronic pain, benefiting select patients. However, we did not observe significant group effects in the Pain Disability Index or Visual Analog Scale.

Tuesday, May 28, 2019
Breakout Session
Deep Brain Stimulation for Pain

38. INS19-0512

CINGULATE STIMULATION

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Chronic pain poses a great socioeconomic burden. Unlike acute pain, chronic pain has been associated with impairment in cognition and attention, development of psychiatric comorbidities such as depression and anxiety, dependence on opioid analgesia, and decline in social functioning. Further, many chronic pain states, such as neuropathic pain, remain difficult if not impossible, to treat with available therapeutics. Chronic pain is an integrated experience of sensory (pain perception), affective (response or interpretations of pain) and cognitive aspects.

Anterior cingulate cortex (ACC) has been known to be a key structure for the affective aspect. The dACC(dorsal) has been implicated in circuits involving decision making, emotional salience, learning, reward processing, empathy, attention, intention, addiction, and affective aspects of pain. This region has been targeted successfully with lesioning techniques for the treatment of affective disorders, obsessive-compulsive disorder, and chronic refractory pain, highlighting the diversity of neurological processes in which it is involved. The role dACC has been further clarified by the new age imaging. fMRI Studies have consistently demonstrated increased activation of dACC during both empathic and experienced pain. Studies have shown that each chronic pain syndrome evokes a unique pattern and it generally activates brain regions that are more involved with emotional and motivational states, than acute nociception, such as dACC. There has been additional neurophysiological data to support the role of dACC in chronic pain. This has led to the recent interest in exploring DBS of dACC.

Lesioning of the anterior cingulate gyrus has been performed, with acceptable outcome, for more than 60 years to treat cancer pain. The first report of DBS was published in 2007, where a patient showed better response to dACC stimulation than to the periventricular gray matter stimulation. This was followed by a case report from the Oxford group in 2013 and a case series from the same group in 2017. In a follow up of 22 patients undergoing dACC DBS (12 patients having a mean follow-up of 38.9 months) various outcome measures were evaluated. Six months post-surgery, there was statistically significant improvement in the mean numerical rating score for pain, McGill pain questionnaires, EuroQol-5D and Short-form 36 quality of life scores. The authors concluded that dACC alleviates chronic pain and improves quality of life.

The presenter will discuss the role and future of dACC DBS.

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Breakout Session
Deep Brain Stimulation for Pain

39. INS19-0466

DEEP BRAIN STIMULATION FOR PAIN: CON

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DBS for pain was first described in 1954. It therefore represents one of the earliest uses of neurostimulation. However, instead for pain, DBS for movement disorders is currently widely used in the routine. Literature offers many case series reporting limited overall effects of DBS in patients with various chronic pain conditions. Placebo effects are significant in this population. Since the technique remains "Off-label" only a small number of surgeons report DBS for pain. No RCT's are available. The only RCT which was ever established beginning of the 2000 (Concept trial Medtronic) failed due to a limited patient recruitment. There are no biomarkers or predictors for pain relief. DBS may be employed for a number of nociceptive and neuropathic pain states, including cluster headaches, LBP, Brown Sequard, FBSS, peripheral neuropathies, facial deafferentation pain, and pain due to brachial plexus avulsions.

In a recent review (Levy R. et al., 2016) of seven studies, 163 patients were identified with those heterogeneous conditions. All were case series with major limitations, such as retrospective data collection, poor selection criteria, lack of accurate diagnosis of neuropathic pain and poor reporting of adverse events. They used heterogeneous methodological approaches and targeted structures.

Although the mean pain intensity reduction approached 50%, results were imprecise (large confidence intervals) and inconsistent, with large variations in reported pain relief across studies. It was also impossible to define subgroups according to specific diseases. However, the best DBS results were obtained with stimulation of the somatosensory thalamus in patients with peripheral neuropathic pain. DBS has thus far been aimed largely at the sensory pathways, which mediate only a portion of the overall pain experience. Medial pathways are more affected by burst stimulation, which was not tested for DBS yet. Given the very low quality of evidence and the current uncertainty on DBS effects, the recommendation for DBS in neuropathic pain is inconclusive. There is a need for:

- RCT's proving reliable evidence on DBS efficacy;
- to define efficacious DBS target and stimulation algorithms
- to use diagnostic tools to better define subtypes of pain which might respond to stimulation in order to improve selection criteria
- to include a large patients cohorts with similar pain conditions to determine

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40. INS19-0503

MOTOR CORTEX STIMULATION FOR PAIN AND RELATED CONDITIONS: PRO

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While there exists a large body of literature reporting the significant efficacy of MCS for chronic pain therapy, several investigators have more recently discussed their frustration with MCS as a long term successful therapy. Is MCS a panacea for neuropathic pain or is the effect merely placebo?

Chronic stimulation of the precentral cortex for the treatment of pain was first reported by Tsubokawa in 1991. A number of reports have followed describing the use of MCS for intractable pain syndromes including post-stroke pain, phantom limb pain, spinal cord injury pain, postherpetic neuralgia, and neuropathic pain of the limbs or face. MCS has shown particular promise in the treatment of trigeminal neuropathic pain and central pain syndromes such as post-stroke thalamic pain syndrome, for which there are few other effective treatments. Based upon these reports, post-stroke pain responds well to MCS, with approximately two-thirds of reported patients achieving adequate relief. Several studies have reported excellent results of using MCS for the treatment of trigeminal neuropathic pain, with 75% to 100% of patients achieving good to excellent pain relief. A review of the literature has corroborated these results, showing that 29 of 38 (76%) reported patients with neuropathic facial pain achieved ≥ 50% pain relief with MCS.

Apparently negative results with MCS for pain have also appeared. These studies have largely reported overall positive results for pain relief but report blinded periods of no stimulation during which pain scores remain depressed from baseline. While this has been suggested to reflect a placebo effect of MCS, a more plausible explanation leading to a type II error is that either no or insufficient washout periods were used in these studies. More than once I have had the experience of a patient returning with complaints that their MCS has stopped providing pain relief. After taking a careful history and performing some calculations of expected battery life based upon stimulation parameters, it became clear that the battery should have expired several months before the return of pain. More notably, pain relief returned with replacement of the pulse generator. This raises the equally likely possibility that the MCS effect, when successful, can be quite long lasting and can thus confound clinical trials that do not take it into account.

Other issues requiring discussion include the need for trialing, either with navigated rTMS or implanted leads, proper lead targeting, surgical technique and MCS programming. While MCS thus appears to hold great promise for patients with trigeminal neuropathic pain, post-stroke pain, and pain which has failed to respond to other less invasive forms of neurostimulation, MCS for intractable pain requires further rigorous, prospective study.

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Breakout Session
New Developments in Neuromodulation for Gastrointestinal Conditions

41. INS19-0469

NEW METHODS AND APPLICATIONS USING THE SCIENCE UNDERLYING GI NEUROMODULATION: LOW AND HIGH RESOLUTION MAPPING

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Rhythmic and ordered electrical slow wave patterns in the gastrointestinal tract are critical for the efficient breakdown and transportation of ingested food. Disordered slow wave activity in the stomach has been associated with a number of functional motility disorders, including: gastroparesis, chronic unexplained nausea and vomiting and functional dyspepsia. Such disorders can have delayed or compromised gastric emptying and the patients have a compromised quality of life due to consistent nausea, bloating and vomiting.

The first electrical recordings from the gastrointestinal tract were made almost 100 years ago. Traditionally, a limited number of electrode sites (low-resolution recordings) have been used. More recently, the use of hundreds of electrodes placed in a regular grid (high-resolution recordings) has provided improved spatio-temporal details about the underlying slow wave propagation patterns. The use of external electrical stimuli to treat functional motility disorders has been widely proposed but the majority of studies investigating the electrophysiological effects of such therapies have historically been limited to low-resolution recordings. The combined use of external electrical stimuli with high-resolution electrical mapping allows the efficacy of stimulation parameters to be more comprehensively evaluated and quantified.

Two broad categories of external stimuli have been proposed: gastric electrical stimulation (using high-frequency, low energy stimuli, in the range of 1-5 s period, 5-20 mA, 0.33-0.45 ms pulse width at a rate of 15-55 Hz) and gastric electrical pacing (using low-frequency, high energy stimuli, in the range of 18-22 s period, 2-6 mA, 50-500 ms pulse width). Recent acute, inter-operative studies have shown that high-frequency stimulation methods were unable to alter the underlying gastric slow wave patterns. Equivalent studies utilizing high-energy pacing methods in pigs and humans have shown the ability to rapidly change and control the underlying slow wave patterns and frequencies. Longer-term studies have shown that stimulation methods were able to alleviate a patient's symptoms, but not improve gastric emptying rates. There have been a limited number of long-term studies using pacing methods, and further investigation is now needed to optimise protocols and to validate therapeutic benefit.

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Breakout Session
New Developments in Neuromodulation for Gastrointestinal Conditions

42. INS19-0383

ELECTROCEUTICALS FOR MAPPING AND MODULATING GUT ACTIVITY: TOWARDS CLOSED-LOOP MANAGEMENT OF GASTROPARESIS

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Gastrointestinal (GI) motility is coordinated by underlying bio-electrical events known as slow waves. High-resolution (HR) mapping of the slow waves has become a fundamental tool for accurately defining electrophysiological properties in gastroenterology, including dysrhythmias in gastric disorders such as gastroparesis, chronic nausea and unexplained vomiting, and functional dyspepsia. Currently, HR mapping is achieved via acquisition of slow waves taken directly from the serosa of fasted subjects undergoing invasive abdominal surgery.

As in cardiac electrophysiology, implantable pulse generators have been used for stimulating the stomach. Conventionally, two types of pulses have been applied for potential therapeutic effects for gastroparesis: short pulses (high frequency/low energy) and long pulses (low frequency/high energy). Low-energy stimulation is typically delivered with a pulse-width in the order of a few hundred microseconds, at frequencies ranging from 5 to 100 Hz, and may improve symptoms such as nausea, vomiting, and bloating. High-energy stimulation (or pacing) is typically delivered with a pulse-width in the order of milliseconds (10-600 ms), at frequencies akin to the natural gastric frequency (i.e., 3 cpm). High-energy stimulation has demonstrated potential to pace slow waves and improve motility. Due to high energy consumption the latter stimulation method has not been widely used.

We have developed novel bioelectronics that can be used for HR mapping and modulating of the gut activity in small and large animals. These devices are implantable and can wirelessly communicate with a computer station to visualize the recorded signals in real time. Operator can also use the graphical user interface on the computer to modify the electrical stimulation parameters. The implant can be wirelessly recharged through inductive coupling transmission. The system has been validated in small and large animals. We have been able to map the stomach activity wirelessly in high resolution, and modulate the stomach activity in various paces. Also, we have used the system –with lower number of channels– to record slow wave signals from patients with gastroparesis. We are planning to integrate the mapping and modulating technologies into a closed-loop therapy, and to translate the developed technologies to human.

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Breakout Session
New Developments in Neuromodulation for Gastrointestinal Conditions

43. INS19-0451

NEUROMODULATION FOR INFLAMMATORY BOWEL DISEASE

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Introduction: The vagus nerve (VN), the longest nerve of the organism, is a mixed nerve containing 80% and 20% of afferent and efferent fibres respectively. The VN has a dual anti-inflammatory properties via its afferents through the hypothalamic–pituitary–adrenal axis and efferents through the cholinergic anti-inflammatory pathway (anti-TNF effect). Thus neuromodulation of the VN through VN stimulation (VNS), as a non-drug therapy, could be of interest in the treatment of inflammatory bowel disease [IBD; Crohn's disease (CD) and ulcerative colitis] where anti-TNF drugs are presently the gold standard. We have reported that *i)* vagal tone is blunted in CD patients and is associated with a high plasmatic TNF level, *and ii)* VNS improves colitis in rats. Consequently, in a translational approach, we performed a pilot study of VNS in CD patients.

Patients and Methods: Nine patients (5M, 4W) with mild/moderate CD were selected based on clinical (CDAI), biological (CRP/fecal calprotectin) and endoscopic (CDEIS) criteria. VNS was performed with an electrode around the left cervical VN under neurosurgical intervention and connected to a neurostimulator (Cyberonics, Lyon, France). Neurostimulation parameters were: 10 Hz, 500 micros, 0.5 mA, 30 sec ON, 5 min OFF in continuous cycles. Patients were followed-up for 1 year on the above criteria. Plasmatic concentrations of cytokines/chemokines involved were assayed on inclusion and at one year.

Results: At baseline, all patients had active CD, eight had an over-endoscopic scoring and seven had abnormal CRP and/or fecal calprotectin. Two patients were removed from the study at 3 months post-implantation and treated pharmacologically or surgically for persistent active CD. Post-VNS assays of these two patients were performed at month 3. By comparison to a cytokinergic profile of 12 controls, patients showed an increase of the following cytokines: 7 out of 9 patients had IL6 level increased by 2.5 to 10 fold; 6 out of 9 patients had IL23 level increased by 2 to 15 fold; 5 out of 9 patients had IL1beta, IL17 and IL12 levels increased by 2 to 5.5 fold, 2 to 5 fold and 2 to 6 fold respectively. 4 out of 9 patients had interferon-gamma and MIP1alpha levels increased by 2 to 4.5 fold and 2 to 2.5 fold respectively; 3 out of 9 patients had TNFalpha increased 2 to 4 times. After 12 months of VNS, the 9 patients were still under stimulation. Seven patients had only VNS as a treatment. The seven patients who completed the study had a clinical score lowered from 80 to 230 points (delta CDAI), five of them had an endoscopic score decreased from 50 to 100%. Six out of nine patients had IL6 level decreased from 29 to 97%. 5 out of 9 patients had TNFalpha level decreased by 36 to 70%. 5 out of 9 patients had an IL23 level decreased from 5 to 51%, but did not reach normal values. 4 out of 9 patients had IL12 and MIP1alpha levels decreased by 3 to 44% and 3 to 32%, respectively, but did not reach normal values. Finally**,** IL17, IL1beta, interferon gamma and IL10 had a decreased rate for 3 out of 9 patients.

Conclusion: VNS appears as an interesting therapeutic alternative to conventional drug therapy for patients with mild to moderate CD. The results of this pilot study partially confirm the anti-TNF effect of VNS which also appears to impact other cytokines such as IL6 and IL23. These preliminary data warrant further investigation in a larger longitudinal cohort of CD patients. Data, except cytokinergic profile, on the first seven implanted patients after 6 months of VNS have been published previously (Neurogastroenterol Motil 2016;28:948-53).

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Declaration: no financial disclosure for the present work.

Tuesday, May 28, 2019
Breakout Session
New Developments in Neuromodulation for Gastrointestinal Conditions

44. INS19-0494

NEW APPLICATIONS FOR MID GUT STIMULATION FOR METABOLIC DISORDERS: GI STIMULATION FOR DIABETES AND OBESITY

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Obesity is one of major public health problems in the world. In 2015-2016, 39.6% US adults are obese and 7.7% are extreme obesity. Obesity is a major risk factor for diabetes; currently 9.4% US population had diabetes which costs $327 billion in 2017. While various methods have been investigated or introduced, the bariatric surgical procedures are the only effective long-term therapies for treating obesity. Due to mortality and morbidity, the bariatric surgery is only limited to a small portion of patients with extreme obesity. Gastric electrical stimulation (GES) has been reported as a potential therapy for obesity from both basic and clinical research; the mechanisms of action are hypothesized to be related to the delayed gastric emptying, activation of satiety neurons in the ventral medial hypothalamus and the suppression of hunger hormone ghrelin. GES therefore resulted in the decreased appetite and increased satiety and then the reduced food intake and body weight. Intestinal electrical stimulation (IES) has been reported to delay gastric emptying, accelerate small bowel transit and reduce fat absorption; it was also shown that IES reduced gastric ghrelin and increased the release of glucagon-like-peptide-1. Accordingly, IES can be considered as an electronic counterpart of bypass therefore has the therapeutic potential for both obesity and diabetes. Several implantable gastrointestinal electrical stimulation devices for treating obesity and diabetes are introduced, and their effects on food intake, body weight and glucose level are presented, followed with the discussion on the limitation of the devices and the study design. Finally, our viewpoint on potential of GES and IES for obesity and future development of the GI stimulation therapy are provided.

Tuesday, May 28, 2019
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New Developments in Neuromodulation for Gastrointestinal Conditions

45. INS19-0456

NEW NEUROMODULATION THERAPIES FOR COLONIC DISORDERS

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Incontinence and constipation are significant pathologies of the large bowel. In the last 15 years, studies using electrodes implanted onto sacral nerves or using temporary electrodes on the skin have shown that large bowel function can be modified by neural stimulation. While still in its infancy, this area of research is beginning to show promise.

Sacral nerve stimulation using implanted electrodes has shown good results for incontinence but mixed outcomes for constipation. The technique requires surgical implantation of the electrodes and stimulator and is well developed. Temporary placement of electrodes is used to determine if patients are responders, then permanent stimulators are implanted in the buttocks. The technique is expensive but where effective, has major impact for the patient.

Studies in the early 2000's reported that transcutaneous electrical stimulation (TES) could modify large bowel function and improve constipation. There has been an increasing number of centres worldwide investigating the potential for non-invasive electrical stimulation of the large bowel using TES. Studies have been in children and adults with slow transit constipation, anorectal retention and spina bifida, with variations in number and position of electrodes and electrical current frequency. Effects include increased colonic contractions and defecation frequency, reduced soiling, straining and laxative-use, improved stool consistency, sensory awareness, health-related quality of life and overall bowel function measured with questionnaires. Stimulation of the large bowel may also have effects upstream in the stomach.

Many studies are pilots with low quality data but RCTs are appearing. Stimulation has been performed 20-60 mins/day, 3-7 times/week for 1-6 months. Effects take weeks to months to occur, and last for months to years after stimulation ceases suggesting neuronal modulation. Studies are becoming more sophisticated, including control and comparator arms and measures of physiological changes in the bowel and nervous system (parasympathetic, sympathetic, sensory and central awareness).

Transcutaneous Electro-Acupuncture (TEA) on classic acupuncture sites (ankle and knee) have also produced improvement in constipation. Recent studies suggest that TEA increases vagal activity and decreases sympathetic activity adjusting autonomic function balance. TEA was effective in the prevention of stroke-induced constipation.

Transcutaneous stimulation is non-invasive and cheap. Future directions include examining mechanisms of action, optimal stimulation parameters, which patient groups respond and if combination with other treatments such as diet or physiotherapy could be additive and development of specific devices. The next 10 years will produce higher quality studies and data on neuromodulation of the bowel.

Wednesday, May 29, 2019
Plenary
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46. INS19-0470

CURRENT CONCEPTS AND EVIDENCE IN NEUROMODULATION FOR HEADACHE

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Current Concepts and Evidence for Neuromodulation for Headache

Peter J Goadsby, NIHR-Wellcome Trust King's Clinical Research Facility/SLaM Biomedical Research Center, King's College Hospital and King's College London, UK

Neuromodulation of primary headache disorders has advanced significantly in the last decade (1). By exploiting pathways that have been explored in the laboratory (2), clinicians have developed approaches that now benefit many highly disabled patients. Techniques can be broadly divided into invasive and non-invasive, and I will cover approaches used in practice, recognising other modalities, which are currently largely experimental, are also being studied. Invasive approaches include occipital nerve stimulation for migraine and cluster headache, and deep brain stimulation and sphenopalatine ganglion stimulation for cluster headache. Non-invasive approaches include single pulse transcranial magnetic stimulation for migraine, non-invasive vagus nerve stimulation for migraine and cluster headache, and external trigeminal (supraorbital) nerve stimulation for migraine. Patients often seek non-pharmaceutical treatments; neuromodulation offers opportunities to treat patients in novel and effective ways.

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Wednesday, May 29, 2019
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47. INS19-0513

PROSPECTIVE 12 MONTH OUTCOMES OF MULTI-CENTER TRIALS OF 10 KHZ SPINAL CORD STIMULATION IN THE TREATMENT OF ARM AND NECK PAIN (AUSTRALIAN AND NORTH AMERICAN CENTERS)

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Background: Intractable neck and upper limb pain has historically been challenging to treat with conventional spinal cord stimulation (SCS) being limited by obtaining effective paresthesia coverage[1]. The goal of this study is to assess the safety and effectiveness of the 10 kHz SCS system, a paresthesia-independent therapy[2,3], in the treatment of neck and upper limb pain.

Methods: Subjects with chronic, intractable neck and/or upper limb pain of ≥5 cm (on a 0-10 cm visual analog scale [VAS]) were enrolled in three Australian centers (ACTRN12614000153617) and six US centers (NCT02385201) following investigational device exemption (IDE) from Food and Drug Administration (FDA) and institutional review board (IRB) approval. Each subject was implanted with two epidural leads spanning C2-C6 vertebral bodies. Subjects with successful trial stimulation were implanted with a Senza® system (Nevro Corp., Redwood City, CA) and included in the evaluation of the primary safety and effectiveness endpoints. Results are presented as mean ± SD.

Results: A total of 38 and 55 subjects were trialed and 31 and 46 subjects received a permanent implant (89.1% and 82.6% success rate) in Australia and the US, respectively. At the 3-month primary endpoint, 23 of 30 (76.7%) and 39 of 45 (86.7%) subjects were responders with at least 50% pain relief from baseline. One study-related SAE in Australia and two study-related SAEs in USA were reported. No neurological deficits or paresthesias from 10 kHz SCS were reported in either study.

Baseline neck pain scores of 8.1±1.2 cm (N=27) and 7.4±1.5 cm (N=45) improved to 2.2±2.0 cm (N=27) and 1.5±1.6 cm (N=37) at 12 months (74.2%±22.6% and 79.1%±23.7% pain relief), respectively. Baseline upper limb pain scores of 7.3±1.2 (N=18) and 7.1±1.4 cm (N=24) improved to 2.8±2.4 cm (N=17) and 1.0±1.1 cm (N=20) at 12 months (61.8%±32.4% and 85.9%± 15.2% pain relief) respectively. Responder rates were 85.2% (N=23/27) and 89.2% (N=33/37) for neck pain and 76.5% (13/17) and 95.0% (N=19/20) for upper limb pain respectively. Disability, as measured by pain disability index score, decreased from 42.6±14.7 (N=31) and42.4±11.8 (N=45) at baseline to 21.2±18.3 and 16.9±12.8 (N=39) at 12 months post-implant, respectively.

Conclusions:

Results indicate 10 kHz SCS can provide durable and long-lasting relief to patients with upper limb and neck pain.

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Wednesday, May 29, 2019
Plenary
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48. INS19-0444

CURRENT STATE OF BATTERY-FREE SYSTEMS

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Along with continued development of multiple waveforms to enhance pain relief responses to implanted neuromodulation devices comes a renewed interest in applying evolving device technology for SCS, DRG and PNS applications using external power sources as alternatives to implanted battery/generators. Battery-free neurostimulation devices offer a variety of external/wearable power solutions avoiding traditional tunneling and pocketing of IPG hardware. This can be an attractive alternative for certain patient subsets with targeted neuromodulation indications and provides new device technology rather than repurposing conventional spinal cord stimulator systems.

Wednesday, May 29, 2019
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49. INS19-0448

RECOMMENDATIONS OF THE JOINT INS, ION AND IMMPACT GROUP

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Improving the quality of clinical research is a shared goal of The International Neuromodulation Society (INS), the Institute of Neuromodulation (IoN), and the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT). The three organizations organized a two-day meeting in Washington, DC in November, 2018 to develop consensus reviews and recommendations for improving the design, execution, and interpretation of clinical trials of spinal cord stimulation (SCS) for pain. Invited participants came from multiple specialties in clinical practice, academia, regulatory agencies, consumer groups, and industry. The proceedings of the meeting will appear in full on the IMMPACT.org website, along with 21 previous meetings. Consensus recommendations for improving the design, execution, and interpretation of clinical trials of SCS for pain are currently under development.

Wednesday, May 29, 2019
Breakout Session
Neuromodulation for Pain: Sensing and Feedback

50. INS19-0481

USING WEARABLE SENSORS AND IMPLANTABLE NEUROMODULATION DEVICES TO MEASURE FUNCTION

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Neuromodulation is a scientifically validated method for reducing pain in people with neuropathic back and leg pain. Studies to date that provide the robust scientific evidence of the clinical utility of neuromodulation have focused on pain reduction as the primary end point to demonstrate efficacy. It is presumed that a reduction in pain would likely translate to improvements in physical function in those patients with disability. Secondary endpoint data analysis of subjective assessment of disability (typically using a validated scoring system such as the ODI or Roland Morris Disability Questionnaire – [RMDQ]) has thus far confirmed this presumption. While this is a pleasing trend to observe, there are some factors that require careful consideration. The measures used are subjective and therefore a risk of information bias exists. Clinical research has demonstrated that ODI and RMDQ do not correlate well with objective measures of activity in people with chronic pain who tend to either over-estimate or under-estimate their functional prowess [15]. An ideal tool for assessing the function and ability of pain patients implanted with neuromodulation devices would be capable of providing objective measurements of activity. There are currently a number of external wearable biosensor monitors of clinical grade that could be used in this fashion [5-14]. There is also an implantable neuromodulation impulse generator (IPG), Intellis™implantable [JP1] neurostimulator, that has an embedded accelerometer capable of recording such data. To date none of these tools have been validated to measure function in patients using neuromodulation to manage their pain.

This presentation will explore the limitations of subjective tools for measuring function and disability. Clinical-grade devices that objectively measure function will be explored. A validation study to correlate functional measurement with an external wearable sensor (VitalPatch) and a neuromodulation IPG (Intellis™implantable neurostimulator) will be presented. Future studies will aim to provide clear evidence that neuromodulation for chronic pain improves objective measures of function and thereby reduce disability. The benefit of such research will assist in maintaining a clear value-based health care argument for the ongoing use of neuromodulation for chronic pain sufferers the world over.

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Wednesday, May 29, 2019
Breakout Session
Neuromodulation for Pain: Sensing and Feedback

51. INS19-0496

FEEDBACK STIMULATION OF THE DORSAL COLUMNS

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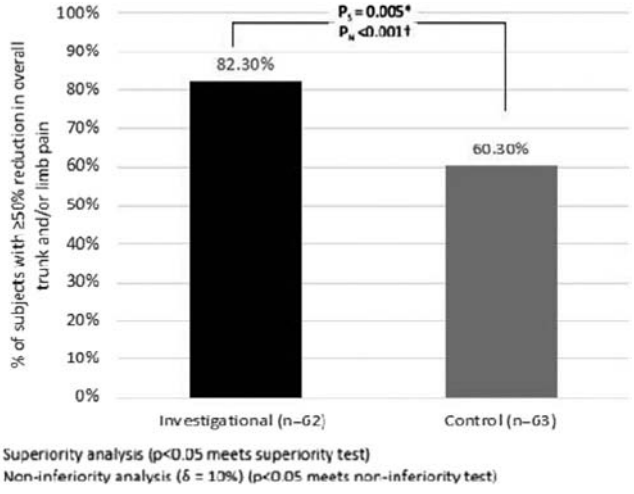
Introduction: Spinal cord stimulation (SCS) activates large, myelinated primary afferent fibers located in the dorsal column (DC) of the spinal cord to provide analgesia. All current SCS technologies are fixed-output systems that deliver stimulation without monitoring the DC activation ("open-loop"). The relationship between the SCS electrical field and DC is dynamic; any change will impact the magnitude of DC activation and potential therapeutic effect. Closed-loop SCS uses evoked compound action potential (ECAP) measurement as a tool to control and maintain therapeutic DC activation in real time, modulating energy delivered with each stimulus.

Methods: This abstract presents a protocol of an ongoing, multicenter, prospective, randomized, double-blinded, pivotal trial comparing closed-loop (CL) (EvokeTM; Saluda Medical, Sydney, Australia) with open-loop (OL) SCS. Adult patients (n=134; aged 18-80 years) with chronic low back and leg pain; Visual Analogue Scale (VAS) score ≥6 cm for leg, back, and overall pain; and Oswestry Disability Index score of 41 to 80 (severely disabled or crippled) at baseline were included.

Results: Study execution and design resulted in the same care for both treatment groups, along with the maintenance of the blind in all patients. The randomization generated directly comparable treatment groups in not only baseline characteristics, but also in neurophysiological properties, supporting the validity of comparisons between the groups. The study demonstrated CL-SCS met superiority at the 3-month primary outcome (% of subjects with ≥50% reduction in overall trunk and limb pain without increase in baseline medications (Figure 1)). Neurophysiological measurements showed statistically significant differences in SC activation (Figure 2 and Figure 3) and time in the therapeutic window (Figure 4) compared to open-loop SCS.

Conclusion: The Evoke closed-loop SCS, which utilizes ECAP measurements to capitalize on the mechanisms of action of SCS by objectively identifying, optimizing, and maintaining individualized therapeutic SC



activation levels during physiological changes and movement, has proven to have comparable safety to existing SCS ystems and in the clinical trials conducted to date deliver superior overall pain relief to the compared open-loop SCS. This ongoing study continues to evaluate the safety and efficacy of closed-loop SCS in a double-blinded, controlled fashion. Continued monitoring of human neurophysiological recordings is leading to a deeper understanding of the mechanism of action of SCS.

Wednesday, May 29, 2019
Breakout Session
Neuromodulation for Pain: Sensing and Feedback

52. INS19-0478

LONG-TERM OUTCOMES FROM THE AVALON STUDY: A PROSPECTIVE MULTICENTER STUDY EVALUATING CLOSED-LOOP SCS IN THE TREATMENT OF CHRONIC BACK AND LEG PAIN

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[5]*Precision Brain, Spine and Pain Centre, Melbourne, Australia*
[6]*Inner West Pain Centre, Sydney, Australia*
[7]*Saluda Medical, Sydney, Australia*

Objective: Current SCS systems deliver stimulation with a fixed output to the dorsal columns without adjusting to the spinal cord's response. A new SCS system measures evoked compound action potential (ECAP) and responds on every stimulation pulse to optimize spinal cord activation within a subject's therapeutic window. The effectiveness of this closed-loop SCS system for pain relief and other outcomes was investigated.

Methods: Chronic pain subjects who were successfully trialed with a closed-loop SCS system received a permanent system. Subject ratings of pain (100-mm visual analogue scale [VAS] and Brief Pain inventory [BPI]), function (Oswestry Disability Index [ODI]), sleep (Pittsburgh Sleep Quality Index [PSQI]), and quality of life (EuroQol [EQ-5D-5L]) were collected at baseline and follow-up visits. Objective neurophysiological measures based on ECAPs were also evaluated. These included therapeutic window, magnitude of ECAP amplitude, and other neurophysiological properties. All subjects have reached the 12-month endpoint and 90% of subjects have reached the 18 months.

Results: Outcomes were maintained long-term with 77% of subjects experiencing ≥50% back pain relief and 79% of subjects with ≥50% leg pain relief at 12 months. Traditionally back pain is difficult to treat and within the back pain cohort 56% of subjects were high responders (≥80% pain relief) Significant improvements in secondary outcomes (BPI, ODI, PSQI, and EQ-5D-5L) supported the profound response in pain (Table 1). At 12 months, the median time in the therapeutic window was 85%, and

Table 1. Patient reported outcomes.

	Back Pain Reduction (mean)	Leg Pain Reduction (mean)	Significant reduction in BPI Severity*	Significant reduction in BPI Interference*	Significant ODI Reduction†	PSQI Reduction (mean)
3 months	69%	76%	89%	76%	70%	3.5
12 months	72%	72%	91%	84%	77%	3.1
18 months	76%	74%	97%	83%	80%	3.4

*Significant reduction considered a 1-point change in BPI. The percentage represents subjects with >1-point change in BPI.
†Significant reduction considered a 10-point change in ODI. The percentage represents subjects with >10-point change in ODI.

Table 2. Percent time in therapeutic window and other device measures (median values presented).

	Percent Time in Therapeutic Window	Percent Time above Therapeutic Window	Percent Time below Therapeutic Window	Mode ECAP Amplitude [μV]	Conduction Velocity [m/s]	Chronaxie [μs]	Rheobase [mA]
3 months	97%	0.02%	3%	23	56	356	5.2
12 months	85%	0.15%	5%	29	53	317	3.4
18 months	98%	0.10%	2%	27	56	320	3.1

the mode ECAP amplitude was 29μV. A median conduction velocity of 53 m/s was measured, which is within the reported range of 16-100 m/s for Aβ sensory fibers (Table 2).

Conclusions: The majority of subjects experienced profound and sustained pain outcomes through 12 months, a result of maintenance of spinal cord activation within the therapeutic window. In addition, the potential clinical application of neurophysiological measurements may be to monitor compliance with the therapy, to provide the ability to evaluate the integrity of the spinal cord, to give insight into the interaction between medications and stimulation, and to evaluate changes in neural activation and conduction properties over time. The study is ongoing with updated results will be presented at the congress. In addition, a multicenter, double-blind, randomized controlled trial in the United States is further investigating neurophysiology and pain outcomes (clinicaltrials.gov ID #: NCT02924129) with the data also being presented at INS in Sydney.

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

Wednesday, May 29, 2019
Breakout Session
Neuromodulation for Neuro-Rehabilitation and Stroke

53. INS19-0482

NEUROMODULATION FOR NEUROREHABILITATION OF MOTOR DISORDERS FOR STROKE AND SPINAL CORD INJURY: AN OVERVIEW

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The International Neuromodulation Society has defined therapeutic neuromodulation as "the alteration of nerve activity through targeted delivery of a stimulus, such as electrical stimulation or chemical agents, to specific neurological sites in the body" (1). Therapeutic neuromodulation can improve functional recovery and relieve neurological symptoms associated with stroke and spinal cord injury (SCI), which has been highlighted by a tenfold increase in the number of studies cited in this field (Institute for Scientific Information, January 2019). However, the overall quality of these studies needs to be assessed to facilitate better evidence-based choices about health interventions, especially as recent advances in this field has attracted intense online media attention (Altmetric. Bodleian Oxford Library, January 2019).

In this workshop leading international researchers in the field of therapeutic neuromodulation for SCI and stroke will present their latest results for improving motor system neurorehabilitation using both invasive and non-invasive neuromodulation techniques, ranging from repetitive magnetic motor cortex, transcutaneous spinal and deep brain cerebellum stimulation. Each speaker will highlight the clinical impact of their research line and the priority areas that need to be addressed for further technical development. Results from a systematic review of non-invasive transcutaneous spinal cord stimulation for SCI motor neurorehabilitation will be presented, with a special emphasis on stimulation parameters, clinical trial design and outcome measures. Finally, two ongoing research projects at the Hospital Nacional de Parapléjicos and the Universidad Castilla-La Mancha will be introduced to the audience. The NEUROTRAIN project will apply lumbosacral transcutaneous electrical spinal stimulation in combination with intensive cycling, with the aim of potentiating gait function and controlling spasticity for patients with incomplete SCI. In parallel the RECODE project will assess how non-invasive transcutaneous spinal and transcortical direct current stimulation, synchronized with robotic exoskeletons, can potentiate gait rehabilitation after SCI.

Acknowledgements: Funding support provided by the NeuroTrain (FIS 2017) and Recode project (Explora Ciencia/Tecnología 2017 DPI2017-9111-EXP).

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Wednesday, May 29, 2019
Breakout Session
Neuromodulation for Neuro-Rehabilitation and Stroke

54. INS19-0464

NONINVASIVE BRAIN STIMULATION FOR STROKE

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Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation that has a long history of development. Since the beginning of the 20th century, tDCS has been applied in various neurological diseases. The position of the electrodes may modulate the neuronal excitability differently. Anodal tDCS (a-tDCS) results in corticomotor depolarization and increases motor cortex excitability. On the other hand, cathodal tDCS (c-tDCS) leads to hyperpolarization and reduces the excitability. Nowadays experimental tDCS protocols, which are considered safe in humans, suggest a stimulating currents of 1-2 mA using electrode sizes between 25(5*5) and 35(5*7) cm^2 for durations of 10 to 20 min. After Stroke, the activity of the ipsilesional hemisphere further decreases while the activity of the contralesional hemisphere increases due to interhemispheric inhibition. It has been demonstrated that ipsilesional hemisphere activity could be increased by a-tDCS application and the contralesional hemisphere activity decreased by c-tDCS application. Therefore, a-tDCS and c-tDCS were applied to result in balanced hemispheric activity and motor functional improvement. Recently, studies further combined tDCS with other interventions to result in long term effect on motor function. Although, recent studies showed a strong therapeutic potential of tDCS for post-stroke motor rehabilitation, its neurophysiological mechanisms are not fully understood. In conclusion, tDCS may modulate brain activity to improve motor performance, and its effect could be enhanced by combining with exercise. However, effects of tDCS may be influenced by patient's characteristics, such as lesion site or post-stroke duration.

Wednesday, May 29, 2019
Breakout Session
Neuromodulation for Neuro-Rehabilitation and Stroke

55. INS19-0488

INVASIVE BRAIN STIMULATION FOR STROKE

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We have previously proposed chronic activation of the widespread projections of the net excitatory, glutamatergic dentatothalamocortical pathway as a therapeutic approach to upregulate perilesional cortical excitability and promote both functional cortical reorganization and post-stroke motor rehabilitation. Our work in preclinical models of middle cerebral artery (MCA) ischemia supports the beneficial effects of chronic stimulation of the dentatothalamocortical pathway on motor recovery; with physiological and histological data pointing to potential mechanisms that involve changes in cortical excitability as well as enhanced synaptogenesis and expression of markers of long-term potentiation. Our first-in-human clinical trial of DN deep brain stimulation (DBS) to treat upper extremity hemiparesis in chronic (> 12 months), post-MCA ischemia patients is providing a unique opportunity to extend our understanding of the effects of DN DBS on cerebral cortical activity.

Six patients have been enrolled and implanted in the clinical trial, with no significant adverse events related to surgical lead placement or chronic stimulation encountered to date. DN DBS-evoked cortical potentials were observed in all patients with substantial variation observed in the timing and topography of responses across subjects. Within subjects, physiological effects are highly dependent on contact topography and direction within the DN target. Partial outcome data will be available for the six patients by the time of the meeting.

DN DBS has been well tolerated in the first-in-human use. DBS-induced changes in cerebral cortical activity may be used to guide stimulation parameter selection. This is important in this application as no acute clinical changes are noted during programming to guide chronic parameter selection. In the present study, differential effects were observed both across patients and within patients, across stimulation settings. Variability across patients likely reflects differences in post-stroke cortical pathway integrity, while within subject variation as a function of DBS parameters suggests differences in activation within the target region.

Wednesday, May 29, 2019
Breakout Session
Under the Hood: Mechanisms of Action Aspects

56. INS19-0449

BEYOND THE GATE

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Spinal Cord Stimulation for Pain Inhibition: New Paradigms and Mechanisms Beyond the Gate.

Patients who suffer chronic neuropathic pain are often the most difficult to treat. Both conventional paresthetic spinal cord stimulation (SCS) and new paresthesia-free SCS are viable neurostimulation modalities for pain control. Yet, the respective mechanisms underlying their pain inhibitory effects are only partially known. This presentation will introduce the history of SCS for pain treatment, review recent progress in pre-clinical mechanistic study of SCS for pain treatment, especially new evidence suggesting mechanisms beyond traditional gate control theory, and discuss strategies that may improve SCS therapy.

Wednesday, May 29, 2019
Breakout Session
Under the Hood: Mechanisms of Action Aspects

57. INS19-0461

BURST AND HIGH FREQUENCY STIMULATION: MECHANISMS OF ACTION

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Theta Burst Stimulation (TBS) and high frequency stimulation (HFS) are important new sub-perceptible innovations in spinal cord stimulation (SCS)[1]. Although these programming strategies employ very different waveforms to introduce their highly salient signals to the nervous system, they appear to share some biochemical processes. This session will review the current clinical and neurophysiological literature and share practice recommendations based on empirical observations.

Divergent mechanisms: In TBS, the electrical field appears to increase in size and charge across the surface of the dorsal spinal cord and with each pulse. At the center of the *cathodic* field, evoked compound action potentials (eCAPs) appear to be generated; at the rim of the cathodic field, sub-threshold perturbations in membrane potentials can occur. Conversely, at the center of the *anodic* field, membrane potentials are hyperpolarized, whilst eCAPs may well be generated at the rim[2]. Both orthodromic and antidromic eCAPs have compounding central and peripheral consequences via neurotransmitter release at the up- and down-stream axon terminals[3], resulting in rapid-onset therapy. Cervical-based therapy for both 4-extremity and low back neuropathic pain is easily obtainable in a sub-perceptible manner[4].

HFS has a longer wash-in period before therapy is apparent, which strongly suggests gradual biochemical alterations in localized areas of the cord, quite likely involving neuronal and glial function. Any generation of eCAPs appear to be epiphenomenal and purely secondary via network reflexes. The primary mechanisms appear to involve neuroinflammatory, interstitial ionic currents[5], and neuronal ion-channel functionality effects.

Convergent mechanisms: In both waveforms, neuroimmunity genomics [6] and altered ionic environments likely play major roles. Therapy-linked alterations in glial-generated biomarkers obtained from CSF, plasma, and sputum are seen during SCS therapy. Consistently, too-intense application ('Overstimulation') mimics viral flu, with clinically obvious systemic neuroimmune features; systemic infection can precipitate Overstimulation through transient sensitization of the CNS[7]. Teasing out the subtleties of this complex interaction is a major focus in the basic sciences that is now influencing the clinical sciences.

Conclusions: TB harnesses the primary effects of eCAP generation for a rapid global CNS effect. In contrast, HFS alters the spinal ionic and immune milieu in a slower and more focal distribution. Neuroimmune processes appear to be at the heart of both novel and conventional SCS waveforms.

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Wednesday, May 29, 2019
Breakout Session
Under the Hood: Mechanisms of Action Aspects

58. INS19-0497

DEEP BRAIN STIMULATION MECHANISM OF ACTION REVIEW

C. McIntyre BS PhD [1]

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Deep brain stimulation (DBS) is a successful clinical therapy for a wide range of neurological disorders; however, the exact physiological mechanisms of DBS remain unresolved. While many different hypotheses currently exist, recent scientific interest has concentrated on dissecting the effects of DBS on synchronous network activity. That work has demonstrated that tonic ~100 Hz stimulation is generically effective at disrupting lower frequency network oscillations in the brain, which at times can be considered pathological. This disruption of network activity is the result of stimulation-induced changes in neural firing at the cellular level. Changes at the cellular level occur because the applied electric field manipulates the opening and closing of voltage-gated sodium channels in cells near the electrode, generating stimulation-induced action potentials, and subsequently controlling the release of neurotransmitters in the directly activated neural pathways. As such, a basic mechanism of DBS that can be defined at the level of the synapse may be the ubiquitous phenomenon of high frequency stimulation-induced suppression of synaptic transmission. This loss of synaptic communication between directly stimulated neurons and their network, acts to limit the propagation of synchronous oscillations through the network, which decreases the ability of the pathological network to negatively impact behavior.

Thursday, May 30, 2019
Breakout Session
New Targets, New Diseases

59. INS19-0460

THE CASE FOR CORDOTOMY VS. NEUROMODULATION FOR CANCER PAIN: (PRO-CORDOTOMY)

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Percutaneous cervical cordotomy (PCC) is a minimally invasive neurosurgical procedure for relief of intractable cancer pain below the level of the neck. Pain is one of the most common and debilitating symptoms in cancer patients. Despite best medical treatment a subset of cancer patients continue to suffer from pain that is refractory to all treatments. Patients suffering from unilateral localized pain may benefit from cordotomy, which refers to the selective disconnection of the spinal pain pathways in the spinothalamic tract. The advantage of cordotomy lies in its ability to provide immediate and effective pain relief for intractable nociceptive pain. In patients with a limited life expectancy and advanced disease, implanting hardware such as morphine pumps is often not optimal, being both expensive and labor intensive. PCC is performed using radiofrequency ablation under CT guidance, usually in awake patients for physiological verification of the lesioning target. With appropriate patient's selection, the procedure has a high success rate in achieving pain control in the most difficult to treat cancer pain syndromes. Complications although potentially serious are relatively rare. The aim of this talk will be to highlight current indications, advantages and also limitations of cordotomy.

Thursday, May 30, 2019
Breakout Session
New Targets, New Diseases

60. INS19-0455

THE CASE FOR CORDOTOMY VS. NEUROMODULATION FOR CANCER PAIN: (CON-CORDOTOMY)

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In line with advances in interventional radiology and intra-operative neuroimaging, the techniques, accuracy, efficacy, and safety of cordotomy procedures for pain relief in advanced cancer have improved substantially over the past 20 years. Nevertheless, prospective trial data and patient numbers remain limited, while clinical indications are narrowly defined, being generally confined to those with short longevity and with focal or unilateral nociceptive pain.

The risks and benefits of intrathecal drug delivery in cancer patients have been well documented. Neurostimulation would appear potentially to be applicable to a wider variety of cancer pain conditions and in cancer survivors and is of low operative risk. However, high quality, prospective data including cost effectiveness and comparison with best possible medical management are also lacking.

"Modern" cordotomy, punctate myelotomy, and neurostimulation may all have a place in the treatment of cancer pain. The use of each must depend, above all, on careful patient selection and timing of intervention. It will be dictated also by local economic factors, the results of early and appropriate medical treatment by a dedicated pain management team, and by the availability of suitably trained radiological/neurosurgical personnel.

Thursday, May 30, 2019
Breakout Session
New Targets, New Diseases

61. INS19-0498

SPHENOPALATINE GANGLION STIMULATION THERAPY: PROCEDURAL CHALLENGES

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Background: Headache disorders are amongst the most common of the nervous system disorders with a prevalence of 48.9% in the general population[1]. Two of the most disabling headaches are Migraine and Cluster Headache with a prevalence of 15%[2]and 0.1%[3]respectively. Cluster headache (CH), one of the most excruciating primary headaches, has unilateral pain occurring up to eight times daily and lasting 15–180 minutes. Both disability and impairment are high and lead to reduced quality of life[4,5]. Abortive (subcutaneous and nasal triptans or oxygen) and preventative treatments (verapamil, lithium, topiramate, corticosteroids or greater occipital nerve injections[6,7]tend to be less effective in the considerable proportion of patients and the complications of systemic side effects limit the efficacy of these therapies.

Headache disorders can be treated with non-invasive and invasive Neuromodulation. Among invasive therapies, occipital nerve stimulator (ONS) and SPG stimulator is being used in Europe and US.

Introduction: SPG is the largest extracranial parasympathetic ganglion. With its connections to Trigemino-cervico-complex, it is responsible for the clinical features of cluster headache and migraine including autonomic features. Sphenopalatine ganglion stimulation is currently CE marked for chronic cluster headache and chronic migraine with autonomic features. Electrical stimulation of the SPG relies on an implantable on-demand stimulator that is activated by the patients themselves. The safety and effectiveness of the system were first investigated in the Pathway CH-1 study, a multicenter randomized trial[4]. This study found the therapy to have dual clinical benefits of acute pain relief and attack prevention while demonstrating an acceptable safety profile comparable to similar surgical procedures. Further SPG stimulation effectiveness was proven in Pathway CH-2 RCT[5].

Sphenopalatine Ganglion (SPG) Stimulation: It is a miniaturized device to stimulate the SPG. It is designed to fit facial anatomy. The system is implanted under general anaesthesia using a minimally invasive, trans-oral, gingival buccal technique and takes almost 60-90 minutes. Prior to implant each subject received a parasinus computed tomography (CT) scan to aid in the surgical planning. It is On-demand, patient-controlled therapy and has got whole-body MRI conditional labelling.

Conclusion: Sphenopalatine Ganglion Stimulation is becoming an established neuromodulation treatment for patients with Chronic Intractable Cluster Headache. Treatment should be proposed after experts consensus through the multidisciplinary meeting to ensure homogeneous and appropriate patient selection. Governance arrangements are necessary to ensure measurement of patient's outcomes ie clinical response, long term quality of life, device-related complications and morbidity for learning and education.

Thursday, May 30, 2019
Breakout Session
New Targets, New Diseases

62. INS19-0459

THE APPROACHES IN PERIPHERAL NERVE STIMULATION OF BRACHIAL PLEXUS

G. De Carolis MD[1]

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Safety and Effectiveness of Peripheral Nerve Stimulation of Brachial Plexus Nerve Roots for Chronic Refractory Neuropathic Pain of the Upper Limb: a multicentric cohort study

Introduction: Brachial plexus injury (BPI) often causes severe neuropathic pain that becomes chronic and difficult to treat pharmacologically or surgically.

Objective: We report the outcome of 14 patients consecutively enrolled suffering from chronic medically-refractory neuropathic pain of the upper limb topographically limited, treated with brachial plexus peripheral nerve stimulation (PNS).

Data were collected in the Pain Therapy Unit of Santa Chiara University Hospital, Pisa (IT) and in the National Scientific and Practical Institute for Neurosurgery, Moscow (RU).

Materials and Method: A specialized psychological evaluation was performed to rule out untreated major psychiatric comorbidity contraindicating an implant. The technique consisted in ultrasound-guided percutaneous implantation of a quadripolar cylindrical lead via anterior supra-clavicular approach. Electromyography showed non complete avulsion of BP for all patients.12 out of 14 patients underwent a positive trial stimulation before lead connection to a subcutaneous IPG. Bipolar stimulation mean parameters were: frequency 24 Hertz, voltage 1 Volts, 244 μs. The voltage was set below the threshold inducing muscle contractions or paresthesias. Patients' pain rating (0-10 NRS) and quality of life (SF -12) were assessed for up 18 months.

Results: Analysis of the data 18 mths following permanent PNS implant indicates that there was an improvement in pain intensity in all participants (8.1 ± 1.4 vs 5.3 ± 2.6). Concomitantly patients showed changes in psychological variables. At 18 mths follow up SF -12 Mental Component Summary scores was higher compared to baseline (41.2 ± 16.6 vs 51 ± 12.9). Ten patients had a pharmacological therapy before the implant, 9 out of 10 reduced drugs intake. At last follow-up, 6 out of 12 patients were very satisfied, 4 were satisfied, and 2 were poorly satisfied. No adverse events occurred.

Conclusion: Peripheral Nerve Stimulation of Brachial Plexus Nerve Roots via anterior supra-clavicular approach for chronic refractory neuropathic pain of the upper limb seems to provide a safe, durable and effective option for upper limb neuropathic pain. Further data are needed.

Thursday, May 30, 2019
Breakout Session
New Targets, New Diseases

63. INS19-0445

MECHANISMS OF ACTION OF DORSAL ROOT GANGLION STIMULATION FOR PAIN

C. Hunter[1]

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I will present the present state of knowledge of the mechanisms of action of dorsal root ganglion electrical stimulation

Thursday, May 30, 2019
Breakout Session
New Targets, New Diseases

64. INS19-0452

NEW INDICATIONS FOR DORSAL ROOT GANGLION STIMULATION

F. Huygen MD PhD FIPP FFPMCAI (hon),[1]

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Around 2004 Mir Inram and Daniel Kim came up with the idea to stimulate the Dorsal Root Ganglion. The DRG plays a pivotal role in the processing of peripheral pain. The DRG was already a well-known target for invasive pain treatment. For the continuous stimulation of the DRG, new leads, a delivery system and a specific stimulator had to be developed.

In 2013, the first study in humans was published[1]. Followed by the safety and efficacy study in which a variety of indications were studied [2,3]. Case series and case reports followed with all kinds of indications such as phantom limb pain and groin pain [4,5]. It became clear that previously difficult to reach areas for neurostimulation such as the trunk were accessible for DRG stimulation.

High quality evidence was provided for superiority of DRG stimulation in the accurate study[6].

New indication areas are still being discovered, such as low back pain via L2 stimulation [7].

All these new indications need to be further researched in controlled studies to better determine their effectiveness and ultimately allow these therapies to qualify for reimbursement.

Proper use of DRG stimulation is described in a recent review [8].

1. A prospective study of dorsal root ganglion stimulation for the relief of chronic pain. Deer TR, et al. Neuromodulation. 2013 Jan-Feb;16(1):67-71.

2 A multicenter, prospective trial to assess the safety and performance of the spinal modulation dorsal root ganglion neurostimulator system in the treatment of chronic pain. Liem L, et al. Neuromodulation. 2013 Sep-Oct;16(5):471-82.

3 One-year outcomes of spinal cord stimulation of the dorsal root ganglion in the treatment of chronic neuropathic pain. Liem L, et al. Neuromodulation. 2015 Jan;18(1):41-8.

4 Dorsal Root Ganglion (DRG) Stimulation in the Treatment of Phantom Limb Pain (PLP). Eldabe S, et. al. Neuromodulation. 2015 Oct;18(7):610-6.

5 Spinal cord stimulation of the dorsal root ganglion for groin pain-a retrospective review. Schu S, et al. Pain Pract. 2015 Apr;15(4):293-9.

6 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. Deer TR, et al. Pain. 2017 Apr;158(4):669-681.

7 Stimulation of the L2-L3 Dorsal Root Ganglia Induces Effective Pain Relief in the Low Back. Huygen F, et al. Pain Pract. 2018 Feb;18(2):205-213.

8 The Neuromodulation Appropriateness Consensus Committee on Best Practices for Dorsal Root Ganglion Stimulation. Deer TR, et al. Neuromodulation. 2019 Jan;22(1):1-35.

Thursday, May 30, 2019
Breakout Session
Advances in Neuromodulation for Refractory Epilepsy

65. INS19-0517

NEUROBIOLOGY OF NEUROMODULATION OF EPILEPSY

A. Velasco MD[1]

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Neuromodulation for epilepsy is performed in several epilepsy surgery centers. Different patient selection (those with focal seizures vs generalized seizures, catastrophic epilepsy) neural targets (hippocampus (Velasco et al, 2001, 2007), primary motor cortex foci (Fisher and Velasco 2013), thalamus, cerebellum, vagal nerve), stimulation parameters (high vs low frequency stimuli, open vs close loop, high vs low amplitude) are used. Obviously different outcomes are reported, all of them show diverse seizure improvement, none of them show seizure increase or permanent neurologic deficit, if present, adverse effects are reversible. Best of all, there are hints that neuromodulation could even improve patient´s cognitive function and quality of life. A broad number of targets have been stimulated and new ones continue to be proposed for stimulation. We can resume all of them in two groups: direct epileptic foci stimulation in case of focal seizures with a well-defined focus localization; and propagation blockage, in case of generalized seizures, multifocal epilepsy and currently, in case of sclerotic tissue. What are the mechanisms that explain seizure reduction? One of our studies (Velasco et al, 2000), was performed in patients that had a transitory hippocampal stimulation trial for mesial temporal lobe seizures. This study was performed in patients who had mesial temporal lobe epilepsy and, as part of their diagnosis for lobectomy, underwent amygdalo-hippocampal electrode implantation. All patients agreed to sign a consent letter (approved by the General Hospital Research and Ethics Committees) to participate in the therapeutic stimulation trial previous to the lobectomy. Once the focus was localized, we performed a two-week period of focus stimulation. Before and after this trial, we carried out fast 60 per second stimulation to obtain after-discharges. We observed that after-discharges were blocked and consequently seizures did not occur ("quenching" phenomenon described in animal model by Weiss et al, 1998); paired pulse stimulation that show that pulses are importantly diminished in amplitude after weeks of stimulation; SPECT studies showed basal ipsilateral temporal hypometabolism, post therapeutic stimulation produced an important increase of the hypometabolism only comparable to the post-lobectomy one. Additionally, post-lobectomy benzodiazepine receptor studies comparing tissue with non-epileptic patients and with other lobectomy tissues in non-stimulated patients, showed a significant increase in benzodiazepine receptors in the stimulated tissue. All studies point to an inhibitory effect of stimulation. Recent studies using PET-CT scans with flumazenil support this mechanism. More studies are needed to explain the neurobiology of neuromodulation in epilepsy, but a huge path has been advanced.

Thursday, May 30, 2019
Breakout Session
Advances in Neuromodulation for Refractory Epilepsy

66. INS19-0510

RESPONSIVE VAGAL NERVE STIMULATION

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[1]*Clinica de Epilepsia de Sao Paulo, Neurosurgery, Sao Paulo, Brazil*

Vagus nerve stimulation in refractory epilepsy

VNS has been used to treat a variety of epilepsy syndromes and seizure types. More than a hundred thousand of individuals has been implanted so far, but the best patient population who would be good candidates for the procedure is not yet adequately established. A fifty percent of responders (at least 50% seizure frequency reduction) could be expected. VNS appears to be more effective in paediatrics series, especially so in children with Lennox-Gastaut syndrome. Cost-effectiveness has been reported in different ways, including a reduction in emergency room visits and high reimplantation rates. Standard mortality rates are reduction in patients using VNS; it is not clear if SUDEP rates are modified by VNS use. More recently, a cardiac-based closed-loop system has been released in the market. Two pivotal studies, one coming from Europe and another one from the US suggested efficacy, but adequate comparison of this new system to the old one is lacking.

Thursday, May 30, 2019
Breakout Session
Advances in Neuromodulation for Refractory Epilepsy

67. INS19-0505

RESPONSIVE DEEP BRAIN STIMULATION - Not included in the main Scientific program (No CME/CPD credit)

M. Morrell MD[1]

[1]*Stanford University/NeuroPace, Neurology, Palo Alto, USA*

Neuromodulation for the Treatment of Epilepsy: Brain Responsive Stimulation and Insights from Long-term Ambulatory ECoG Monitoring

Martha J. Morrell MD

Clinical Professor of Neurology and, by courtesy, Neurosurgery Stanford University, Chief Medical Office, NeuroPace

Neurostimulation is an increasingly important treatment modality for disorders of the nervous system. Most neurostimulation devices are open-loop; stimulation settings are pre-programmed and do not automatically respond to changes in electrophysiological signals or the patient's clinical symptoms. In contrast to open-loop stimulation devices, responsive (or closed-loop) neurostimulation devices modulate or adapt therapy in response to physiological signals, and may be more efficient, effective, and better tolerated than open-loop stimulation. A recently FDA approved product provides scheduled stimulation to the vagus nerve and automatically activates vagus nerve stimulation in response to tachycardia.

The first responsive brain neurostimulator (RNS® System, NeuroPace) is approved as an adjunctive therapy for adults with refractory, partial onset seizures. Stimulation is delivered directly to the seizure focus when abnormal electrocorticographic activity occurs. Quantitative data regarding the frequency and type of epileptiform activity and the electrographic response to treatment, as well as recordings of the electrocorticogram are combined with reports of clinical seizures to individualize treatment for each patient. Median seizure reductions of 44% at one year increase to 75% by 9 years of treatment and are accompanied by improvements in quality of life overall and in areas related to attention, language, memory, as well as work and social function. There is no negative impact on mood or cognition, and some patients experience improvements in some aspects of language and memory. The risk is similar to other implanted medical devices and the neurostimulator can be programmed so that therapeutic stimulation is not perceived.

Neuromodulation, including brain-responsive neurostimulation, has proven an important treatment option for patients with pharmacoresistant partial epilepsy. In addition, the RNS System provides data that may contribute substantially to disease management.

Morrell MJ, Halpern C. Responsive Direct Brain Stimulation for Epilepsy. Neurosurg Clin N Am. 2016 Jan;27(1):111-21.

Thursday, May 30, 2019
Breakout Session
Advances in Neuromodulation for Refractory Epilepsy

68. INS19-0511

HIPPOCAMPAL DEEP BRAIN STIMULATION

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Hippocampal DBS in refractory epilepsy

DBS has been used in an increasing frequency to treat refractory epilepsy. Hippocampal DBS has been used to treat patients with refractory temporal lobe epilepsy who were not good candidates for resective surgery due to bilateral ictal onset, memory concerns, failed previous resection, personal preference, etc. Both continuous or responsive stimulation paradigm had been used. Targetting is usually performed using a posterior approach which can provide ample coverage of the hippocampal head and body with a single entry. Two RCTs have been reported, one using continuous and the other using responsive stimulation, which yielded a 50% and 15% seizure-free rate, respectively. Bipolar, high frequency stimulation is preferred. No additional neuropsychological deficits have been reported even in patients submitted to bilateral hippocampal stimulation. Complications were like those seen in other DBS series (p.e, for treatment of movement disorders).

Thursday, May 30, 2019
Breakout Session
Advances in Neuromodulation for Refractory Epilepsy

69. INS19-0526

SPECIFIC THALAMIC TARGETINGIN DBS

J. Archer FRACP PhD[1], A. Warren[1], L. Dalic[1], K. Bulluss[2], W. Thevathasan[3], A. Roten[2]

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[3]*Royal Melbourne Hospital, Neuroscience, Melbourne, Australia*

Epilepsy is a network disorder in which the electrical and clinical features of epileptic seizures reflect the brain networks predominately driven by epileptic discharges. Thalamic deep brain stimulation probably works by disrupting the propagation of abnormal epileptic activity through intrinsic neural networks. Accurate targeting is important to ensure the neuromodulating effects of DBS are being applied to the relevant networks. Direct targeting based on the patient's own MRI is superior to coordinate based targeting due to variations in patient anatomy. Methods for direct targeting the Anterior nucleus of Thalamus are now established. We have developed a method for direct targeting of the Centromedian Nucleus of Thalamus (CM), that we are using in a formal study of CM DBS for severe generalised epilepsy - 'ESTEL' (Electrical Stimulation of the Thalamus for Epilepsy of Lennox-Gastaut Phenotype)

Thursday, May 30, 2019
Breakout Session
Neuromodulation for Pelvic Organ Motility Disorders

70. INS19-0495

SACRAL NEUROMODULATION FOR THE TREATMENT OF URINARY BLADDER DYSFUNCTION: MECHANISM OF ACTION AND FUTURE DIRECTIONS

B. Blok MD PhD[1]

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Sacral Neuromodulation for the Treatment of Urinary Bladder Dysfunction: Mechanism of Action and Future Directions

Symptoms of bladder dysfunction affects a large portion of the world population, especially the elderly. When conservative treatment has failed, sacral neuromodulation (SNM) is an effective third-line therapy in patients with overactive and/or underactive bladder. Overactive bladder concerns symptoms during the filling or continence phase, like urge, frequency or urge incontinence. Underactive bladder concerns symptoms during the voiding or micturition phase, like post void residue, urinary retention and decreased urinary flow. Although it seems to be counter intuitive that SNM works both in 'spastic' and 'paralyzed' urinary bladders, the working mechanism of SNM can be explained by the neural connections of the lower urinary tract in both overactive as well as in underactive bladder. It is proposed that SNM does not work directly on the central components of the micturition reflex, but indirectly via cortical and subcortical areas, which in turn modulates the micturition reflex components in the caudal brainstem. The clinical use and outcomes of SNM are described for several forms of bladder dysfunction. Some recent new developments are discussed, such as expanded indications, a more effective use of existing nonrechargeable neuromodulators and the introduction of a rechargeable device.

Thursday, May 30, 2019
Breakout Session
Neuromodulation for Pelvic Organ Motility Disorders

71. INS19-0501

INDICATIONS AND CLINICAL RESULTS OF PELVIC FLOOR NEUROMODULATION

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The use of neuromodulation to address a pelvic floor problem has roots dating back to the late 1800s yet it is only in the last 20 years that effective applications have been available for clinical use. These applications can be broadly categorized into disorders of bowel and bladder function but more recently also include pain. Paradoxically, among functional disorders of the bowel and bladder are both storage (e.g. urinary or fecal incontinence) and evacuation applications (e.g. voiding or constipation). While there exists across these applications varying degrees of evidentiary support, there remain many unanswered questions. These questions begin with our incomplete understanding of how precisely neuromodulation works to correct pelvic floor problems but also include practical clinical questions as well. Why does the treatment work in some but not all individuals with similar clinical applications? Why does the therapy stop working in some individuals over time? What demographic or clinical features predict who should use this therapy? To be sure some of the answers to these questions lie in features related to the respective disease states, however, the objective of this presentation is to review the available clinical outcomes literature across all applications of pelvic floor neuromodulation. Having this as background, consideration will be given to practical study designs available to fill in our present knowledge deficits.

Thursday, May 30, 2019
Breakout Session
Neuromodulation for Pelvic Organ Motility Disorders

72. INS19-0453

STANDARDIZATION IN SACRAL NEUROMODULATION TECHNIQUE

S. De Wachter MD, PhD, FEBU[1]

[1]*Antwerp University Hospital UZA - Antwerp University UA, Department of Urology, Edegem - Wilrijk, Belgium*

Sacral neuromodulation (SNM) is a well accepted minimally invasive therapy for pelvic organ disorders such as overactive and underactive bladder and faecal incontinence. Despite its overall success, therapy fails in a number of patients which may be due to inadequate lead placement leading to suboptimal coupling of the electrode and the nerve.

This presentation will describe the main steps to optimal lead placement which resulted from two meetings of an international multidisciplinary working group highly experienced in performing SNM. Furthermore, new data will be presented providing background information to standardization in settings and troubleshooting.

Thursday, May 30, 2019
Breakout Session
Neuromodulation for Pelvic Organ Motility Disorders

73. INS19-0446

SACRAL NEUROMODULATION FOR PELVIC PAIN AND PELVIC ORGAN DYSFUNCTION

T. Vancaillie FRANZCOG, FFPMANZCA[1]

[1]*Women's Health & Research Institute of Australia, n/a, Sydney, Australia*

Sacral Neuromodulation for Perineal Pain and Pelvic Organ Dysfunction – The Sydney Protocol

The Sydney protocol consists of 1] combining trans-hiatal and transforaminal access for sacral neuromodulation with in addition the occasional peripheral pudendal nerve lead; and 2] using multiple modalities of stimulation, such as tonic, sub-threshold and burst-type, in various combinations. The objective of the Sydney protocol is to find the optimal stimulation parameters to treat patients, who present with complex syndromes of perineal pain as well as bladder, bowel or sexual dysfunction.

The presentation will cover the anatomy of the region as well as the physiology of the pelvic organs. Anatomy and physiology form the background which guides the team in choosing optimal placement of the stimulation leads. The results of our near ten year experience will be presented.

Thursday, May 30, 2019
Breakout Session
Neuromodulation for Pelvic Organ Motility Disorders

74. INS19-0450

UPDATES IN PERCUTANEOUS TIBIAL NEUROMODULATION

K. Peters M.D.[1]

[1]*Oakland University William Beaumont School of Medicine- Beaumont Health, Urology, Royal Oak, USA*

Updates in Percutaneous Tibial Neuromodulation

The tibial nerve is comprised of L4, L5, S1, S2 and S3 nerve fibers and is easily accessible along the medial aspect of the lower extremity. Since the 1980's studies have been done by percutaneously stimulating the tibial nerve with an acupuncture-type needle or through a cutaneous patch. The initial studies were all open-label, but consistently demonstrated efficacy. It wasn't until 2010 with publication of a well-designed sham-controlled trial (Sumit) that PTNS was proven to work and became readily available to patients. Since that time, the tibial nerve remains a nerve target of interest. Multiple small studies have been published on OAB, Fecal incontinence, rectal evacuation disorder, sexual dysfunction, anal fissures, combination therapy and neurogenic bladder. This talk will provide an update on tibial neuromodulation, highlight recent clinical trials and discuss emerging technologies designed to create an easily implantable microstimulator to be placed at the tibial nerve for chronic stimulation.

***References*:**

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2. Combination of sacral nerve and tibial nerve stimulation for treatment of bladder overactivity in pigs. Int Urol Nephrol. 2017 Jul;49(7):1139-1145. doi: 10.1007/s11255-017-1587-x. Epub 2017 Apr 18.

3. Percutaneous Posterior Tibial Nerve Stimulation vs Perianal Application of Glyceryl Trinitrate Ointment in the Treatment of Chronic Anal Fissure: A Randomized Clinical Trial., Dis Colon Rectum. 2017 Jan;60(1):81-86.

4. Medium-term outcome of percutaneous tibial nerve stimulation in the treatment of fecal incontinence. Tech Coloproctol. 2018 Nov;22(11):875-879. doi: 10.1007/s10151-018-1892-0. Epub 2018 Dec 18.

5. Sacral nerve stimulation versus percutaneous tibial nerve stimulation for faecal incontinence: a systematic review and meta-analysis. Int J Colorectal Dis. 2018 May;33(5):645-648. doi: 10.1007/s00384-018-2976-z. Epub 2018 Feb 22.

6. Effectiveness and durability of solifenacin versus percutaneous tibial nerve stimulation versus their combination for the treatment of women with overactive bladder syndrome: a randomized controlled study with a follow-up of ten months. Int Braz J Urol. 2018 Jan-Feb;44(1):102-108. doi: 10.1590/S1677-5538.IBJU.2016.0611.

Thursday, May 30, 2019
Breakout Session
Neuromodulation for Pelvic Organ Motility Disorders

75. INS19-0458

PUDENDAL STIMULATION

K. Jottard MD[1], P. Bonnet[2], L. Bruyninx[1], S. Ploteau[3], D.W. Stefan[4]

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[4]*University Hospital Antwerp, Urology, Antwerp, Belgium*

Introduction: Chronic pudendal nerve modulation (CPNM) is a promising alternative in case of sacral nerve modulation failure or as a primary treatment option in case of overactive bladder syndrome, urinary retention or chronic pelvic pain syndrome. Its role in treating patients with fecal incontinence is still unclear. Since pudendal afferents appear to play a role in the clinical effect of sacral neuromodulation, we could expect that CPNM would augment clinical efficiency. However, its clinical efficacy is highly dependent upon optimal lead placement. All the known percutaneous procedures for implantation of pudendal nerve electrodes seem very unwieldly and despite cannot guarantee the precise location and trajectory of the electrode.

Aim: The aim of this article is to describe a minimal invasive trans gluteal endoscopic approach to implant a pudendal electrode for neuromodulation under full visual control.

Methods: Eight trans gluteal approaches were performed on four cadavers. The sacral transforaminal percutaneous technique was performed to implant the electrode. The electrode was then picked up and placed under visual control next to the pudendal nerve.

Results: The first trocar was placed in the upper lateral quadrant of the gluteal region. The 0° optical system was used to help with the pneumodissection to identify the sciatic nerve. At that point a second 3 mm trocar was placed to insert a dissecting grasping forceps. In some cases, a second 3 mm trocar was placed. A step by step dissection, based on anatomical findings, was necessary to be able to locate the pudendal nerve. The electrode, which was placed percutaneously and transforaminal through S3 or S4, was picked up and placed under full visual control next to the pudendal nerve, slightly entering the Alcock's canal. The electrode was placed in an ideal manner, meaning that all 4-contact points of the electrode are in parallel and in contact with the targeted nerve. The electrode was fixed in that ideal position at the level of the sacrospinous ligament. Since we used a transforaminal approach for electrode introduction, the position of the electrode near to S3 or S4 could allow multitarget neuromodulation.

Conclusions: The ENTRAMI technique allows optimal pudendal electrode placement under full visual control. At the time of writing we started a pilot study for pudendal electrode placement by the ENTRAMI technique, in patients operated for pudendal nerve release, in case of chronic perineal pain syndrome. The first results should be available around April 2019.

Thursday, May 30, 2019
Special Session
Neuromodulation in Asia - Part 1

76. INS19-0524

NEUROMODULATION IN MINIMALLY CONSCIOUS STATE

W. Wang MD PhD[1], Y. Xu[1]

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Cervical Spinal Cord Stimulation for the Vegetative State: A Preliminary Result of 12 cases

***Objectives*:** Data on the treatment of the vegetative state (VS) with cervical spinal cord stimulation (cSCS) are limited and prognostic factors are inconclusive. In this study, we present our experience of treating 12 VS patients with cSCS and discuss the prognostic factors.

Methods: Twelve VS patients were enrolled. Preoperative assessments included CT/MRI, PET, brainstem auditory evoked potentials (BAEPs), somatosensory evoked potentials (SEPs), and electroencephalogram (EEG). cSCS surgeries were performed at West China Hospital. The electrode was implanted in the epidural space of the C2–4 vertebrae. Levels of consciousness were evaluated based on the Coma Recovery Scale-Revised (CRS-R) at baseline and during follow-up.

Results: The average follow-up was 11.1 months. The average CRS-R score at the last evaluation was 10.8, which was significantly improved compared with the baseline score (6.25). Five patients achieved responsive outcomes (three recovered and two evolved to a minimally conscious state) and seven achieved unresponsive outcomes (six remained in VS and one died). Age, preoperative CRS-R score, the interval between acute comatose injury and cSCS, and the Vth wave of BAEPs did not differ significantly between the responsive group and the unresponsive group. Appearance of the N20 of SEPs and multifocal abnormalities on CT/MRI and PET were significantly associated with a better outcome, while the etiology of ischemia and anoxia (IAA) was significantly associated with a poor outcome.

Conclusions: cSCS should be a glimmer of hope for VS patients. Patients whose N20 is elicited or whose CT/MRI or PET demonstrates multifocal abnormalities are more likely to benefit from cSCS, whereas those with an IAA etiology have a lower likelihood of recovery after cSCS.

Thursday, May 30, 2019
Special Session
Neuromodulation in Asia - Part 2

77. INS19-0522

COMBAT WITH NEUROMODULATORY THERAPIES IN KOREA AS A PIONEER

Y.C. Kim MD PhD[1]

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Combat with Neuromodulatory Therapies in Korea as a Pioneer

Yong-Chul Kim, MD, PhD

Seoul National University School of Medicine, Korea

In Korea, the prevalence of chronic pain, such as failed back surgery syndrome and complex regional pain syndrome per capita is significantly higher than other Asian countries. Our experiences on the neuromodulatory treatments for those patients might be helpful to other Asian countries. I had deeply involved to introduce such interventions to Korea. There have been several obstacles to treat chronic pain using neuromodulatory interventions in Korea. I think these obstacles may be common problems in Asian Countries. I'll, therefore, share my experience to Asian pain physicians.

The high cost of intrathecal morphine pump (ITMP) implantation may be the main obstacle to its use in chronic pain patients. Since July 2014, the Korean national health insurance (NHI) program began paying 50% of the ITMP implantation cost in selected refractory chronic pain patients. Analysis of the patients who underwent ITMP implantation at a single university-based tertiary hospital between July 2014 and May 2016 showed that ITMP provided effective chronic pain management with high satisfaction. The reasonable financial break-even point of 28 months with 50% insurance coverage by NHI program in Korea. As the coverage of the NHI program is increasing up to 80% of the ITMP cost, more patients would have financial benefit. Only morphine and baclofen can be permitted for intrathecal pump therapy by the Korean FDA, which is also another great obstacle. Spinal cord stimulation has also been widely performed in Korea after 80% coverage by insurance.

Thursday, May 30, 2019
Plenary
Closing Plenary Session: The Future?

78. INS19-0491

VAGUS NERVE IMPLANTS TO OPTIMIZE VAGAL SIGNALS AND FUNCTION - BIOELECTRONIC MEDICINE AS A FUTURE STANDARD OF CARE

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Bioelectronic medicine combines neuroscience, molecular biology, and bioengineering to tap into the nervous system to help the body heal itself. Making effective and targeted bioelectronic medicine devices relies on how much information we have about a condition and its neural signaling. Once we know how the neurons in the vagus nerve are signaling the disruption of homeostasis in various diseases, we can develop devices that will diagnose this disruption in its earliest stages, even before symptoms arise and stimulate the nerve to either stop or modify this signaling and act only when it is needed. This crucial step can be achieved by accessing the information from our bodies' built-in neural reflexes that continuously monitor organ function and maintain physiological homeostasis. Recent studies have started to investigate the possibility of leveraging the sensory arm of these reflexes to diagnose disease states. To accomplish this, neural signals emanating from the body's built-in biosensors and propagating through peripheral nerves must be recorded and decoded to identify the presence or levels of relevant biomarkers of disease. This crucial step will enable the development of closed-loop interfaces that would not only record these neural signals but also modulate them appropriately by applying parametric nerve stimulation. Although the selection of stimulation parameters to consistently up- or down-regulate various biomarkers remains a daunting task, resolving the encoding of these biomarkers by the nervous system can provide valuable insight into the optimization of these parameters. Making effective and targeted bioelectronic medicine devices relies on how much information we have about a condition and its neural signaling. Once we know how the neurons in the vagus nerve are signaling the disruption of homeostasis in various diseases, we can develop devices that will diagnose this disruption in its earliest stages, even before symptoms arise and stimulate the nerve to either stop or modify this signaling and act only when it is needed. By combining neurophysiology, neurotechnology, and machine learning and data analytics, the results emphasize the importance of decoding neural signals and lay the groundwork to provide the first crucial steps toward this important goal.

Thursday, May 30, 2019
Plenary
Closing Plenary Session: The Future?

79. INS19-0473

TRANSCRANIAL STIMULATION FOR A SMARTER YOU

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The Future – Transcranial Stimulation for a Smarter You

Jeff Arle, MD, PhD, FAANS

"Neurotechnology, ethically developed, has the capacity to change every person's daily routines and life for the better. It is the only path forward to ensure humanity can thrive into the future. The last great frontier is inward." These are words from new startup company Kernel CEO and founder Bryan Johnson. The overall media have been sending out items and articles of interest for the last several years now on how we might someday, perhaps some day soon, be able to enhance our innate cognitive abilities. This topic, which seems to be a sidebar of sorts for those of us in the neuromodulaiton field, is thought of differently by Johnson who has also written: "The future of the human race lies in our ability to radically upgrade our cognition".

Can we 'hack' into the brain? Can we find ways to use the various modes of physics we are, at least, currently aware of, to gain a pathway into the workings of our neural circuitry in a way that would 'make us smarter'? And if we can, what are the potential ramifications of that ability? Who gets it and who doesn't? What will it cost, individually and to societies overall?

It's not without peril and caution. The Pew Research Center recently found that 69% of Americans would be worried about brain machine interfaces for cognitive enhancement, a higher percentage than are worried about germline gene editing to reduce disease risk or enhancement via injection with synthetic blood. But others, like DARPA are very interested in shortening learning time in soldiers for new languages and skills, among other things.

What if I could read and comprehend in an afternoon those seventy neuroscience papers awaiting my reading? What if I could learn new skills five times as fast? What if people of differing viewpoints could connect their brain's emotional responses and reconcile their perspectives to build constructive solutions? What if the cognitive fatigue suffered inevitably by judges, politicians, doctors and CEOs could be better managed? What if I was able to control the timing, duration and quality of my sleep and attention?

I explore the status of tDCS/TMS and other current cognitive enhancement approaches, the good, the bad, and the ugly of enhancement ethics, and the inevitable collision course cognitive enhancement will have with AI including thoughts on getting that right.

Thursday, May 30, 2019
Plenary
Closing Plenary Session: The Future?

80. INS19-0493

CYBER SECURITY IN NEUROMODULATION

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Cyber security has become pervasive across many sectors whether it is finance, healthcare, transportation, defense or critical infrastructures. In the area of healthcare, the growth in the use medical devices implanted on patients, whether permanently or temporarily for treating a medical condition or improving the functioning of some body part, has increased the security and privacy risks for the patients. Increasing medical devices such as neuromodulation devices are having connectivity together with computing functionality, especially software capability, which can make them vulnerable to security attacks. On the one hand, such computing capabilities can provide more autonomy to patients as well as allow the medical practitioners to manage and monitor the devices remotely, thereby enabling enhanced patient care as well as timely diagnostics. On the other hand, if appropriate security precautions are not taken, the presence of these devices can be easily detected by other devices (and users) in the network, due to their communication capabilities. This can not only lead to unauthorized disclosure of data from these devices (causing potentially breach of privacy) but also can provide an attacking channel for sending unauthorized commands and messages to these devices (potentially causing them to malfunction). Particular consideration should be given to the context under which software updates occur and what security measures and authorizations are needed.

This talk will discuss the types of security threats and attacks that can arise as well as the security measures that are required to be incorporated in the design of neuromodulation devices to counteract these attacks. Though several security mechanisms and solutions exist, challenges are likely to arise when considering trade-offs between security requirements and clinical demands. Furthermore, as is often the case, when devices are being by different types of patient demographics, they will not be always used as intended by the manufacturers or by the healthcare professionals. This can have some unexpected consequences and open up some vulnerable channels for attacks. Device manufacturers need to ensure that they consider security throughout the design process. It would be useful to incorporate mechanisms that can verify the device is in a trusted state and generate alerts in the case of any anomalous behaviour. There is also a role of regulatory authorities to develop guidelines that encourage good security practice. Increasing the security awareness among the healthcare professionals and patients can create a culture shift, which in turn can help to reduce the risks. With the field of neuromodulation evolving rapidly, it is important for the device manufacturers and practitioners to work with cyber security specialists to ensure that future healthcare innovations are not only effective but also deliver patient safety.

*Pages 94-879: Abstracts from the International Neuromodulation Society's 14th World Congress Sydney, Australia on 25 - 30 May 2019,

(*peer reviewed content)

Poster Presentations - May 27 - May 30

Basic Science

81. INS19-0109

A COMPARISON OF BEHAVIOR AND REPORT OF GENE EXPRESSION MODULATION OF WAVEFORM-DEPENDENT SPINAL CORD STIMULATION IN A RAT MODEL OF NEUROPATHIC PAIN

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Introduction: Spinal cord stimulation (SCS) has emerged as an alternative to address the increased prevalence of chronic pain and mitigate the impact of opioid crisis. Its exact mechanism of action is unclear. This study investigates the effects of phase polarity and recharge balance on behavior and gene expression, to elucidate the mechanism by which variable waveforms induce analgesic effects in a neuropathic pain rat model.

Materials/Methods: Animal procedures were approved by the IACUC at Illinois Wesleyan University. Rats were implanted with a four-contact cylindrical mini-lead. Sixty-seven rats (n=7-11/group) were randomly assigned to two control groups that did not receive SCS - Sham and SNI; and five experimental groups that received current-controlled pulsed signals at 50Hz, intensity at 66% motor threshold, and variable anodic content – Monophasic-Cathodic, Monophasic-Anodic, Symmetric-Biphasic (SymBi), Asymmetric-Biphasic 1:2 (AsymBi 1:2), and Asymmetric-Biphasic 1:0.5 (AsymBi 1:0.5). Mechanical allodynia was assessed at baseline, pre-stimulation, and 24h post-stimulation. RT-PCR was performed to determine relative gene expression for 21 genes. Gene expression, SCS intensity (mA) and behavioral effect (% of baseline, BSPB) were used to generate correlograms (R-Studio). ANOVA-based methods (SPSS) were performed to determine significance ($p<0.05$).

Results: AsymBi 1:0.5 SCS required mA statistically larger than required for other waveforms. BSPB was significantly higher for Sham compared to SNI and SCS groups for both pre-stim and post-stim. BSPB was significantly improved post-stim compared to pre-stim in Cathodic, Anodic, SymBi 1:1 and AsymBi 1:2 groups. Correlograms using gene expression, mA and BSPB showed differential expression level in response to varying SCS waveforms (Figure1). RT-PCR analysis demonstrated significant change in expression of several genes including AIF1, CD74, C1QB, CXCL16, MT2A, TSPO, NADSYN1, TIMP1 and GABBR1 post-exposure to varying waveforms.

Discussion: AIF1, C1QB, CD74, CXCL16, TIMP1, and TSPO are known modulators of the development and maintenance of chronic pain and neuroinflammation. Significant modulation towards baseline values was observed within the treatment groups. Differences in behavioral responses and gene expression levels point to overarching alterations in signaling pathways and global gene expression networks that respond differentially to the electrical characteristics of the waveforms.

Conclusions: Results indicate that SCS modalities operate by differential modulation of underlying molecular mechanisms and open the door for pattern specific therapies.

Objectives

Understand SCS mode of action at molecular level.

Evaluate the differential effects of phase polarity on biological processes.

Determine effects of waveforms on neuroinflammation.

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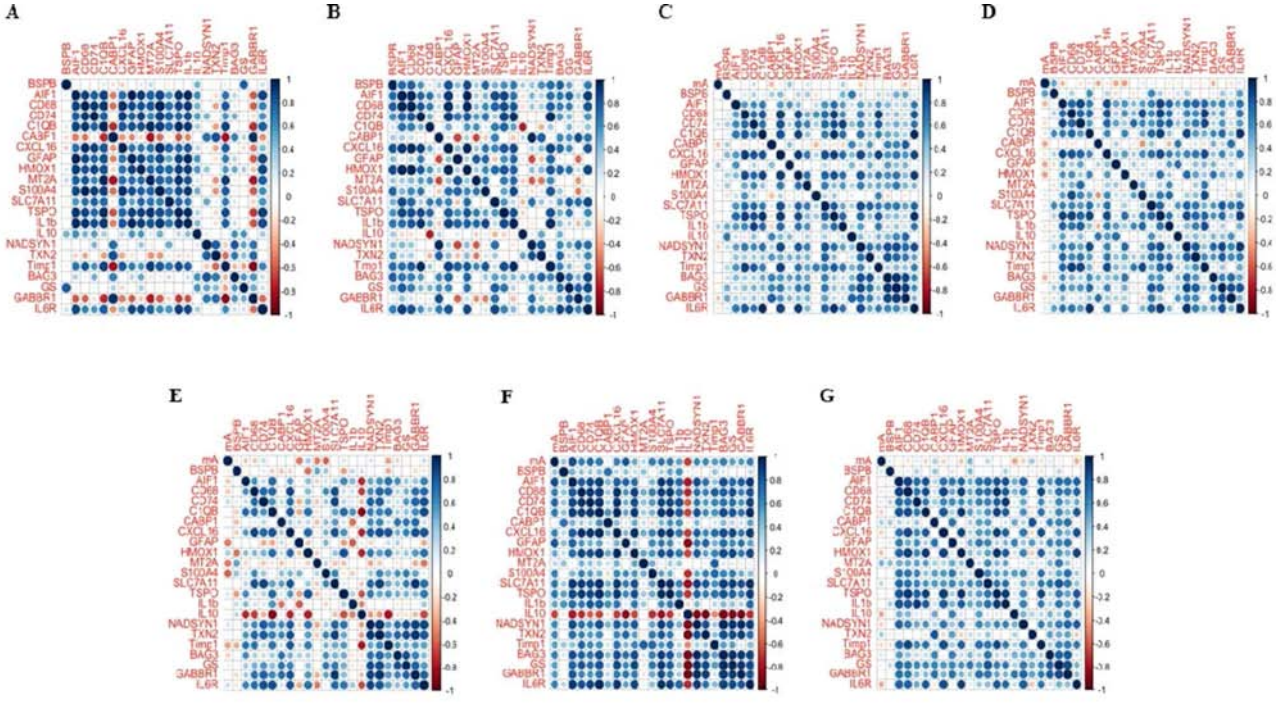

Figure 1. Correlograms between genes, SCS Current (mA), and Behavioral Score as % of Baseline (BSPB). A: Sham, B: No-SCS, C: biphasic symmetric SCS, D: monophasic cathodic SCS, E: monophasic anodic SCS, F: asymmetric biphasic SCS 1:0.5, G: asymmetric biphasic 1:2.

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Basic Science

82. INS19-0116

SPINAL CORD STIMULATION MODULATES PROTEINS IN THE EXTRACELLULAR MATRIX OF THE SPINAL CORD OF AN ANIMAL MODEL OF NEUROPATHIC PAIN

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Introduction: Our pre-clinical studies demonstrated that spinal cord stimulation (SCS) using varying waveforms differentially modulated gene expression and biological processes. These changes in gene expression translate into changes in protein expression. The extracellular matrix (ECM) plays a vital role in pain-related plasticity in peripheral and central nervous system neurons, and changes in number and activity of glial cells. This plasticity can facilitate the transition of pain from acute to chronic form[1]. This study investigates the change in expression of proteins associated with ECM post-treatment with continuous SCS in neuropathic pain (NP) rat model.

Materials/Methods: IACUC at Illinois State University approved all animal procedures. The spared nerve injury (SNI) model was induced in rats (n=10-12) for 4 days and implanted with a quadrupolar mini-lead. SCS was applied continuously for 72hrs using pulses at 50Hz frequency, 20μs pulse-width and intensity at 70% motor threshold. Non-implanted SNI animals served as controls. The stimulated ipsilateral quadrant of spinal cord (SC) was subjected to proteomics using ten-plex isobaric mass tagging. High performance liquid chromatography, tandem mass spectrometry and bioinformatics were used to identify and quantify proteins. Proteins significantly ($p<0.05$) modulated by SCS relative to control were subjected to functional protein association network analysis followed by cluster and pathway analysis.

Results: 5,840 proteins were identified and quantified, with 155 of these significantly changed by SCS relative to SNI animals. Out of these, 51 proteins were identified to have known interactions and involved in biological processes including ECM organization. Thirty-two of these proteins strongly correlates with gene expression changes and 14 of them are a part of ECM (Table1).

ECM Protein	Fold Change (SCS vs SNI)
Col3a1	1.80
P4ha1	1.40
Serpinh1	1.64
Postn	2.10
Plod3	1.33
Pcolce	1.60
Lox	1.53
Efemp2	1.29
Fbln5	1.32
Vtn	1.62
Fbln1	1.89
Itga5	1.35
Ctsg	3.10
Nfkb2	1.29

Table1: Upregulation of ECM proteins after SCS treatment compared to control SNI.

Discussion: The ECM provides structural and biochemical support at the synapse. Degradation of ECM in neural tissue causes maladaptive changes and unbalance of synapses, leading to NP. SCS upregulates proteins associated with ECM in the SC of an animal model of NP. This indicates that SCS mode of action may involve reshaping of the ECM leading to normalization of cell-to-cell interactions and thus, ECM proteins may serve as potential biomarkers and/or therapeutic targets to treat chronic NP.

Conclusions: SCS modulates neural tissue ECM related protein expression in a NP animal model with high correlation to gene modulation.

Objectives

Understand mode of action of SCS at molecular level.

Illustrate the role of ECM in chronic pain.

Recognize the value of molecular techniques.

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Poster Presentations - May 27 - May 30
Basic Science

83. INS19-0205

HUMAN DORSAL ROOT GANGLION PULSED RADIOFREQUENCY TREATMENT MODULATES CEREBROSPINAL FLUID LYMPHOCYTES AND NEUROINFLAMMATORY MARKERS IN CHRONIC RADICULAR PAIN

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Introduction: Pulsed radiofrequency (PRF) applied to the Dorsal Root Ganglion (DRG) is a minimally invasive day-care treatment, which is gaining significant clinical acceptance in a selective group of patients with pure radicular pain. Greater insights into the immunomodulatory effects of this procedure may help to further optimise its application and find alternative treatment options. We have examined its effect on lymphocyte frequencies and secreted inflammatory markers in the cerebrospinal fluid (CSF) and correlated this with clinical outcome to identify clinical markers of chronic radicular pain.

Materials/Methods: 10 consecutive patients were enrolled for the study who had continuous chronic single dermatomal lumbosacral radicular pain. DRG PRF treatment was carried out in the Day Surgery Unit. CSF samples were taken prior to the procedure and three months after. CSF lymphocyte frequencies and levels of cytokines, chemokines and growth factors were quantified using flow cytometry and enzyme-linked immunosorbent assay (ELISA), respectively. Clinical assessment utilised Brief Pain Inventory scores.

Results: 9/10 patients (90%) demonstrated significant reduction in pain severity (p=0.0007) and pain interference scores (p=0.0015) 3 months post-treatment. Our data revealed significant reductions in CD56+, CD3-, NK cell frequencies (p=0.03) and IFN-γ levels (p=0.03) in treatment responders, while CD8+ T cell frequencies (p=0.02) and IL-6 levels were increased (p=0.05). IL-17 inversely correlated with post-treatment pain severity score (p=0.01) and pre and post-treatment pain interference scores (p=0.03, p=0.01).

Discussion: Our findings represent DRG as an important target for pain modulation. The mechanism of action of DRG PRF therapy in highly selective group of patients with chronic radicular pain might be immunomodulatory as evidenced by changes in cytokine levels following the procedure.

Conclusions: This study provides novel information regarding possible immune mediated mechanisms of DRG PRF treatment and potential biomarkers for diagnosis, prognosis and treatment of chronic pain.

***Objectives*:**

Altered CD56+ CD3− NK cell frequencies

Change in IFN-γ and IL-6 levels

Alternative therapeutic potentials in future

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Poster Presentations - May 27 - May 30
Basic Science

84. INS19-0369

PRECLINICAL OUTCOMES OF STIMULATION PARAMETERS FOR SACRAL NEUROMODULATION ON VOIDING AND DEFECATORY DYSFUNCTION: A SYSTEMATIC REVIEW

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Introduction: Stimulation parameters for sacral neuromodulation (SNM) have hardly changed over time. In the clinic, conventional stimulation settings using a frequency of 14 Hz and a pulse duration of 210 μs were originally used to treat voiding dysfunction, and were later adopted for defecatory dysfunction. Conventional SNM showed a positive effect as a treatment for voiding and defecatory dysfunction, but improvements of clinical outcome are still feasible. Currently, in preclinical research new stimulation parameters are investigated to achieve a better and longer effect.

Materials/Methods: The literature search was conducted using three databases: Ovid (Medline, Embase) and PubMed. Articles were included if they reported on stimulation parameters in animal studies for voiding or defecatory dysfunction as a primary outcome. Fourteen articles and five abstracts were eligible for inclusion and various aspects of stimulation parameters were included; frequency, intensity, continuous vs intermittent, and unilateral vs bilateral stimulation.

Results: Results from this systematic review tentatively suggest that low frequency stimulation (LF-SNM; 5, 7.5 or 10 Hz) induced a maximal increase in functional bladder capacity and inhibited bladder overactivity, investigated in feline, ovine and rodent species.

Discussion: LF-SNM at 2 Hz showed a superior effect in anal canal evoked potentials in rodent species. However, high frequency stimulation (HF-SNM; 600 Hz, 12.5 kHz) seems to inhibit the external urethral sphincter and allow voiding, investigated in feline and canine species. In addition, SNM intensity at or above motor threshold resulted in an increased functional bladder capacity in ovine and rodent species.

Conclusions: Even though these results are interesting, the amount of studies available is very limited. With a variety in stimulation parameters, a better effect of SNM could be achieved, but additional research is essential before new stimulation parameters can be applied in the clinic.

***Objectives*:** This systematic review summarized the current status of SNM stimulation parameters and its effect on voiding and defecatory dysfunction in preclinical research and compared the current status of SNM stimulation parameters of the different dysfunctions.

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Poster Presentations - May 27 - May 30
Basic Science

85. INS19-0088

PROGRAMMING STRATEGIES IN POST-IMPLANT CLINICAL SESSIONS: USEFULNESS OF COMPUTER MODEL TO PREDICT THE PARESTHESIA AREA DISPLACEMENT IN THE TRANSVERSAL DIRECTION

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Introduction: Changes in the paresthesia area is a challenge for the clinician when reprogramming SCS devices. Translation of anodes and cathodes along a lead has normally a direct impact in the paresthesia area, in the same direction as the translation of the cathode (rostrocaudal). The problem appears when we must move the area laterally.

Materials/Methods: We used a mathematical model at T8 level, to analyze how the addition of anodes in the opposite lead (also called transverse stimulation) in a two leads configuration, influences the position of the sweet spot (the first activated fiber) and the zone of paresthesia. Guarded Cathode (GC) and Double Guarded Cathode (DGC) with three distances between leads were analyzed in terms of threshold, stimulation area and position of the first activated fiber (sweet spot).

Results: When anodes were added in the opposite lead, we observed an unexpected effect: the stimulation area was laterally moved to the opposite side of the second lead. In addition, the activation area was also reduced when using transverse stimulation. However, as shown in Table 1, the activating area translation depends on distance between leads and polarity (GC and DGC). So, in both polarities the activating area is maximized when leads are closer together (1.2 mm), but the biggest translation in DGC is achieved at 1.2 mm of distance whereas at 3 mm in GC. Both values are maximized when using DGC versus GC.

Discussion: We supposed that the area of stimulation followed the changes in the electric field, i.e., adding an anode in the opposite lead moves the area to the center of the spine between both leads, but it follows the second difference of the electric potential, a parameter not as intuitive as the first one. In consequence, the effect of new anodes in the second lead moves the stimulated fibers just in the opposite direction than expected.

Conclusions: The fact that the stimulation area is moved outside the leads adding anodes in the opposite lead could be a useful strategy in cases were the leads are too medial and it is difficult to move to one of the sides, or other situations where a lateral movement of the stimulation area is desirable.

Objectives

- Show the usefulness of computer models
- Rebate intuitive ideas about stimulated fibers
- Propose new resources for programming neurostimulators

References

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Basic Science

86. INS19-0160

COMPUTATIONAL MODELING OF THE EFFECTS OF STAND-ALONE VS. SIMULTANEOUS PARESTHESIA-BASED AND SUBPERCEPTION SCS ON DORSAL HORN INHIBITION

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Introduction: Despite both paradigms being effective, paresthesia-based and sub-perception SCS exhibit key feature differences—notably lead placement, presence/absence of paresthesia, and pain relief wash-in time—suggesting distinct mechanisms of action and the possibility that applying both modalities simultaneously may improve therapy. This study used computational modeling to test the hypothesis as to whether simultaneous application of paresthesia-based and sub-perception SCS increases dorsal horn inhibition relative to the effects produced by each individual therapy.

Materials/Methods: We simulated the effects of paresthesia-based and sub-perception SCS on dorsal horn inhibitory interneurons (IINs) in a manner that reflected the hypothesized stimulation targets: far-field 50Hz paresthesia-based SCS was modeled as dorsal column-originating synaptic events injected into the dendrites of the IIN. Near-field 1 kHz sub-perception SCS was modeled using a finite element model of SCS and directly coupled to the biophysical IIN model. As IIN activity is hypothesized to relate to dorsal horn inhibition and a greater therapeutic effect, we compared the firing rate of the IIN following each stand-alone modality with effects following simultaneous stimulation.

Results: For some model IIN states, simultaneous stimulation enhanced the response of the IIN to 50Hz even when sub-perception stimulation alone did not produce an effect. For other IIN states, both 50Hz SCS and 1 kHz sub-perception SCS independently increased the firing rate of the IIN from baseline. In the latter states, the effects of 50Hz and sub-perception SCS on the IIN firing rate were additive when applied simultaneously and were sensitive to the strength of the 50Hz synaptic input.

Discussion: The results of this study further underscore the importance of considering the dorsal horn as an inter-connected network and call for investigations of multiple mechanisms as drivers for the therapeutic effects of SCS. More sensitivity analyses and experimental verification are required to confirm these computational predictions.

Conclusions: This computational study supports the simultaneous delivery of multiple waveforms to multiple targets as a method to unmask and/or enhance dorsal horn inhibition by individual SCS modalities.

Objectives

1. Computational modeling was used to assess the effects of stand-alone and simultaneous 50Hz and 1kHz SCS on dorsal horn interneurons.
2. Simultaneous 50 Hz and 1kHz SCS either unmaksed or enhanced the effects of each individual modality in a manner that was sensitive to the state of the cell model.
3. More research is required to understand whether and how the delivery of multiple SCS waveforms to multiple targets may improve therapy.

Poster Presentations - May 27 - May 30
Basic Science

87. INS19-0091

EVOKED COMPOUND ACTION POTENTIALS TO GUIDE LEAD PLACEMENT: A NEUROMONITORING TECHNIQUE—CASE SERIES

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Introduction: SCS has relied on overlapping paresthesia with the patient's painful area. The procedure to place leads at the appropriate location on the spinal cord traditionally required patients to be awake for reporting of device-induced paresthesias. Conversely, neuromonitoring using electromyography (EMG) recording is employed to determine optimal lead location while the patient is under general anesthesia. These techniques have been compared, in both retrospective and prospective studies with regards to safety and efficacy, favoring the use of neuromonitoring (*Neuromodulation*. 2012;14:130-5; *Neurosurgery*. 2018, doi:10.1093/neuros/nyy062). We present an update to data previously reported, with 7 subjects, incorporating the use of Evoked Compound Action Potential (ECAP) recording from implanted electrodes, using a new SCS system, and comparing the results with EMG recording.

Materials/Methods: Standard neuromonitoring protocols were employed at 2 institutions with 2 separate physicians. Once leads were implanted, stimulation current was increased until the following were observed: ECAP and EMG signal (late response [LR]) on the implanted electrodes, and EMG signal on the neuromonitoring EMG electrodes. Stimulation and recording was performed at multiple locations along each lead. An x-ray was obtained; postoperative paresthesia testing was performed to assess coverage obtained at different points along the implanted leads.

Results: Data were obtained from 7 patients, across 2 sites, demonstrating that ECAP and EMG signals can be successfully recorded in patients under general anesthesia. Onset of EMG signals on implanted electrodes and EMG electrodes correlated. Furthermore, the ratio of current amplitude between EMG onset and ECAP onset (LR:ECAP), on implanted leads, provides a potential estimate of lead laterality and objective lead placement. Whereby a ratio <1 indicates leads are too lateral. This technique was used successfully to place leads under general anesthesia (1 case), without utilizing EMG recording as a dermatomal coverage marker.

Discussion: Intraoperative recording of ECAPs and EMG signals from implanted leads may facilitate optimized lead placement, like traditional neuromonitoring, without requiring additional equipment and setup. Furthermore, analysis of ECAP morphology and its relationship with different waveforms could have diagnostic capabilities intraoperatively. This could be correlative with recent results showing the effect of different waveforms on EMG recording (*Neuromodulation*. 2018, doi:10.1111/ner.12781) and would be interesting to replicate while also recording ECAPs and EMG from implanted electrodes.

Conclusions: Further research is required to assess this new technique.

Objectives

1. ECAP recording may facilitate objective lead placement.
2. ECAPs may be a useful diagnostic tool intraoperatively.
3. ECAP recording could eliminate extra EMG recording equipment and personnel requirements.

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Basic Science

88. INS19-0394

DORSAL ROOT GANGLION STIMULATION AND PAIN RELIEF IN A RAT MODEL OF PAINFUL DIABETIC PERIPHERAL NEUROPATHY: BURST AND EFFECT OF AMPLITUDE

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Introduction: Dorsal root ganglion stimulation (DRGS) has recently emerged as a neuromodulation modality in the treatment of chronic neuropathic pain(1). The objective of this study was to compare the efficacy of different Burst-DRGS amplitudes in an experimental model of painful diabetic peripheral neuropathy (PDPN).

Materials/Methods: Diabetes Mellitus was induced in female Sprague-Dawley rats by intraperitoneal injection of streptozotocin (STZ, n=28). Animals were tested for mechanical hypersensitivity ($\log_{10}$ (10.000 x 50% withdrawal threshold (WT) on von Frey test) before, and 4 weeks after STZ injection. PDPN rats (n=13) were then implanted with a unilateral bipolar electrode at the L5 DRG. Animals received Burst-DRGS (interburst frequency=40Hz, intraburst frequency=500Hz, pulse-width=1000µs, interpulse interval=1000µs, burst pulse count=5) at 0%, 10%, 33%, 50%, 66% and 80% of motor threshold (MT) in a randomized crossover design on post-implantation days 2-7 (n=9). Mechanical hypersensitivity was assessed based on Von Frey filaments and hind paw withdrawal before stimulation onset, 15 and 30 minutes during stimulation, and 15 and 30 minutes after stimulation. Two animals were withdrawn from the study due to excessively high MT (>1mA) and two animals were withdrawn due to not displaying neuropathic symptoms following implantation.

Results: Burst-DRGS at amplitudes of 33%, 50%, 66%, and 80% MT resulted in a significant attenuation of STZ-induced mechanical hypersensitivity at 15 and 30 minutes during stimulation, as well as 15 minutes after cessation of stimulation. No effect on mechanical hypersensitivity was observed in animals stimulated at 0% MT and 10% MT. Furthermore, a significant overall effect of amplitude was observed (Figure 1). Responder rates were highest for animals which received Burst-DRGS at 50% MT and 66% MT (at 15 minutes) and 66% MT (at 30 minutes).

Discussion: A significant effect of amplitude was observed in animals stimulated with Burst-DRGS. Burst-DRGS amplitudes of 50% MT and 66% MT resulted in maximal response rates to mechanical hypersensitivity in rats with PDPN.

Conclusions: Further optimization and analysis of DRGS driven by insights into the underlying mechanisms of various stimulation paradigms is necessary.

Objectives: The objective of this study was to compare the efficacy of different Burst-DRGS amplitudes in an experimental model of painful diabetic peripheral neuropathy (PDPN).

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Poster Presentations - May 27 - May 30
Basic Science

89. INS19-0282

SHIFTING THE BALANCE BETWEEN HEMISPHERES OR SINGLE HEMISPHERE STIMULATION FOR RESPONSE INHIBITION

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Introduction: The ability to correctly inhibit response tendencies or stopping an ongoing response is central for goal direct behavior. In the mediation of this response inhibition, the right inferior frontal gyrus (rIFG) plays a central role, as shown by neuroimaging and neuromodulation studies. What remains poorly understood is the possibility of increasing the effects on inhibitory control of the anode over the rIFG, by additionally decreasing activity over the homotopic region. In this experiment we kept the anode over the rIFG and changed the size of the cathode over the left IFG (i.e., 35 or 100 cm2).

Materials/Methods: Sixteen-college volunteers (age: 21.5 ± 4.5, 11females) participated in this study. Participants were randomized and counterbalanced to receive, while performing a prepotent inhibition task, 20-min, of 2mA (i) bi-hemisphere tDCS (35 cm^2 anode over the rIFG and 35 cm^2 cathode over the left IFG -lIFG); (ii) uni-hemisphere tDCS (35 cm^2 anode over the rIFG and 100 cm^2 over the lIFG) or (iii) sham tDCS. A high resolution (1mm) MRI derived finite element method (FEM) model was produced to assess the predicted field intensity and current flow.

Results: Uni-hemisphere tDCS (M = 0.754, SE = 0.827) significantly increased performance compared to bi-hemisphere (M = 2.779, SE = 0.742) (p = 0.002) and sham tDCS (M = 1.885, SE = 0.903) (p = 0.035). Uni-hemisphere tDCS increased response time (M = 42.278, SE = 7.024) compared to bi-hemisphere (M = 6.509, SE = 13.538)(p = 0.015) and sham tDCS (M = 20.212, SE = 10.220) (p = 0.042). Results from FEM showed a symmetrical field intensity for the bi-hemisphere montage and field asymmetry (smaller field intensity/current density under the 100 cm2 electrode) for the uni-hemisphere montage.

Discussion: Uni-hemisphere tDCS increased accuracy at the cost of response time, showing a speed accuracy tradeoff (SAT). Shifting the balance towards the right hemisphere impaired the effects of tDCS over the rIFG, suggesting that bi-hemispheric stimulation may be an appropriate montage for disrupting inhibitory control.

Conclusions: The lack of results of bi-hemisphere tDCS suggests: (i) the potential role of lIFG in inhibitory response control, and (ii) the importance of considering the dual effects of tDCS when choosing the electrode montage.

Objectives:
Understand:
1. Inhibitory control
2. role of the IFG in inhibitory control
3. effects of tDCS in modulating inhibitory control

References

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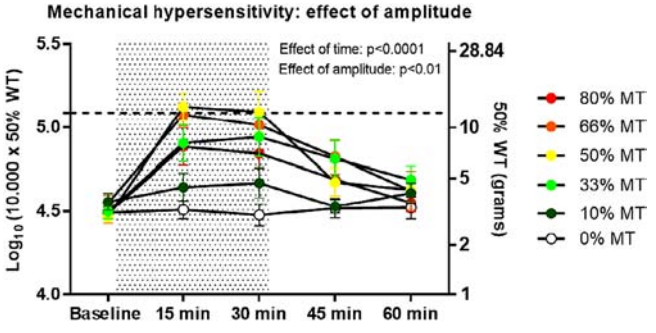

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Basic Science

90. INS19-0324

MODULATION OF CORTICAL EXCITABILITY AND FUNCTION BY RAPID ROTATION OF STRONG PERMANENT MAGNETS IN A WEARABLE BRAIN STIMULATOR

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Introduction: The cerebral cortex can be non-invasively stimulated by a rapidly changing magnetic field. We have recently developed a new method called transcranial rotating permanent magnet stimulation (TRPMS) using a wearable device that involves rapid rotation of strong neodymium magnets. The TRPMS device is capable of multifocal synchronous or sequential spatiotemporal stimulation using a new oscillatory mode that might be better at inducing long-term neuroplastic changes. Here we provide evidence that this device modulates motor cortex excitability and perceptual function.

Materials/Methods: To quantify the effects of TRPMS on motor excitability, we performed electromyographic recordings from the first dorsal interosseous muscle in healthy adults (n = 9) and measured motor-evoked potentials (MEPs) before and after active TRPMS or sham (rotated non-magnetic rod) stimulation over the contralateral motor hotspot using standard conventional transcranial magnetic stimulation (TMS) procedures. To study TRPMS modulation of sensory perception in healthy adults (n = 10) we tested whether active bifocal TRPMS or sham stimulation over the presumed right inferior parietal lobule (IPL) region and presumed right extrastriate body area (EBA) alters the Rubber Hand Illusion (RHI) in the contralateral hand using a proprioceptive hand location test.

Results: Repeated TRPMS stimuli of 100-ms duration delivered every 5 s for 20 min (240 stimuli) caused a 41% increase in the mean MEP amplitude at 20 min post-active TRPMS compared to a 1% increase post-sham stimulation ($p = 0.01$). The same parameters of active TRPMS applied for 10 min over IPL and EBA resulted in an attenuation of RHI, as measured by a significant ($p = 0.0005$) decrease in the mean distance between the real hand and its perceived localization by the subjects.

Discussion: The TRPMS-induced increase in cortical excitability is comparable to that produced by 10 or 20 Hz rTMS and theta burst stimulation in prior studies. Involvement of IPL and EBA in RHI, as indicated by the TRPMS effect, is consistent with previous unifocal stimulation studies using conventional rTMS.

Conclusions: Repeated intermittent stimulation over a single scalp location with the newly developed wearable TRPMS device appears to be comparable to rTMS in the effectiveness of neuromodulation. Given that multiple scalp locations can be simultaneously stimulated using TRPMS, our device therefore has a unique potential for multifocal in-home neuromodulatory therapies.

Objectives

1. Upon review of this abstract, delegates will become familiar with a new wearable multifocal non-invasive brain stimulator;
2. Its mechanism of action; and
3. Its effects compared with those of conventional rTMS.

References

None

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91. INS19-0406

ELECTRICAL STIMULATION PROMOTES NEURAL STEM AND PROGENITOR CELL MIGRATION IN MICE BRAINS

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Introduction: Neural stem and progenitor cells (NSPCs) are found in the periventricular region of the central nervous system. NSPCs proliferate, migrate and differentiate into different neural cell types. NSPCs have been shown to contribute to neural repair following injury. They are electrosensitive cells and their migration can be directed towards the cathode using charge-balanced electrical stimulation *in vitro*. With the goal of enhancing neural repair, we ask if application of electric fields in adult brains can lead to migration of transplanted NSPCs.

Materials/Methods: Fluorescent adult-derived NSPCs were transplanted onto the corpus callosum of adult mice. Intracortical platinum wire electrodes were implanted medial (cathode) and lateral (anode) to the injection site. Mice were electrically stimulated 2-days post-surgery for 4.5 hours over 3 days or 9 hours over 6 days. Mice were perfused after the last stimulation session. The charge-balanced biphasic stimulation waveform is similar to electric field strengths used to direct cell migration *in vitro* (250 mV/mm) (1). Through immunohistochemistry we investigated inflammation in the brain and the migration, proliferation and differentiation of the transplanted cells. The electric potential was measured medial-lateral to the cell transplant region in the corpus callosum of coronal tissue slices.

Results: Charge-balanced electrical stimulation compared to non-stimulated mice increased cathodal (medial) migration over 3 days, but not 6 days, *in vivo*. Inflammatory cell numbers near the electrode/transplant sites and transplanted cell differentiation/proliferation remained unchanged in stimulated vs. non-stimulated brains. The transplanted cells demonstrated preferential lateral migration in the absence of an applied electric field, which correlated with the measured endogenous electric potential being more negative lateral compared to medial.

Discussion: The charge-balanced stimulation did not cause a large inflammatory response or change in proliferation/differentiation of the transplanted cells while it did increase cell migration. The ability to direct NSPCs *in vivo* using electric fields without negatively impacting brain tissue holds promise for electric field application for brain repair. The preferential lateral migration and endogenous electric potential measurements demonstrates a need for optimized electrical stimulation paradigms in different environments.

Conclusions: Biphasic electrical stimulation can direct NSPC migration against electric potential gradients.

Objectives: The adult brain possesses NSPCs that have regenerative potential. These cells are electrosensitive. We can direct exogenous (transplanted) NSPC migration *in vivo* using electric fields.

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92. INS19-0175

LONG-TERM HIGH-FREQUENCY SPINAL CORD STIMULATION (SCS) ATTENUATES NEUROPATHIC PAIN THROUGH MODULATING MICROGLIA ACTIVATION AND POLARIZATION

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Introduction: Background: High-frequency (HF) SCS has been demonstrated to be successful for treating chronic neuropathic pain. However, the mechanism of HF SCS has been unclear. Microglial cells, as a type of important immune cells in the central nervous system (CNS), play an important role in pain regulation. The research regarding its analgesic effect on SCS is still in blank. In this study, we investigated the mechanism of microglial regulation behind the pain relief induced by HFSCS.

Materials/Methods: **Methodology**: Male SD rats weighting 200-230g were allocated to 4 study groups: vehicle group; sham-group; SNI group; SNI+4 days HF SCS. Neuropathic pain model was via spared nerve injury (SNI) surgery. The spinal column of the rat was exposed by a mid-line lumbar incision followed by laminectomy at T12–T13. A custom-made 4-contact electrode (0.9mm diameter; mainland company) was introduced into the epidural space at T13 level. SCS was delivered for 60mins/4 days beginning 2 weeks after SNI as follows: frequency:10khz; pulse width: 20μsec; amplitude: 0.4v (90% motor threshold). The paw withdraw threshold (PWT) was measured by von Frey test each 15min during the SCS. Western blot and immunofluorescence were used to measure the expression and the cellular distribution of CD86/IL-1beta and CD206/Arg-1.

Results: Results Before SNI, baseline PWT was measured. Two weeks after SNI, all groups showed a significant decrease in their PWT ipsilaterally ($p<0.05$, n=6). HFSCS significantly increased the PWT of SNI+HFSCS group at the 1st day($p<0.05$,n=6)and reached the peak at the 4th day ($p<0.01$,n=6) compared with the sham group. The analgesic effect of SCS lasted up to 15 days since the first time SCS, and gradually returned to the same level ($p>0.05$ n=6) as sham group. The expression of IL-1β increased after the long term HFSCS ($p<0.05$ versus sham group) whereas the expression of CD206 and CD86 showed an opposite trend in the SNI +HF SCS group. Furthermore, after long term HFSCS, the activation of microglia was significantly reduced in the SNI+HFSCS group ($p< 0.01$ versus the sham group).

Discussion: Conclusions HFSCS increased the PWT after SNI and the analgesia continued up to 15th days, suggesting that the long term HFSCS may be an effective parameter in clinical. One potential mechanism for HFSCS may be to reduce glial activation, as well as changing the microglia polarization to the M2 type at the level of the spinal cord.

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93. INS19-0347

CREATING A RELATIONAL MAP BETWEEN SPINAL STIMULATION AND LIMB ACTIVATION, PLASTICITY FOLLOWING SPINAL INJURY

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Introduction: Spinal segmental anatomy has a repeated sensorimotor neuro-architecture comprised of motoneurons, sensory fibers and interneurons, constituting canonical motor microcircuits (CMMs) which innervate the entire body. CMMs are an attractive target for electrical stimulation because following spinal cord injury (SCI), segments below the injury site contain the functional elements necessary to generate movements. As such, direct electrical stimulation (DES) of the spinal cord has tremendous therapeutic potential for SCI. However, two major issues need to be addressed. First, DES activates fibers of passage that send projections to multiple segments. Thus, a 'stimulation map' relating DES sites to muscle activation needs to be established. Second, spinal injury not only disrupts descending motor commands, but can also damage descending neuromodulatory inputs from the brainstem. These inputs modulate the excitability of neurons in the CMM and can thus alter the stimulation map. Here we stimulate the lumbar spinal cord of decerebrate cats prior to and after complete SCI. Our results demonstrate that the resulting map changes considerably following injury.

Materials/Methods: A laminectomy exposing the lumbar spinal cord was performed and the dura removed in the decerebrate feline preparation. EMG wires were inserted into selected hind limb muscles across all 3 limb joints (ankle, knee, hip). The spinal cord was stimulated (1ms duration pulses, 1Hz, 10-500uA) at predetermined sites and muscle activations were recorded. Finally, a complete transection (T13-14) was performed and the stimulus paradigm was repeated.

Results: Using DES we are able to effectively generate a map relating stimulation site to muscle activity. Importantly, this map changes substantially after spinal transection. Following transection, individual stimulus locations activate more muscles than pre-injury.

Discussion: Spinal cord motoneurons (MN) display considerable plasticity due to modulation of intrinsic properties by descending brainstem inputs. This plasticity acts as a gain control for MNs but also effectively serves as a filter for synaptic pathways. The normally focused nature of reciprocal inhibition for example is significantly altered following spinalization and loss of these inputs. Here the effect of spinal injury changes the relational map and provides a predictive tool as various other injuries are modeled (dorsal/lateral hemisection etc…).

Conclusions: Functional DES mapping is attainable in the feline preparation. Spinal injury drastically changes this map.

Objectives: Demonstrate the importance of descending neuromodulatory inputs. Demonstrate a mechanism of electrical stimulation of the SC. Reveal the effectiveness of DES.

References

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94. INS19-0341

10 KHZ ELECTRICAL STIMULATION OF THE SPINAL CORD SUPPRESSES LASER-EVOKED AFFERENT NEURAL HYPERACTIVITY

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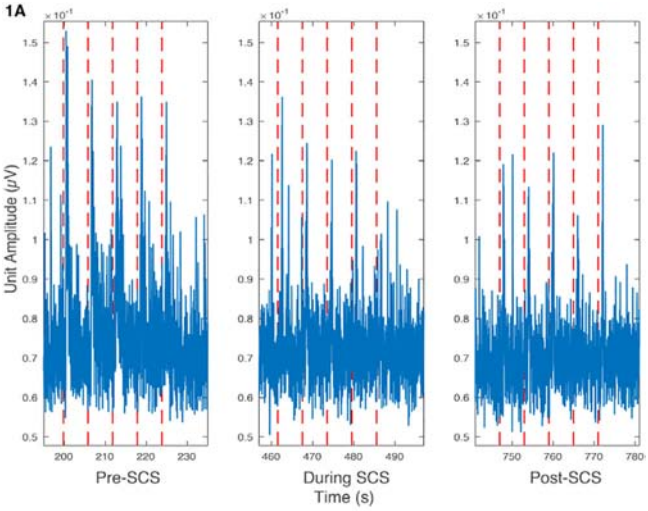
Introduction: Hyperexcitability of wide dynamic range spinal dorsal horn (DH) neurons has been associated with chronic pain states. Past experiments have demonstrated the usefulness of methods such as brushing, poking, and pinching of cutaneous sites to evoke neural responses from hyperexcitable DH neurons. However, these techniques activate neurons via a 'sensory size principle', where using ostensibly painful high intensity mechanical stimuli always activate low-threshold innocuous afferents simultaneously with high-threshold noxious afferents. This may result in mixed responses when studying pain mechanisms. In an effort to focus solely on DH response to nociceptors, we used a laser to study both optical/thermal evoked responses as well as the influence of low intensity high frequency 10kHz spinal cord stimulation (10kHzSCS) on DH neurons.

Materials/Methods: A normal adult male Sprague Dawley rat was anaesthetized with urethane in a Nevro-run facility. After a multilevel laminectomy, 10kHzSCS was applied via a micro-sized in-line quadripolar electrode array positioned epidurally over the L5-L6 dorsal spinal segments (innervating the left hind paw). A 16-contact extracellular recording electrode was plunged into the superficial DH (300±50um below cord surface) within 1mm of the active contacts on the quadripolar SCS array. To characterize the response of DH neurons to various types of stimuli and determine the effect of 10kHzSCS on laser evoked potentials, we used the following sequence of stimuli on the ipsilateral hind paw: 1st: innocuous brush; 2nd: painful laser (500ms duration, ~120mW power, 2mm^2 spot diameter), 3rd: painful laser & 10kHzSCS (20% of motor threshold), 4th: painful laser, 5th: innocuous brush.

Results: Brush stimulation reliably evoked responses from DH neurons both before and after laser stimulation. Laser stimulation (indicated by red dashed lines) evoked an initial neural response by an afterdischarge response (left panel, Fig 1A). In the presence of 10kHzSCS, while the laser still evoked short-latency potentials, this afterdischarge was suppressed (middle, 1A). Even ~250s after 10kHzSCS is removed, the afterdischarge remains largely suppressed (right, 1A). Across 9 units that showed at least 3Hz response in the 3s following each of 5 laser pulses, the median firing rates for before, during, and after 10kHzSCS were 121, 29.9, and 31.5 Hz, respectively (Fig 1B).

Discussion: Conclusions: Painful laser stimulation on the skin reliably evokes responses from DH neurons. In the presence of subthreshold 10kHzSCS, the afterdischarge is suppressed. This DH afterdischarge suppression may help explain the mechanism by which subthreshold 10kHzSCS reduces pain clinically. Further investigations are underway to validate these early observations.



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95. INS19-0328

RAT FMRI BRAIN RESPONSES TO NOXIOUS STIMULATION DURING TONIC, BURST, AND BURST-MICRODOSING SPINAL CORD STIMULATION

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Introduction: Spinal cord stimulation (SCS) is used to treat various chronic pain conditions. Different stimulation patterns have been proposed to optimize efficacy. Here, we compare three clinically-relevant stimulation temporal patterns in a preclinical model, including animals with neuropathic pain, and evaluate efficacy by mapping the integrated response of pain-activated brain centers to these SCS treatments using functional magnetic resonance imaging (fMRI), which avoids limitations of pain testing by simple reflex behaviors.

Materials/Methods: Both naïve adult male rats and ones 2wk post tibial nerve injury (TBI), had a custom SCS electrode (0.005in Pt/Ir 2.5mm apart) inserted to T13. During anesthesia (dexmedetomidine/pancuronium), 9.4T imaging was performed using Gradient Echo-Planar Imaging (EPI; TR=2s, TE=19ms, FOV=35mm, 128x128 matrix, 1mm slices). Noxious stimulation ("Nox") was administered to the ipsilateral toes as blocks (20s ON, 40s OFF, total 3min 40s). Acquisitions included Nox alone, then Nox during SCS (90% motor threshold). SCS was either Tonic (0.3ms, 40Hz), BurstDR (five 1ms pulses at 500Hz, repeated at 40Hz) [1], or BurstDR microdosing (mBurstDR; 5s ON, 5s OFF). EPI acquisitions were used to create activation maps (F-test on the time series, block design as regressor; $p<0.005$ threshold). Activated voxel time-courses from specific ROIs were averaged across animals; treatment effects were mapped using paired t-tests ($p<0.05$, cluster of >20 voxels) to identify affected regions.

Results: For naïve animals, Nox produced dominant signal changes in three regions. Primary somatosensory cortex (S1HL, sensory/discriminative) showed modest reduction of activation by Tonic, but greater, comparable effects of Burst and mBurst. For caudate putamen (emotional/motivational), Burst and mBurst nearly eliminated Nox-induced changes, whereas Tonic has a moderate effect. Anterior cingulate (Cg, cognitive/affective) showed a similar pattern. Nox-induced thalamus activation was unaffected by SCS. Comparable findings were observed in TNI animals, with most marked effects by Burst and mBurst, especially in S1HL and Cg.

Discussion: These findings show that all tested patterns of SCS suppress brain activation induced by pain, in animals with and without neuropathic pain. Considering what is known about homologous brain centers in humans, these observed changes may represent analgesia in the behaving rat, allowing comparison of stimulation patterns.

Conclusions: Our data indicate that Burst stimulation reduces pain activation more effectively than tonic stimulation, and that mBurst is comparable to Burst.

Objectives

1. Understand fMRI pain imaging.
2. Recognize selective pain roles of specific brain regions.
3. Appreciate efficacy differences in SCS stimulation patterns.

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96. INS19-0420

EFFECTS OF LACTATE RELEASED BY ASTROCYTES ON NEURAL ACTIVITIES IN THE MEDIAL VESTIBULAR NUCLEUS

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Introduction: The pathogenesis of vertigo caused by saccharometabolism or impaired blood flow may be happened by abnormal energy metabolism of astrocytes in the central vestibular system. From this hypothesis, we verified whether controlling metabolism of astrocyte in the central vestibular system of rats can regulate the excitability of metabolism and neural plasticity in the central vestibular system. The astrocyte provides lactate to neurons through monocarboxylate transporter (MCT). Moreover, L-lactate has been known as a main fuel for neuronal activities. In this animal experiment, we used MCT blocker α-cyano-4-hydroxy-cinnamate (4-CIN) to verify the role of astrocytes to control neuronal activities in the medial vestibular nucleus (MVN).

Materials/Methods: *In vitro*. Rats (4~5 weeks) were anesthetized with urethane and then decapitated. The brain was rapidly removed and put in ice-cold artificial cerebrospinal fluid. After that, the brain was cut by a vibratome. Cut slices were transferred to a holding chamber. A MVN slice was placed on the Multi-Electrode Array (MEA). Field potentials were evoked by injecting bipolar single pulse (200 μs width) through an electrode placed on MVN. EPSPs (excitatory postsynaptic potentials) were monitored at 30 seconds intervals under no 4-CIN or various 4-CIN concentration (200 μM, 500 μM) with 2.5 mM glucose.

In vivo. All rats (300 ~470 g) were anesthetized with urethane solution. 2 tetrode electrodes were placed in the MVN. Action potentials were continuously recorded before and after injecting 4-CIN (25μg/ml) into MVN.

Results: 200μM 4-CIN had no significant effect at EPSPs in the MVN. On the other hand, 500μM 4-CIN inhibited EPSPs in the MVN. In addition, spontaneous firing rates of type I and II neurons in MVN decreased over one hour after the injection of 4-CIN (25μg/ml) into MVN.

Conclusions: We propose that the lactate provided from astrocytes plays a pivotal role for an essential energy source and the regulator of vestibular system. Therefore, the abnormal activity of astrocytes may be one cause of vertigo. Moreover, the stabilization of metabolism in vestibular system may be a possible approach for an alternative treatment of vertigo.

Objectives

To understand the role of astrocytes in vestibular system
To verify effects of lactate on neurons in vestibular nucleus
To know how to measure neuronal activities in the MVN

References

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97. INS19-0064

PAIRED ASSOCIATIVE STIMULATION IN THE VISUAL CORTEX

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Introduction: Neuroplasticity in the visual cortex is essential for cognitive functions associated with visual processing. In humans, pathophysiological alterations of visual cortical excitability are observed in migraineurs. Visual plasticity can be induced via light deprivation or non-invasive brain stimulation protocols over the visual cortex. However, a synapse-specific plasticity, which is suggested as the key component in learning and memory processing, has not been demonstrated in human visual cortex so far.

Materials/Methods: In this study, we investigated neuroplasticity in the primary visual cortex using paired associative stimulation (PAS). PAS was applied with the combination of flash stimulus and single-pulse transcranial magnetic stimulation (TMS) over the visual cortex at inter-stimuli interval (ISI) 110ms or 85ms for the induction of excitatory or inhibitory plasticity respectively. In addition, two extra conditions with only visual stimulation or TMS were also implemented as experiment controls. Visual evoked potentials (VEPs) and phosphene thresholds (PT) were recorded from sixteen healthy adult participants.

Results: PAS with ISI 85ms (PAS85), which induces desynchronized stimulation of the visual cortex via TMS and visual stimuli, generated a significant decrease of visual cortex excitability. PAS at ISI of 110ms (PAS110) did not generate significant change in cortical excitability at the whole group level. However, subjects who received synchronous paired stimulation, as selected according to the individual VEP latency, revealed significant increase of cortical excitability PAS110. Both flash- and TMS-only conditions did not show any effect on cortical excitability.

Discussion: Our results revealed an induction of visual plasticity similar to the spike-timing-dependent plasticity (STDP) in animal studies, which is suggested as physiological basis of learning process.

Conclusions: In conclusion, in our study PAS85 induced a decrease of the visual cortical excitability, while PAS110 led to an increase of visual cortical excitability, establishing the transferability of PAS protocol to the visual cortex.

Objectives

1. Extending knowledge about visual cortical plasticity in humans
2. Transferability of PAS protocol in visual cortex
3. Providing possible clinical application

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98. INS19-0254

ELECTRICAL ACTIVITY EVOKED BY 10KHZ SPINAL CORD STIMULATION ON SUPERFICIAL DORSAL HORN NEURONS IN NEUROPATHIC PAIN RATS

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Introduction: Paresthesia-free 10kHz spinal cord stimulation (10kHzSCS) has Level I clinical evidence demonstrating clinically-superior, long-term pain relief. Recent studies in normal rats have suggested that 10kHzSCS selectively modulates interneurons in superficial dorsal horn (SDH). In order to see how 10kHzSCS may evoke responses on SDH neurons, we investigated the electrical activity of SDH neurons during 10kHzSCS field stimulation in a spinal cord slice preparation from neuropathic pain rats.

Materials/Methods: Neuropathic pain was induced by tight ligation of the L5 spinal nerve (SNL) in 8-14-week-old male Sprague Dawley rats. After sacrifice, the spinal cord ipsilateral to the site of injury was extracted and sliced (400-550 um thick) on the parasagittal plane with dorsal roots attached. Whole-cell patch-clamp recordings were obtained from dorsal horn lamina I/II neurons using MultiClamp 700B amplifiers. 10kHzSCS field stimulation electrodes using bipole cylindrical contacts (1mm length with 1mm separation), were placed parallel to the slice. Firing patterns of cells were identified by current injection and categorized into 'Tonic', 'Phasic', or 'Delayed/Irregular' firings. Charge-balanced biphasic square pulses at 10kHz were delivered in duty cycle mode (3-200ms ON with 2s OFF) at various amplitudes. The recorded signal from each patched-cell was filtered to remove high-frequency artifacts. Post-synaptic potentials, either excitatory (EPSP) or inhibitory (IPSP), evoked by 10kHzSCS, were categorized into 'EPSP', 'IPSP' or 'EPSP followed by IPSP'.

Results: Twenty-five SDH neurons were recorded and categorized into Tonic (40%), delayed/irregular (28%) and phasic (32%) firing patterns. In response to 10kHzSCS: Tonic firing neurons had post-synaptic responses as 54%(EPSP), 38%(IPSP) and 8% (EPSP-IPSP); Phasic firing neurons had 20% (EPSP), 20%(IPSP) and 50% (EPSP/IPSP); and Delayed/irregular firing neurons showed 78%(EPSP), 11%(IPSP) and 11% (EPSP-IPSP).

Conclusions: Duty-cycled 10kHzSCS field stimulation evoked a variety of post-synaptic potential responses in SDH neurons. A train of 10kHzSCS pulses evoked EPSP in the majority of tonic firing neurons, and IPSP (or EPSP->IPSP) in most phasic firing neurons. While these responses were recorded at 10kHzSCS amplitudes that would translate to higher values than those used clinically, these results suggest different sensitivities of SDH neurons to 10kHzSCS electrical fields and may provide insights into the electrophysiological characteristics of neural responses to 10kHzSCS in the spinal cord.

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99. INS19-0256

COMPARING THE FIRING PATTERNS OF SUPERFICIAL DORSAL HORN NEURONS EVOKED BY ROBOTICALLY AUTOMATED AND HUMAN MANUAL BRUSHING AND VON FREY HAIR STIMULATION

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Introduction: Investigations into the response of spinal dorsal horn (SDH) neurons to afferent inputs typically employ various types of mechanical stimulation to peripheral structures (e.g., a rodent paw). Most often, these stimuli are applied manually to a receptive field; manual application may contribute to inconsistent variation in the parameters of the stimulus: temporal timing, duration, location, etc. We compared the spinal dorsal horn neural response between manual and custom robot-based brushing/Von Frey stimulation system.

Materials/Methods: A robot with four degrees of freedom was programmed to brush the hind paw of an anesthetized rat. Multichannel electrodes were placed in the ipsilateral SDH (lamina II-III, the spinal segment L4-6) to monitor single unit firings evoked by a similar brushing motion and Von Frey stimulation performed by the robot and from a trained examiner. The robot brushing was programed to brush in an arc motion at different depths (0.5, 1, 2 and 3mm), speeds (50, 100 and 200mm/s) and directions (proximal to distal vs. distal to proximal). Von Frey hair stimulation was applied with 2, 6, 10 and 15g hair for 1.5s. This research was done at animal facility under provision of InterVivo (Mississauga, ON, Canada) with IACUC approval.

Results: Qualitatively, automated brushing and Von Frey generated consistent and repeatable patterns of multiunit SDH activity. Manual forward brushing was most similar to the automated brushing with depth=2mm, speed=100mm/s in terms of firing rate and duration. Manual Von Frey duration had during of 0.76±0.12s with intension of 1 s stimulation duration, while automated Von Frey had duration of 1.4±0.02s. Mean firing rate from manual Von Frey was ~10% higher than automated stimulation. Interestingly, it appeared that most recorded neurons, activated by manual brushing or Von Frey hair were also fired by automated brushing, but certain neurons were activated more by manual mode or the other.

Conclusions: Standardization of the sensory stimulus using this novel robot tool may allow for fewer trials of applied afferent input and greater sensitivity to detect subtle changes in response in sensory experiments or intervention such as spinal cord stimulation.

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100. INS19-0247

HIGH FREQUENCY KHZ SPINAL CORD STIMULATION (SCS) MODULATE SPINAL DORSAL HORN NEURONS IN NEUROPATHIC PAIN RATS

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Introduction: Paresthesia-free 10kHz spinal cord stimulation (10kHzSCS) has Level I clinical evidence demonstrating clinically-superior, long-term pain relief. Recent studies in normal rats have suggested that 10kHzSCS selectively modulates interneurons in superficial dorsal horn (SDH). In order to see how 10kHzSCS might modulate spinal interneurons to relieve neuropathic pain, we investigated brush and von Frey (VF) evoked responses (firing rate) of SDH neurons in neuropathic pain model rats.

Materials/Methods: Neuropathic pain was induced by tight ligation of the L5 spinal nerve (SNL) in 9-week-old male Sprague Dawley rats. 10-14 days after SNL surgery, electrophysiological recordings were made under urethane anaesthesia. In all experiments, bipolar 10kHzSCS at 30% of motor threshold (MT) was applied via a micro-sized in-line quadripolar electrode array positioned epidurally over the L5-L6 dorsal spinal segments. A 16-contact extracellular recording electrode was plunged into the SDH (depth from cord surface: 300±50um) within 1mm of the active contacts on the SCS array. First, we used brush and innocuous VF (10g) stimuli on the ipsilateral hindpaw to find the receptive-field center, and to characterize the type of responsive SDH neurons by their firing pattern. We then applied brush and VF (1, 2, 6, 10, 15g) to investigate the input-output relationship (I/O) of SDH neurons before (Baseline) and during 10kHzSCS. This research was done at animal facility under provision of InterVivo (Mississauga, ON, Canada) with IACUC approval.

Results: In 5 rats, a neuropathic pain condition was confirmed by clear expansion of the receptive field compared to normals. Also, brush-evoked responses of SDH neurons in SNL rats were reduced by ~40%. Three different cell types (Adapting, Non-Adapting, and After-discharging) were identified by 10g VF in neuropathic pain rats, whereas only two types (Adapting and Non Adapting) were previously identified in naïve rats. Compared to Baseline, during 10kHzSCS, there was reduction of slope of the I/O relationship in Adapting cells while the increase of Y-intercept was observed in Non-adapting cells with no change of slope.

Discussion: Per previous studies, Adapting and Non-adapting cells might be regarded as excitatory and inhibitory interneurons, respectively. These data suggest an underlying pain signal pathway and functional relationship between neurons in SDH, which is modulated by 10kHzSCS: Activity(excitatory neuron) = Primary Afferent Input/Activity(inhibitory neuron).

Conclusions: Thus, any increase in inhibitory interneuron activity (e.g., by 10kHzSCS), will reduce the influence of afferent drive on excitatory interneurons, and hypothetically provide a profound reduction in pain transmission in SDH.

Objectives: Mechanism of Action

References

Prescott, S.A. (2002)

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101. INS19-0251

DIFFERENTIAL MODULATION OF SPINAL DORSAL HORN NEURONS BY VARIOUS SPINAL CORD STIMULATION STRATEGIES

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Introduction: In spinal cord stimulation (SCS) for chronic pain, various stimulation strategies (10 kHz, asymmetric burst, and passive burst) have been clinically applied, though only 10kHz has shown long-term clinically-significant pain relief for back and leg pain [Kapural et al, Deer et al]. The mechanisms for these various strategies are not yet clear. Here, we investigated the responses of superficial dorsal horn neurons (SDHN) classified as adapting & non-adapting neurons (presumed excitatory & inhibitory interneurons, respectively) to different SCS strategies.

Materials/Methods: Adult male Sprague Dawley normal rats (N=5) under urethane anaesthesia were used. In all experiments, after multi-level laminectomy, SCS was applied via a micro-sized, in-line quadripolar electrode array positioned epidurally over the L5-L6 dorsal spinal segments (innervating the left hind paw). A 16-contact extracellular recording electrode (NeuroNexus) was plunged into the SDH (depth from cord surface: 300±50um) within 1mm of the active contacts on the quadripolar SCS array. First, we defined the receptive field center of SDHN by their most active response to brush and von Frey (VF) stimuli onto the ipsilateral hind paw. Then, we identified the neurons as adapting (n=9) and non-adapting cells (n=10) by their firing response to 10g VF, depth of location, etc. Twenty trials of each SCS strategy (10kHz, asymmetric burst, passive burst) at 30% of motor threshold were applied for 20sec with an intervening 2sec no-stim interval. At least 5min of quiescence was allowed between application of different strategies. Mean firing rate of neurons were analyzed as the response to SCS.

Results: Mean firing rate of non-adapting cells was increased about 5x Baseline during 10kHz, about 2.5x Baseline during asymmetric burst, while passive burst had no significant effect. In contrast, the mean firing rate of adapting cells was increased approximately 4.2x Baseline with asymmetric burst, whereas 10kHz and passive burst has no significant effect.

Discussion: We observed, at stimulation intensities that would ostensibly not activate dorsal columns (i.e. "paresthesia-free"), that (1) 10kHz selectively activates non-adapting cells, (2) asymmetric bursting nonspecifically activate SDHN, and (3) passive bursting SCS stimulates no SDHN.

Conclusions: This suggests that 10kHz may uniquely drive inhibitory cells, where burst strategies were ineffective or mixed excitation & inhibition in their effects on SDHN.

Objectives: Mechanism of Action and finding better strategy.

References

Kapural L et al.; Comparison of 10-kHz High-Frequency and Traditional Low-Frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain. Neurosurgery. (2016).

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102. INS19-0133

EFFECTS OF A NOVEL, PULSED EPIDURAL STIMULATION PATTERN ON WDR NEURONS IN THE DORSAL HORN OF RATS

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Introduction: Application of electrical fields to the dorsal surface of the spinal cord in the treatment of chronic pain has undergone significant change with respect to the stimulation parameters that are being utilized. Altering both patterning and frequency of stimulation has potential clinical benefits for both efficacy and utility. We tested the influence of a novel spinal cord stimulation pattern on pain processing neurons in the dorsal horn of the spinal cord.

Materials/Methods: Neuropathic pain was established in Male, Sprague-Dawley rats (n=8) utilizing a spared nerve injury model and confirmed through von Frey testing. Single-unit, extracellular recordings were obtained from wide dynamic range (WDR) neurons in the dorsal spinal cord laminae. Recordings were obtained through a tungsten microelectrode inserted into the spinal cord at 4 - 5thlumbar segments. A silver ball-type electrode was surgically placed on the dura (~T5) and connected to a programmable stimulator to deliver various stimulation parameters. Stimulation patterns included:1) 40-Hz tonic stimulation; 2) 10kHz tonic stimulation;3) 500 Hz burst pulse trains and 4) 3 novel, phasic stimulation patterns. Responses of WDR neurons were recorded before and after delivery of each of the stimulation waveforms for 5 min. Spontaneous activity and responses evoked by mechanical stimuli were observed before and after the various stimulation patterns in the same individual neurons.

Results: The novel, phasic stimulation pattern produced the most profound reductions in WDR neuronal firing when compared to other stimulation paradigms in the same cells. On average, discharge rates were reduced by more than 50% in evoked responses with the phasic stimulation pattern, which is greater than with other patterns. Moreover, the recovery time until returning to baseline firing was greater with the phasic pattern, suggesting a prolonged impact on synaptic and/or cell membrane physiology.

Discussion: The activity elicited in WDRs before and after each of the SCS patterns demonstrates the ability of various stimulation paradigms to influence response in the neurons recorded. In the current study, multiple stimulation patterns were tested in the same neurons, proving an opportunity to compare and contrast the effects of stimulation on both spontaneous activity and evoked responses. The novel, phasic pattern evoked the largest impact on neuronal functioning. These results provide complimentary mechanistic findings to clinical results from similar novel, phasic SCS in humans.

Conclusions: Continued research into this unique combination of stimulation paradigm elements will help understand how to best utilize this emerging and provocative stimulation pattern.

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103. INS19-0228

SACRAL NERVE STIMULATION INHIBITS THE MAPK/NF-KB SIGNALING PATHWAY AND PROMOTES TREG-TH1/17 CELL BALANCE IN TNBS-INDUCED INFLAMMATION IN RATS

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Introduction: TNBS is known to induce inflammation through triggering the MAPK/NF-kB pathway and activation of T helper cells. Stimulating of sacral nerve (SNS) was reported to improve the inflammation in TNBS-induced colitis in rats. The aim of this study was to investigate whether the SNS anti-inflammatory effect was mediated via the MAPK/NF-kB pathway and/or balancing Th1/17-Treg cells. We also explored if SNS could alter self-renewal of neurons in myenteric plexus.

Materials/Methods: Forty male Sprague-Dawley rats were implanted wire electrodes unilaterally at sacral nerve (S3). One week later, the rats were administrated with TNBS intra-rectally. Five days later, 20 of the rats were treated with SNS 1 hour daily for 10 days with the optimized parameters and the other 20 rats were treated with sham-SNS (exactly the same setting but SNS at 0mA). Additional 20 rats were treated with intra-rectal injection of saline, serving as controls. Various inflammatory factors were assessed by the disease activity index (DAI), macroscopic score, microscopic score, fluorescence-activated cell sorter and western blot. Longitudinal muscle myenteric plexus (LMMP) was studied by immunohistochemistry.

Results: 1) compared to sham-SNS, SNS significantly decreased DAI (area under the curve: 64.3±3.8 vs. 49.5±3.2, P<0.01), macroscopic scores (5.85±0.9 vs. 2.55±0.6, P=0.03) and microscopic scores (4.6±1.1 vs. 2.7±0.8, P=0.04) and normalized the colon length; 2) in colon tissues, compared with sham-SNS, SNS reduced the percentage of Th1 cells (8.87±2.32% to 5.40±1.39%, P=0.04) and Th17 cells (12.35±1.61% to 9.75±1.17%, P=0.04) but increased Treg cells (15.73±2.81% to 20.15±2.24%, P=0.03); 3) SNS reduced the percentage of the phosphorylation of MAPKs compared to Sham-SNS (p-ERK/ERK: 22.5%, P=0.03; p-JNK/JNK: 25.6%, P=0.04) and prevented the nuclear translocation of NF-κB p65 by 40.7% (P=0.02, vs. sham-SNS); 4) the percentage of choline acetyltransferase (ChAT) neurons were decreased by TNBS but reversed by SNS (19.06±2.07% to 25.68±3.56%, P=0.02).

Discussion: SNS is effective in inhibiting colon inflammation through the inhibition of the MAPK/NF-kB pathway, balancing of Th1/Th17-Treg cells, and also improving the LMMP neuronal self-renewal and regeneration.

Conclusions: SNS is effective in inhibiting colon inflammation through the inhibition of the MAPK/NF-kB pathway, balancing of Th1/Th17-Treg cells, and also improving the LMMP neuronal self-renewal and regeneration.

***Objectives*:** IBD is a worldwide healthcare problem with a continually increasing incidence. SNS could ameliorate the IBD symptoms through inflammatory pathways.

References

1. Optimization of sacral nerve stimulation for colonic inflammation in TNBS-induced colitis in rats. 2. Centrally mediated vagal efferent pathway involved in anti-inflammatory effects of sacral nerve stimulation

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104. INS19-0130

WIKISTIM.ORG UPDATE

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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. WIKISTIM 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.

Free CME credits are available for data abstraction.

A monthly email newsletter lists new citations for each stimulation target.

Access to WIKISTIM is free after registration.

Results: Current status (as of November 2018):

Registrants = 807.

DBS = 4624 entries; DRG = 86; GES = 476; PNS = 53; SCS* = 2254; SNS = 907. All lists are comprehensive except PNS, which is only comprehensive for peripheral nerve field stimulation.

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, 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.

Objectives

Improve access to primary neurostimulation data.

Improve the evaluation and comparative analysis of published data in the field of neurostimulation.

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.

References

North RB, Shipley J. WIKISTIM.org: an on-line database of published neurostimulation studies. Neuromodulation in press.

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105. INS19-0139

SYNERGISTIC MECHANISMS OF ACTION IN A NOVEL, PULSED SCS PATTERN

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Introduction: Newer spinal cord stimulation (SCS) techniques are employing higher pulse frequencies as well as bursting pulse trains. While there are many similarities in the outcomes between these stimulation patterns, such as a lack of paresthesias and the potential for improved analgesia, there are important, divergent physiologic mechanisms that are likely being activated. More recently, a novel stimulation pattern has evolved that encapsulates multiple phasic components. By combining crucial elements of stimulation patterns, synergistic effects may be observed both in terms of underlying mechanisms and clinical utility.

Materials/Methods: A critical review of the literature was completed to construct a comparison between the physiologic effects of various SCS patterns. At the same time, results from recent research on the neurophysiologic mechanisms and clinical outcomes of a novel, phasic SCS pattern was also compared and contrasted to prior stimulation patterns. Translational hypotheses are generated regarding the potential physiologic impact and potential of utilizing a stimulation pattern that comprises important individual patterned elements.

Results: Contemporary thoughts on SCS patterns diverge on underlying mechanisms producing analgesia. High-frequency stimulation (>1KHz) tends to cause reversible blockade of axons at high enough pulse amplitudes and can impact underlying tissues near the dorsal spinal cord. These effects include direct effects on dorsal column conduction, direct effects on structures in the dorsal horn and adjacent dorsal surface structures such as Lissauer's tracts. Burst stimulation frequencies are closer to the physiologic range of dorsal structures and, due to the phasic nature of the stimulation, may induce enhanced effects on dorsal column fibers and synaptic connectivity in pain processing pathways. The effects of combining phasic elements has shown potentiated effects on neurons in the spinal cord and also clinical effects that are consistent with these findings.

Discussion: Both basic and clinical research has substantiated findings that a novel stimulation pattern that incorporates multiple phasic stimulation elements can produce enhanced modulatory effects on neurons in the dorsal spinal cord. At the same time this same stimulation pattern produces analgesia in chronic pain patients that is substantially better than traditional SCS. These translationally relevant findings help verify the potential similarities and difference of this novel stimulation pattern in the treatment of chronic pain. Ongoing research will help further elucidate the clinical potential of this newly established and tested pattern.

Conclusions: Utilizing SCS patterns that can evoke a wide range of underlying analgesic mechanisms of action may provide a better approach in the treatment of chronic pain.

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106. INS19-0315

EFFECT OF HIGH-FREQUENCY ALTERNATING CURRENT PERCUTANEOUS STIMULATION OVER THE MEDIAN NERVE ON EVOKED PAIN AND MUSCLE STRENGTH: A SAFETY AND FEASIBILITY STUDY

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Introduction: In recent years a number of experimental animal studies have demonstrated that alternating currents applied at unmodulated frequencies of greater than 1 kHz produce a rapid and reversible peripheral nerve block without damage to the nerve itself [1]. Clinical studies to date have only investigated non-invasive transcutaneous stimulation protocols leading to an increase in somatosensory thresholds [2] and a decrease in the maximum manual grip strength [3]. The objective of this study was to determine the safety and viability of percutaneous ultrasound-guided stimulation of the median nerve with alternating currents of 30 kHz, in addition to determining its effect on pressure pain threshold and voluntary hand muscle strength in healthy subjects.

Materials/Methods: A case series of healthy volunteers is presented who were stimulated for 15 mins at 30 kHz with two acupuncture needles guided by ultrasound on both sides of the median nerve. Current intensity was adjusted to evoke a strong but comfortable tingling sensation, just below motor threshold. Measures included pain pressure threshold (PPT N/cm^2) recorded at T1 before, at T2 during the 10-minute intervention and at T3 immediately after the intervention. Hand grip strength (N) was recorded before (T1) and after the intervention (T3).

Results: Seven subjects participated (4 women and 3 men) with a mean age of 21.3 years (SD=2.5) with an average body mass index of 22.1 Kg/m2 (SD=2.9). The 30kHz stimulation increased PPT at the T2 by 6.5N/cm2 (SD=2.1, p = 0.069) and by 10.3N/cm2 (SD=2.5, p = 0.018) at T3 compared to T1. No effect was observed on manual grip strength. No adverse effects were recorded in the subjects recruited.

Discussion: Although, high frequency current to skin surface has shown some effect for blocking nerve fiber conduction, one of its limitations is poor penetration of the current [3]. In contrast other studies support the use of an ultrasound-guided invasive approach to better stimulate the nerve [4].

Conclusions: Echo-guided invasive stimulation of the median nerve using high-frequency alternating current is a safe and feasible technique that could be applied for the management of pain. Controlled studies with higher sample sizes will be needed to validate this paradigm.

Objectives

1) Evidence for percutaneous high-frequency nerve stimulation.
2) Safety and viability of new technique.
3) Sensory versus motor effects of nerve stimulation,

References

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107. INS19-0326

EFFECTIVENESS OF NON-INVASIVE SPINAL ELECTRICAL STIMULATION FOR THE FACILITATION OF QUADRICEPS MOTOR EVOKED POTENTIALS

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Introduction: Epidural spinal electrical stimulation at the lumbar level evokes rhythmic and alternating muscle activation patterns, attributed to the central pattern generator [1-4]. However, the role of non-invasive spinal stimulation for the activation of lower limb muscles is not yet clear. Here we investigated the effect of non-invasive spinal stimulation on quadriceps motor evoked potentials in healthy subjects.

Materials/Methods: A 10Khz modulated base current applied at 30Hz for 6 minutes was applied to healthy subjects. Two cathodes were placed bilaterally at vertebrae T11-T12 and two anodes placed on both sides of the navel, with the stimulus applied at a maximum tolerable intensity. Quadriceps motor evoked potentials (MEP) were recorded following transcranial magnetic stimulation during a submaximal 20% voluntary contraction. Peak-peak MEP amplitude was recorded before, during and after spinal stimulation.

Results: Five men and one woman were recruited with an average age of 40 years (SD=10). The current was perceived as tolerable but uncomfortable. No adverse effects were found after the application of the current. Quadriceps MEP increased from 0.31 ± 0.17mV ($p=0.006$) during and after 0.30 ± 0.16mV ($p=0.01$) spinal stimulation, compared to the baseline condition (0.24 ± 0.12mV).

Discussion: Non-invasive spinal stimulation facilitates corticospinal activation of the Quadriceps muscle with its effect lasting beyond the stimulation. However, although this approach may be viable to increase motor activity, recordings from other muscles would be necessary to determine specific activation of the central pattern generator.

Conclusions: Non-invasive lumbar spinal stimulation facilitates lower limb MEP lasting beyond the intervention. Further studies will be needed to determine the viability of using non-invasive spinal stimulation for the activation of the central pattern generator.

Objectives

1. Describe the method of non-invasive spinal stimulation to facilitate lower limb muscle activity.

2. Discuss methodological details to record Quadriceps motor evoked potentials with non-invasive spinal stimulation.

3. Reveal long-lasting effect of improving corticospinal activation of lower limb muscles after non-invasive spinal stimulation intervention.

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108. INS19-0111

MODULATION OF THE NEUROGLIA INTERACTION USING DIFFERENTIAL TARGET MULTIPLEXED SPINAL CORD STIMULATION IN AN ANIMAL MODEL OF NEUROPATHIC PAIN

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Introduction: Glia constitute the majority of cells in the spinal cord and play a vital role in regulation of synaptic transmission, neuron repair, and protection. Glia activation and potentiation are essential in development and maintenance of chronic neuropathic pain (NP). Glia responds to electrical stimuli, therefore is plausible to treat NP with spinal cord stimulation (SCS) using waveforms combined in a multiplexed manner to differentially target glia and neurons. This study evaluates the efficacy of differential-target multiplexed (DTM-SCS) approach in providing pain relief and compared it to low-rate (LR) SCS and high-rate (HR) SCS.

Materials/Methods: Procedures were approved by the IACUC at Illinois Wesleyan University. Male Sprague-Dawley rats, implanted with a four-contact cylindrical mini-lead, received the spared nerve injury (SNI) NP model (n=10-13/group). DTM-SCS (proprietary signals), LR-SCS (50Hz, 150μs) or HR-SCS (1200Hz, 50μs) was applied continuously for 48h at 70% motor threshold. Naïve rats (n=9) were also evaluated. Pain behavior (mechanical and thermal hypersensitivity) was assessed before SNI, and before and after SCS. Spinal cord tissues adjacent to lead were harvested and subjected to RNA-sequencing. Weighted gene co-expression network analysis (WGCNA) and gene ontology enrichment analysis (GOEA) identified biological processes affected by SNI and SCS. Statistical analysis (SPSS) was performed. $p<0.05$ was considered significant.

Results: DTM-SCS relieved mechanical hypersensitivity significantly better than HR-SCS and LR-SCS. DTM-SCS significantly relieved hypersensitivity to thermal stimuli, while neither HR-SCS nor LR-SCS reduced it significantly. WGCNA and GOEA indicate that SNI significantly affected expression of genes in biological processes such as regulation of immune system, ion transmembrane transport, and signal transduction. Although all SCS modalities modulated the expression of different genes towards levels in naïve animals, DTM-SCS modulated significantly more processes than HR-SCS and LR-SCS.

Discussion: DTM-SCS provided better relief of pain behavior than HR-SCS and LR-SCS. DTM-SCS significantly affected glial-mediated immune response, cell-to-cell communication, and neurotransmission that are central to homeostasis of neuroglial interaction, thus to chronic pain. DTM-SCS modulated expression of genes in these processes towards naïve levels more effectively than LR-SCS or HR-SCS.

Conclusions: Clinical efficacy of DTM-SCS for pain relief may involve a mode of action in which the homeostasis of neuroglial interactions is normalized.

Objectives

Identify molecular pathways associated with SCS.

Demonstrate the importance of neuro-glial interactions related to pain and SCS.

Understand the mode of action of SCS to improve patient outcomes.

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109. INS19-0184

TRANSLATIONAL COMPARISON OF RODENT AND SHEEP MODELS OF CONTINUOUS DIFFERENTIAL TARGET MULTIPLEXED SPINAL CORD STIMULATION

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Introduction: Spinal cord stimulation (SCS) is a safe and effective way to treat chronic neuropathic pain. Pre-clinical research allows exploration of multiple variables to better understand the mechanism of action underneath clinical effects. Recently, our group reported behavioral and molecular changes under different SCS waveforms in a rodent model. When compared with other modalities, differential target multiplexed SCS (DTM-SCS) uses combined pulses between 20 and 1,200Hz and pulse width below 500μs showed better behavioral results and unique modulation of relevant genes. Translation of those observations represents challenges, which may be overcome with a large animal model. We report the first translational comparison of rodent and sheep models of DTM-SCS in validated neuropathic pain models.

Materials/Methods: Procedures were approved by IACUCs at Illinois Wesleyan University and Medtronic Physiological Research Laboratory. The spared nerve injury (SNI) model was induced in rats (n=13) and the peroneal nerve injury (PNI) in sheep (n=4). Rats were implanted with a quadrupole cylindrical minilead (0.62mm diameter) and sheep were implanted with two octapole cylindrical human leads. DTM-SCS was applied continuously for 48 hours using equivalent parameters. Each sheep was retrialed three times, following a washout period, in order to obtain six data sets. Mechanical hypersensitivity (MHS) was tested before and after SCS using von Frey filaments. Repeated-measures ANOVA analysis were used to determine significant differences ($p<0.05$) relative to pre-stimulation scores.

Results: Consistent with literature, PNI and SNI models produced a marked decrease in MHS. Relative to pre-stimulation, DTM-SCS significantly relieved MHS (78.6% at 24h, 77.3% at 48h) in the rat model. These observations were reproduced in the sheep model where DTM-SCS also relieved MHS (84.8% at 24h, 73.7% at 48h) relative to pre-stimulation.

Discussion: This is the first study reporting consistent improvement in pain-like behavior after SCS among different species, validating the results. Transcriptomics results previously reported indicate that DTM-SCS improves mechanical hypersensitivity by modulating biological processes associated with neuro-glia interactions such as regulation of cell communication, signal transduction, and ion transport. Given the similarity in behavioral results in rodents and large animals under similar conditions, we hypothesize that pain relief in the large animal model involves similar processes.

Conclusions: DTM-SCS consistently improves pain-like behavior in rodent and sheep models suggesting similar effects across different species.

Objectives

Describe models of chronic neuropathic pain.
Understand translational value of animal models of continuous SCS.
Evaluate DTM-SCS in animal models

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Poster Presentations - May 27 - May 30
Basic Science

110. INS19-0329

EFFECTS OF DIFFERENT FREQUENCY-PULSE WIDTH COMBINATIONS IN A LARGE ANIMAL MODEL OF SPINAL CORD STIMULATION

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Introduction: Scientific discoveries for spinal cord stimulation (SCS) have come from rodent models using customized equipment scaled down to size. However, the development of a large animal model would allow for objective assessment of human grade devices with greater translational capabilities. In this exploratory study, we developed a SCS therapy model in sheep with a neuropathic nerve injury and tested clinically-relevant parameters.

Materials/Methods: A peroneal nerve injury was induced in sheep according to literature. Quantitative sensory testing was used to confirm the presence of hypersensitivity. Sheep were implanted with leads in lumbar segments. Motor thresholds (MT) were tested to confirm location and viability of leads. Conventional stimulation was tested to validate the model. Parameters used were 60 Hz frequency, pulse width of 200 μs and an amplitude of 80-90% of MT. A combination of higher frequencies (200-1200 Hz) and pulse widths (200-1000 μs) were tested at lower amplitudes (40-50% MT). The testing of these parameters took place over 5 days of continuous stimulation.

Results: Nerve injury induced hypersensitivity persistent for up to 1-year post-injury, manifested as a decrease in sensory threshold. Application of conventional parameters of SCS reduced the hypersensitivity confirming the sensitivity of our methodology to detect sensory changes. The week-long testing of higher frequencies and pulse widths revealed a biphasic change in hypersensitivity. There was an initial rise on the withdrawal threshold in the first 15 minutes of application with a second peak observed after 24 to 72 hours of continuous stimulation. The time course of withdrawal threshold was parameter dependent.

Discussion: This is the first study to evaluate the response to clinically relevant parameters in a large animal model. Conventional parameters increased sensory thresholds demonstrating the sensitivity of the methodology. Higher frequency-pulse width combinations yielded a biphasic effect on hypersensitivity with continuous stimulation over several days showing the need for longer-term studies. This can be achieved with the sheep model.

Conclusions: We have developed a relevant large animal model of SCS therapy in the sheep. This model can be used as a platform for longer time course studies investigating the effects of novel paradigms of stimulation and/or new device prototypes.

Objectives

Understand validation of animal model
Understand methodology to test stimulation effects
Understand effects of novel stimulation parameters

References

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Poster Presentations - May 27 - May 30
Basic Science

111. INS19-0350

THE IMPACT OF A VISUAL AID ON SPINAL CORD STIMULATOR (SCS) PATIENTS THEATRE EXPERIENCE

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Introduction: All patients benefit from having pictures combined with spoken or written text as part of health education (Houts et al, 2018). Chronic pain patients require information to prepare them for their SCS implant. A PowerPoint teaching aid has been devised to assist clinicians with information giving to patients in SCS education clinics. The purpose of this study was to evaluate the efficacy of the PowerPoint presentation on the experience of SCS patients.

Materials/Methods: For the purpose of this study, adult patients who had an SCS system implanted and followed up in a specialist pain centre in the North West of England between 2017 (n=36) and 2018 (n=30) were included.

To help identify the relevant pre and post PowerPoint data, SCS Patients returned for routine follow up appointments at 3 months and completed patient experience questionnaires. The data was analysed and inputted into a Microsoft Excel spreadsheet.

Results: IN 2017 64% (n=23). of patients strongly agreed that they had enough information to prepare them for their procedure, however 5% (n=2) felt they were not told what to expect before and after the procedure. In 2018 after the introduction of the presentation 74% (n=22) of patients strongly agreed that they had enough information and 26% (n=8) agreed they had enough information to prepare themselves for the procedure.

Discussion: Collecting patient experience feedback has demonstrated that the introduction of a PowerPoint presentation into education sessions has shown to significantly improve patient outcomes. All patients reported that the PowerPoint presentation helped to provide enough information compared to the previous education session which did not have any visual content, but it is unclear as to why a small number patients do not strongly agree that the presentation has made a difference, but suggest this could be an area for further research.

Conclusions: The introduction of a PowerPoint presentation has proved to have a positive effect on patients and their theatre journey. This bespoke tool has been developed for this centre, yet similar tools could be developed in other centres to enhance patient care.

Objectives

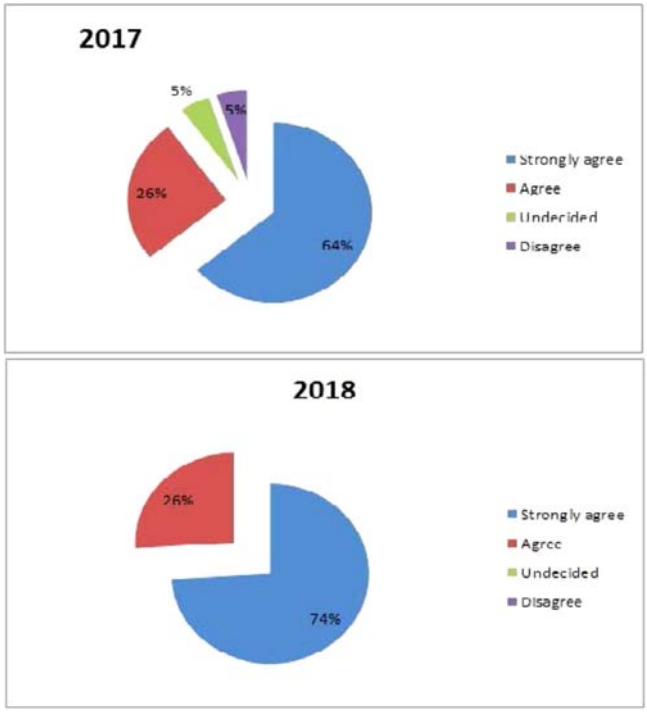
To evaluate the PowerPoint presentation as an educational tool.

To identify the effectiveness of patient feedback to assist with quality improvement.

Does education make a difference to the patient and their outcomes?

References

Houts PS1, Doak CC, Doak LG, Loscalzo MJ.(2006) The role of pictures in improving health communication: a review of research on attention, comprehension, recall, and adherence *Patient Education and Counseling*. ;61 (2):173-90



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Basic Science

112. INS19-0425

SPINAL CORD STIMULATION IS EFFECTIVE IN REDUCING OPIOID CONSUMPTION IN PATIENTS WITH CHRONIC PAIN

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Introduction: The ongoing trend for opioid prescribing within chronic pain continues to contribute to reduced health and quality of life outcomes. Spinal Cord Stimulation (SCS) has shown to reduce pain scores, improve function and quality of life in patients with chronic pain (Sanders et al 2016). The purpose of this study was to evaluate whether Opioid Consumption (OC) reduced after SCS implantation.

Materials/Methods: Adult patients from an SCS database who had an SCS system implanted between a period of 2016 and 2017 in a specialist centre in the North West of England were identified (n=50) patients who did not proceed to the completion procedure were excluded from the analysis (n=5). Opioid consumption was measured pre-trial then at a 3 month, 6 month and 12 month end point. Any reduction in any opioid dose was considered a successful outcome.

Results: 55 % (N=25) of patients reduced or stopped their opioids following SCS implant at 12 months. 20% (N=10) of patients have remained at the same opioid dose and 2% (N=1) had their dose increased. Data was missing from 14 %(N=7) and 2% (N=1) of patients were not taking opioids pre implant.

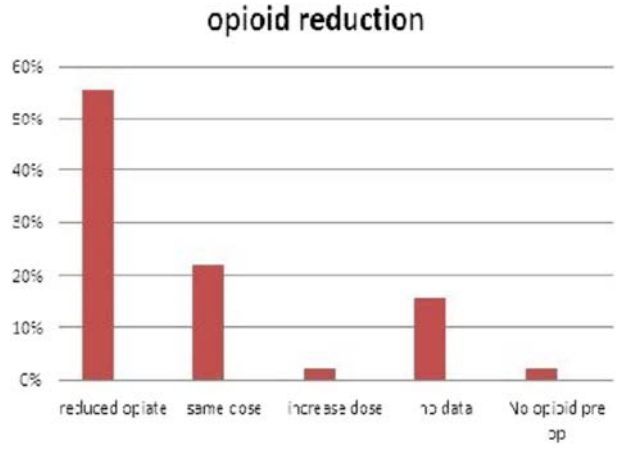
Discussion: SCS can potentially reduce opioid consumption in a significant number of patients. It is unclear why some patients could not stop it completely. This could be an area of future research. It has been shown that outcomes might be superior when SCS is used without opioids. A greater understanding of factors influencing ability to stop opioids could enhance SCS effectiveness.

Conclusions: The results have demonstrated that SCS can be an effective tool in reducing OC in chronic pain patients.

Objectives

-Demonstrate the relationship between SCS and the role it plays in opioid reduction.

-The importance of opioid usage being monitored and reduced post SCS implant in chronic pain patients to reduce the risk of escalation.



- Educating patients about the importance of opioid reduction pre-implant may have a greater success of reducing opioids post implantation.

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Basic Science

113. INS19-0398

LOW FREQUENCY STIMULATION OF ENDOPIRIFORM NUCLEUS IN THE CONTROL OF CHRONIC FOCAL EPILEPSY IN RATS

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Introduction: Deep brain stimulation (DBS) is a new neuromodulation method for controlling intractable epilepsy. However, the mechanism, the optimal stimulus target, and the optimal stimulation parameters are still unclear. In this study, we used a self-developed micro-neurostimulation system deliver continuous low-frequency (1Hz) electrical stimulation to bilateral endopiriform nuclei (EPN). We want to explore new stimulation targets and parameters that can control focal epilepsy.

Materials/Methods: Adult male Sprague-Dawley rats were stereotactic surgical implanted a segment of cobalt wire (1. 0 mm in diameter and 1. 5 mm in length) into the left motor cortex. Two screw electrodes and two tungsten depth electrodes were symmetrically implanted into the bilateral motor cortex and hippocampal CA1 for EEG recording. Then two bipolar tungsten stimulation electrodes were implanted into bilateral EPN. We stimulated each side of the EPN separately and recorded the evoked potential from the ipsilateral hippocampal CA1 region to confirm the stimulating electrodes were accurately implanted in the EPN. Final stimulus parameters were adjusted to the intensity produced half-maximal evoked. Three days later, video-EEG monitoring and bilateral EPN were stimulated with low frequency (1Hz) sustained stimulus was started. The stimulation was stopped after three consecutive days without seizures. At the end of the experiment, all rats were euthanized, their brains were quickly removed and fixed in 4% paraformaldehyde solution. After removed the cobalt wire, the whole brain was imaged using 7.0T magnetic resonance. Subsequent histological examination of brain was done to confirm the stimulation and recording electrodes are in the right place. Finally, the EEG was analyzed and compared between the groups, and behavioral seizures were assessed by Racine scale.

Results: Results show that the average seizures/day in the EPN stimulation group was significantly reduced (3.2±0.2/d) compared to the control group (8.1±1.0/d, P<0.001) and sham stimulation group (7.6±0.8/d, P<0.001). The seizure behavioral score (Racine scale) in the EPN stimulation group was lower (3.0±0.2/d) than the control group (4.1±0.1/d, P<0.001) and sham stimulation group (4.0±0.2/d, P<0.001). EEG spectral analysis showed that the power of theta band of seizures in EPN stimulation group was significantly reduced compared to the control group and sham stimulation group (P<0. 01).

Discussion: None

Conclusions: Our results demonstrate that sustained 1 Hz low frequency stimulation of bilateral EPN can reduce the number of seizures and the seizure behavioral score in chronic focal epilepsy in rats, which suggests that EPN may be a potential target for clinical DBS for drug refractory epilepsy.

Objectives: DBS control seizures.

References

None

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114. INS19-0288

NEUROMODULATION OF INTRINSIC AND NETWORK-DEPENDENT NEURONAL DISCHARGES IN THE BASOLATERAL AMYGDALA

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Introduction: Epilepsy involves unpredictable interruption of normal brain rhythms by paroxysms of aberrant discharges in large-scale neuronal networks (1). Abnormal functions of voltage- or neurotransmitter-gated channels have been reported for the abnormal discharges in different epileptic seizures (2-3), but in most cases the causal relations and especially their underlying mechanisms remain obscure. Innocuous electrical stimulation administered repeatedly in limbic structures such as basolateral amygdala (BLA) can eventually turn normal brain epileptic (4-5). BLA is thus an ideal system for the exploration of the biophysical rationales of abnormal excitation-inhibition oscillations and thus the basic mechanisms underlying epileptogenesis and its neuromodulation.

Materials/Methods: The BLA circuitry comprises interconnected pyramidal neurons and interneurons. We sought to characterize different types of BLA neurons, and investigated the intrinsic membrane properties that govern their network-dependent activities by pharmacological and genetic manipulations, step-current injection, and electrical stimulation with whole-cell patch-clamp recordings in acute mouse BLA slices.

Results: The pyramidal neurons can be identified morphologically with a soma diameter of >10 μm and electrophysiologically with relatively low-frequency firing activity in response to current injection. In contrast, the interneurons are of smaller size and mostly fire high-frequency spikes during depolarizing currents. Intra-nuclear rapid repetitive electrical stimulation or delivery of negative constant current in the BLA results in target cell-dependent oscillation of both pyramidal neurons and interneurons. Higher discharge frequency and more synchronized activities occur across all neuronal types, with greater extent of synchronization when more interneurons are involved. In addition, the stimulus-induced oscillation is distance-dependent.

Discussion: BLA pyramidal neuronal discharges (especially discharge patterns) are regulated by the interneurons. The activities of interneurons are in turn critically dependent upon the presynaptic glutamatergic input from pyramidal neurons. The closely and mutually interactive circuits of pyramidal neurons and interneurons are further rewired in an intracircuit activity-dependent fashion to assume different physiological and pathophysiological roles.

Conclusions: Distinct intrinsic membrane properties of BLA neurons may differentially contribute to their physiological/pathophysiological activities and network-dependent oscillations. BLA neurons, while known for the low spontaneous activity, can be transiently aroused in response to repetitive stimulations. Pyramidal neurons and interneurons can then be rewired in a target-cell activity-dependent fashion and may require local depolarization of neural mass.

Objectives: Biophysical rationales of abnormal network oscillations; Cellular mechanisms underlying epileptogenesis and its neuromodulation; The extension of the reverberating excitation-inhibition in the network of BLA

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Basic Science

115. INS19-0234

AIRWAY SENSORY UNIT IS NOT ONLY A TRANSDUCER BUT ALSO AN INTEGRATOR

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Introduction: Conventionally, researchers believe that one single afferent fiber of the vagus nerve is connected with only one mechano-sensor. Therefore, a sensory unit is merely a transducer. Activation of a given type of sensors sends their afferent signals to specific parts of the central nervous system to elicit unique reflex responses.

Materials/Methods: In anesthetized, open-chest and mechanically ventilated rabbits, we recorded electrical activities from single afferent fibers in the cervical vagus nerve and examined their responses to lung inflation and deflation.

Results: We found two major types of mechanical sensors, inflation activated receptors (IARs) and deflation activated receptors (DARs). According to adaptation rate during a sustained stimulation (constant pressure inflation or deflation of the lung) the sensors can be sub-divided into rapidly adapting IARs (rIARs), slowly adapting IARs (sIARs), rapidly adapting DARs (rDARs) and slowly adapting DARs (sDARs). We further demonstrated that a single afferent fiber can be connected with any combination of the four types of sensors (or encoders). Each type of the sensors can be selectively blocked by injection of lidocaine into the receptive filed.

Discussion: Since different types of encoded information is transmitted, a sensory unit is not only a transducer but also a processor. Significant information integration occurs in sensory units. Our findings challenge conventional view on how airway sensory information is processed at the central nervous system (CNS). While the details regarding how neurons in the CNS can decode the information is unknown, the CNS should be able to decode heterogeneous information. For example, multiple decoders specific for different variables may decipher the encoded information. The information transmitted by rIARs and sIARs can be decoded discriminately because they have different discharge patterns. In addition, activities from IARs can easily be differentiated from those of DARs at the central level because they arrive during different respiratory phases.

Conclusions: A single afferent fiber is connected with a functional unit, which contains multiple sensors (rIARs, sIARs, rDARs and sDARs) in any combination. This heterogeneous information is transmitted in the same pathway to produce respective reflex responses. Thus, studies are required to explore how the sensory information can be decoded at the relay neurons.

Objectives

1. Challenging the conventional view on airway sensors
2. Providing a new concept of airway sensory unit
3. Challenging the conventional view regarding central decoding

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Poster Presentations - May 27 - May 30
Brain: Cognitive Disorders

116. INS19-0336

CAN TDCS FACILITATE WEIGHT LOSS IN OBESITY? OBSERVATIONS FROM TWO CLINICAL TRIALS (N=78, >950 SESSIONS)

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Introduction: Transcranial direct current stimulation (tDCS) is a well-studied technique for noninvasive modulation of the human brain. Due to its safety, tolerability, portability and low cost, it represents an attractive approach to rebalance brain abnormalities in obesity. tDCS targeted to the dorsolateral prefrontal cortex (DLPFC) can reduce food craving, appetite and, possibly, body weight. However, there is need for a better understanding of mechanisms of action and factors that could affect response to tDCS. We compared findings from two clinical trials to address the role of age and dopamine availability status.

Materials/Methods: Randomized, double-blinded, sham-controlled clinical trials to examine tDCS effects on appetite and body weight (ClinicalTrials.Gov: NCT03351426 and NCT02953353). tDCS montage was anode left DLPFC/cathode right supraorbital. NCT03351426: 40 middle-aged women (45-65y, BMI 25-35kg/m^2) from Alcalá de Henares, Spain underwent a 4-week intervention with 8 tDCS sessions (weeks 1-2), combined with an outpatient hypocaloric diet (goal: 5% weight loss at 3 months) (weeks 2-4). NCT02953353: 38 young women (20-40y, BMI 30-40kg/m^2) from Ribeirão Preto, Brazil underwent 17 tDCS sessions, organized as: target engagement (1 tDCS session), 2-week tDCS-only (10 sessions, outpatient), and 2-week tDCS (6 sessions) + hypocaloric diet (goal: 30% energy intake reduction, inpatient); follow-up was 6 months. Study outcomes: appetite, body weight and performance in food-specific cognitive tasks. Additionally, NCT02953353 included evaluation of Catechol-O-methyl transferase (*COMT*) Val158Met polymorphism, a major determinant of extracellular dopamine availability and prefrontal dopaminergic tone.

Results: In NCT03351426, we found overall greater weight reduction in the active tDCS group (p=0.020). At study completion, weight change was sham: -1.29%, active: -2.32% (p=0.029). Additionally, there was a significant improvement in performance accuracy in cognitive tasks evaluating working memory and inhibitory control under the presence of food (p-values: 0.001-0.040), with no change in the sham group (p-values: 0.2-0.9). These findings contrasted with NCT02953353, where there were no significant group differences regarding appetite or weight. However, we found a critical influence of *COMT* genotype on tDCS response. Specifically, active tDCS only caused a reduction of appetite in Met carriers (hunger p=0.038; prospective consumption p=0.009). Non-Met carriers had consistently high appetite throughout the study, and sham tDCS subgroups did not change.

Discussion: Conclusions: We conclude that there is potential for DLPFC-targeted tDCS to facilitate diet-induced weight loss in obesity. tDCS effects may be mediated by dopamine circuits. Middle-aged women, in general, or younger women with Met-containing COMT may respond better to tDCS. These sources of variability should be considered in future efficacy trials.

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117. INS19-0142

RELATIONSHIP BETWEEN CORTICAL RESECTION AND VISUAL FUNCTION AFTER OCCIPITAL LOBE EPILEPSY SURGERY

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Introduction: In this study, the authors investigated long-term clinical and visual outcomes of patients after occipital lobe epilepsy (OLE) surgery and analyzed the relationship between visual cortical resection and visual function after OLE surgery.

Materials/Methods: A total of 42 consecutive patients who were diagnosed with OLE and underwent occipital lobe resection between June 1995 and November 2013 were included. Clinical, radiological, and histopathological data were reviewed retrospectively. Seizure outcomes were categorized according to the Engel classification. Visual function after surgery was assessed using the National Eye Institute Visual Functioning Questionnaire 25. The relationship between the resected area of the visual cortex and visual function was demonstrated by multivariate linear regression models.

Results: After a mean follow-up period of 102.2 months, 27 (64.3%) patients were seizure free, and 6 (14.3%) patients had an Engel Class II outcome. Nineteen (57.6%) of 33 patients had a normal visual field or quadrantanopia after surgery (normal and quadrantanopia groups). Patients in the normal and quadrantanopia groups had better vision-related quality of life than those in the hemianopsia group. The resection of lateral occipital areas 1 and 2 of the occipital lobe was significantly associated with difficulties in general vision, peripheral vision, and vision-specific roles. In addition, the resection of intraparietal sulcus 3 or 4 was significantly associated with decreased social functioning.

Conclusions: The authors found a favorable seizure control rate (Engel Class I or II) of 78.6%, and 57.6% of the subjects had good visual function (normal vision or quadrantanopia) after OLE surgery. Lateral occipital cortical resection had a significant effect on visual function despite preservation of the visual field.

Objectives: In this study, the authors investigated long-term clinical and visual outcomes of patients after occipital lobe epilepsy (OLE) surgery and analyzed the relationship between visual cortical resection and visual function after OLE surgery.

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Poster Presentations - May 27 - May 30
Brain: Cognitive Disorders

118. INS19-0304

REVISION OF RESPONSIVE NEUROSTIMULATION DEVICES FOR NEUROMODULATION OF EPILEPSY AT A SINGLE INSTITUTION

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Introduction: While resective surgery for the treatment of intractable focal-onset epilepsy has historical precedent for seizure freedom, neuromodulation affords the opportunity to provide operative therapy to patients with epilepsy who would otherwise not meet criteria. The Food and Drug Administration approved the responsive neurostimulator (RNS) in 2013 (1) to provide closed-loop neuromodulation for intractable focal-onset epilepsy in adults with one or two seizure foci who are not resective candidates. As RNS is a novel technology, publications regarding repositioning of lead placement have been limited. We present our experience with revision of the RNS system.

Materials/Methods: Between August 2015 and November 2018, 26 RNS devices were implanted in 25 discrete patients.

Results: Seven patients required revision of their RNS systems. One patient required explantation and revision due to infection with *Propionibacterium acnes,* and a second had wound breakdown requiring surgical revision. The third patient had delayed traumatic subdural and intraparenchymal hematoma, and the fourth patient had an additional electrode placed. The final patients underwent right temporal lobectomy based on closed-loop data with preservation and repositioning of the right temporal strip electrode in one case, preservation of a hippocampal depth electrode in another, and placement of a new subdural strip in the third. Follow-up periods have been insufficient to draw meaningful conclusions about seizure outcomes.

Discussion: Revisions of intracranial neuromodulation devices pose novel technical challenges. As evinced by our experience, among others (2, 3) latent infection may require device explantation. One patient at our institution was successfully reimplanted after a course of intravenous antibiotics, and another's electrode was salvaged by placement of a bactiseal catheter. The third patient's delayed traumatic hematoma necessitated explantation to evacuate the hematoma. The remaining patients' lead additions, preservation, and repositioning warrant further discussion of technical considerations not described elsewhere in the literature. Other potential causes for revision cited in the literature include lead damage upon exiting the skull (2) and initial stereotaxy error. (4)

Conclusions: RNS is a promising technique for patients with refractory focal epilepsy who do not meet criteria for resective surgery. Understanding the potential causes for and technical considerations involved in revising the leads is increasingly relevant.

Objectives

-Identify potential complications of RNS
-Identify situations in which RNS revision is indicated
-Discuss technical nuances of such surgery

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Poster Presentations - May 27 - May 30
Brain: Cognitive Disorders

119. INS19-0061

MAGNETIC RESONANCE-GUIDED LASER INTERSTITIAL THERMAL THERAPY FOR THE TREATMENT OF NON-LESIONAL INSULAR EPILEPSY IN PEDIATRIC PATIENTS: THERMAL DYNAMIC AND VOLUMETRIC FACTORS INFLUENCING SEIZURE OUTCOMES

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Introduction: Insular epilepsy presents definite diagnostic and therapeutic challenges stemming from anatomic barriers to exploration. Minimally invasive techniques have gained popularity due to greater accessibility, increased precision and an improved safety profile. Stereoelectroencephalography (sEEG) directed magnetic resonance-guided laser interstitial thermal therapy (MRgLITT) is one such technique that utilizes thermal energy to disrupt epileptogenic foci (Fig. 1).

Materials/Methods: A single-institution, retrospective review of pediatric patients with non-lesional insular epilepsy who underwent sEEG directed MRgLITT over a ten month period was performed. Seizure outcomes were determined based on Engel score (Engel I versus Engel II-IV). Insula and ablation volumes were measured, and the proportion of insula volume ablated was calculated. Thermal energy was calculated in Joules.

Results: Four patients underwent sEEG directed MRgLITT of insular epileptogenic foci. The ablation volume was higher in patients with Engel I outcome (3.93 cm3) compared to Engel II-IV outcome (1.02cm3). The proportion of insula ablated was lowest in the Engel II-IV outcome group (25.10%). Thermal ablation energy and ablation volume (R2 = 0.884) showed a linear trend. Over a mean follow-up period of 104 days, three patients were seizure-free (Engel I), and one patient saw significant improvement in seizure frequency (Engel III).

Discussion: The proportion of insula ablated, as well as the volume of ablation itself, were found to be related to seizure outcome, with increasing ablation volumes corresponding to improved seizure control. A simple, intuitive explanation was that larger ablation volumes are more likely to disrupt a wider array of epileptic networks resulting in large-scale signal disruptions. The linear trend between thermal ablation energy and ablation volume suggested that larger ablation volumes could be achieved either by increasing the wattage, by applying this thermal energy for a longer duration, or both. Our outcomes were comparable to open resection without any postoperative complications.

Conclusions: sEEG directed MRgLITT is a safe and effective minimally invasive technique for the treatment of medically refractory non-lesional insular epilepsy in pediatric patients. Ablation volume, laser thermal energy and seizure control outcomes appear to be related. The extent of this association needs to be quantified.

Objectives

To investigate the safety and efficacy of sEEG directed MRgLITT in medically refractory insular epilepsy in pediatric patients, define the relationship between ablation volumes and seizure control and analyze the relationship between thermal energy and ablation volumes.

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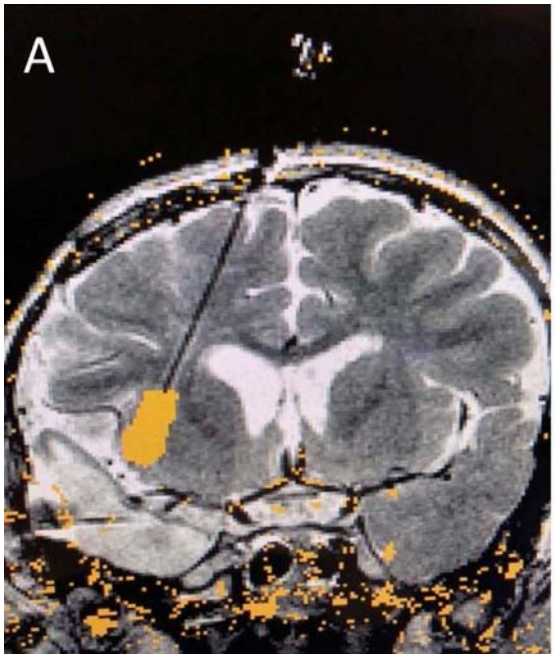

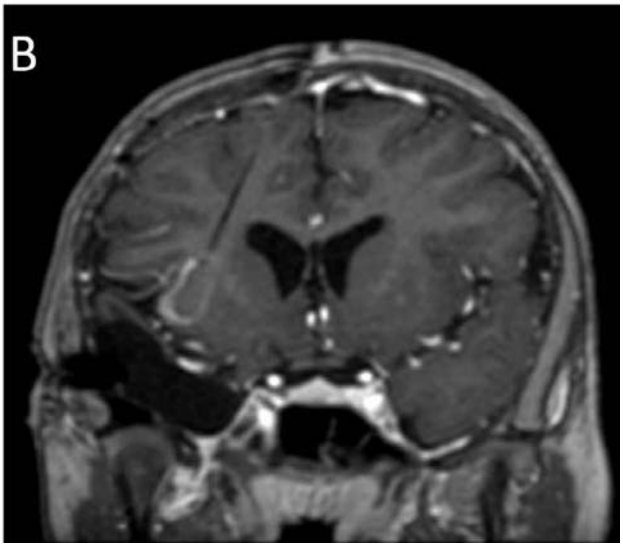

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Brain: Cognitive Disorders

120. INS19-0157

PSYCHOLOGICAL DISTRESS PREDICTS DISABILITY IN NEUROMODULATION PATIENTS

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Introduction: Psychological distress contributes to illness related disability in chronic health conditions such as stroke and spinal cord injury.

Up to 50% of patients referred for neuromodulation present with clinically significant psychological distress.

Given the high prevalence of psychological distress in this patient group this study set out to investigate the influence that psychological distress might have on patients' overall level of disability and consider the implications of this for pre and perioperative support.

Materials/Methods: Design: Repeated measures, questionnaire. Patients completed questionnaires pre operatively and on average 102 weeks following surgery.

Participants: 353 consecutive patients (193 female, 160 male) referred for neuromodulation surgery including Spinal Cord Stimulation (n = 164), Dorsal Root Ganglion Stimulation (n = 120), Occipital Nerve Stimulation (n = 42) and Peripheral Nerve Stimulation (n = 20).

Measures: Hospital Anxiety and Depression Scale (HADS), McGill Pain Questionnaire (MPQ), Pain Catastrophisation Scale (PCS) and Functional Limitations Profile-Self reported (FLP-S)

Analysis: Stepwise linear regression, SPSS

Results: Complete data was available for 205 of 353 patients. Clinically significant anxiety and depression was present in 48% of the patients assessed. A stepwise/linear regression found a significant model ($F(1,204) = 74.26$, $p<.001$) where depression emerged as a significant and independent predictor of disability. Depression was found to independently predict 26% of the variance in post-surgical pain relief. Severity of pain (MPQ Total Score) added an additional 6% of variance to the model.

Discussion: Clinically significant psychological distress was present in 48% of patients referred for neuromodulation surgery. Regression analysis indicated that depression was a significant and independent predictor of disability in neuromodulation patients. This finding is consistent with the literature on the role that mood can play in other chronic health conditions such as stroke and spinal cord injury.

Conclusions: The high prevalence of psychological distress and the influence it has on patients' disability highlights the important of the need for psychological assessment and support for patients through their neuromodulation pathway.

Objectives

Highlighting patient disability prevention before surgery

Importance of psychological assessment pre-surgery

Caution of high prevalence of psychological distress in neuromodulation patients

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Brain: Cognitive Disorders

121. INS19-0159

PAIN CATASTROPHISATION AND PAIN REDUCTION FOLLOWING NEUROMODULATION

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Introduction: Neuromodulation has proven effectiveness in treating neuropathic pain; however, there can be significant variations between reported levels of pain relief between individuals. A number of factors have been proposed to explain this variation including hardware or technical complications, the subjective nature of visual analogue scales and psychological factors.

The appraisals that patients make about their illness play a significant role in how they cope with their condition and the level of disability they experience in day to day life. In the context of pain, pain catastrophisation (excessive and maladaptive cognitions about pain has been shown to influence how they manage their condition and how they engage with treatment. This study aimed to investigate the role of pain catastrophisation in neuromodulation patients.

Materials/Methods: Design: Repeated measures, questionnaire based

Participants: 353 patients of John Radcliffe hospital (193 female, 160 male) assessed before and after neuromodulation surgery

Measures: Hospital Anxiety and Depression Scale (HADS), McGill Pain Questionnaire (MPQ) and Pain Catastrophisation Scale (PCS)

Analysis: SPSS

Results: Complete data was available for 80 of 353 patients. Over the whole sample patients reported a significant reduction in pain following surgery ($t = -2.801$). A linear regression produced a significant model ($F(1, 79) = 7.843$, $p<0.01$). Pain catastrophisation independently predicted 10% post-operative pain relief. Factors such as Age, MPQ scores, Anxiety and Depression added an additional 18% variance but were not independent predictors.

Discussion: Pain catastrophisation predicted a significant proportion of the variance in pain relief following neuromodulation surgery with greater catastrophisation predicting less pain relief. Pain catastrophisation represents one aspect of how a patient makes sense of and thinks about their illness. These cognitive processes are potentially amenable to intervention through treatments such as Cognitive Behaviour Therapy or Acceptance and Commitment Therapy. It is possible; therefore, that pain catastrophisation could be targeted prior to surgery in order to enhance patients' outcomes.

Conclusions: How patients think about pain influences their reported level of pain relief following surgery. This could represent a new target for pre-surgical intervention to enhance outcomes.

Objectives

New targets for pre-surgical intervention

Discussion on how patients view pain

Suggestions for successful pain relief following surgery

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122. INS19-0063

IS PHYSICAL CHANGE EFFECT? FOR LINKAGE FALL POST−OPERATIVE STN-DBS AND PRE −OPERATIVE BADS RESULT

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Introduction: Deep brain stimulation therapy (STN - DBS) is often selected as an effective treatment for Parkinson 's disease (PD). However, many patients tend to fall after STN-DBS and consequently their daily lives become challenging. In our previous study, the relationship between fall post−operative STN-DBS and preoperative results of BADS (behavioral evaluation of performance dysfunction syndrome). According to the results of BADS, it was classified into two groups, "above-average/average", "below-average /disable ", and compared, we found that the latter group are significantly increased the postoperative falls, but we didn't mention the change in physical function.

Materials/Methods: In 18 patients underwent STN - DBS at the hospital and performed BADS as pre-operative assessment, we studied about changes in physical function post-operative, in all cases. We used UPDRS III for assessment of physical functions. We studied there is or not difference, improvement body function in two groups. In addition, regardless of the results of BADS, we also studied about improvement body function in the two groups, with fall or not, in post-operative. We also studied, there was no difference in physical function in each 4 groups (BADS result "above-average/average" and "below-average /disable", falls or not in post-operative), at the time of before STN-DBS",

Results: In all cases, post-operative UPDRS III scores were improved. There was no significant difference in UPDRS III scores improvement in two groups, pre-operative BADS scores, "above-average/average ", "below-average /disable ". There is no significant difference was found in groups with fall or not, in post-operative. Also, even before STN-DBS, there was no difference in UPDRS III between each groups.

Discussion: As a factor of the fall post STN-DBS, we think about that there is an influence of the frontal lobe function, such as the performance dysfunction at the time of the pre-operative, regardless of the improvement of the physical function after STN-DBS.

Conclusions: They didn't have any difference in pre-operative, and in spite of improvement physical as same after STN-DBS, someone fall. But BADS result was different each other. Physical improvement is not effect for linkage fall post−operative STN-DBS and pre−operative BADS result. We provably consider about pre-operative fall at the time of pre-operative assessment.

Objectives: Prior to pre-operative evaluation, Frontal lobe function affect physical, We must to consider about post-operative life

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123. INS19-0232

THE EFFECT OF DEEP BRAIN SITIMULATION ON SLEEP QUALITY

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Introduction: In Advanced Parkinson Disease (aPD), non-motor symptoms are often ignored. However, these non - motor symptoms often affect quality of life directly.

The most forgotten area of non-motor symptoms of aPG is mostly sleep.

Not only the sleep Quality (SQ), but also autonomic dysfunction, cognitive impairment, and advanced movement problems are intertwined.

We aimed to clarify the effects of DBS on the SQ of aPD.

Materials/Methods: A total number of 33 patients applied DBS were included in this study. From 2012 March to November 2018, the patients followed at Selcuk University, School of Medicine, Department of Neurology, Movement Disorders Subunit and Department of Neurosurgery, Dokuz Eylul University, all patients were applied DBS.

Each patient was evaluated for SQ on behalf of sleep architecture with Polysomnograpy and also Parkinson Disease Sleep Scales (PDSS).

All scores were collected before the DBS and after the intervention with a 6 month periods.

Results: The most common disturbance of aPH was difficulty staying asleep through the night, however, may actually affect any aspect of sleep. Other co-occurring sleep disorders, such as sleep attacts in diurnal life period, REM behavior disorder, and restless legs syndrome are also very common.

PDSS was 63.5; it is very high in comparison with age - matched 30 healthy control group (PDSS was around 27,8). Polysomographic values did not differ with apneo - hypopnea indexes (AHI). REM period, sleep stages and Leg movements were all differed from healthy group.

All the scores before and after DBS were compared. All the SQ values, sleep stages, REM period, leg movements, Willis Ekbom syndromes were differed and improved with DBS.

Discussion: The aPD affects the QoL, the effects created on sleep should not be ignored. These sleep problems are associated with a poor QoL.

The etiology of sleep problems in aPD is multi-factorial.

Previously, established causes include, advanced age, nocturnal motor symptoms, and psychiatric complications such as depression and hallucinations, and also medication effects, which may disrupt the sleep architecture and lead to motor fluctuations. Also, there is a strong effect of DBS on SQ

Conclusions: DBS improves SQ in aPD.

Objectives

DBS improves SQ

All aPD patients should be evaluated for Sleep Quality.

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Brain: Movement Disorders

124. INS19-0399

BILATERAL GPI DBS FOR A PARKINSONIAN PATIENT WITH DVA IN THE REGION OF THE BASAL GANGLIA

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Introduction: Drug resistant Parkinsonian patients are candidates for deep brain stimulation (DBS). The primary target is the subthalamic nucleus (STN), however, these patients may benefit from bilateral internal globus pallidus (GPi) DBS implantation as well.

Materials/Methods: We prepared a 45 years old male patient with Parkinson's disease for DBS surgery due to severe fluctuation. Our primary target was the subthalamic nucleus on both sides. However, the preoperative MRI scan showed a developmental venous anomaly (DVA) in the region of the basal ganglia on the left side, and consequently safe trajectory could not be defined reaching the subthalamic nucleus. We decided to target the GPi on both sides. After meticulous planning we could define one trajectory passing between the branches of the DVA. We determined the optimal position of the electrode based on the results of the single channel microelectrode recording and macrostimulation. On the right side we applied 5 channel microelectrode recording and macrostimulation, as usual in our practice. We used Leksell frame (Elekta) for the surgery, and Surgiplan (Elekta) software for the planning.

Results: No adverse events occurred during or after the surgery. UPDRS III scores without medication dropped from 30 to 5 with stimulation on, the scores with medication were 0 preoperatively and postoperatively as well. Levodopa equivalent dose was reduced from 600mg to 400 mg. Postoperative MRI scan showed the left electrode passing safely between the branches of the DVA.

Discussion: Meticulous planning preparations and precise surgery can offer safe solutions for patient with certain intracranial structural anomalies. When these structural changes affect the feasibility of reaching the primary target, alternative regions could be considered based on the patient's disease and symptoms.

Conclusions: Meticulous planning preparations and precise surgery can offer safe solutions for patient with certain intracranial structural anomalies. In special cases alternative regions could be considered based on the patient's disease and symptoms.

Objectives

1. Different targets to be considered
2. Detailed planning processes are to be applied
3. Long-term follow up results are to be used for evaluating the optimal lead and contact position

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125. INS19-0220

GENDER DIFFERENCE IN OUTCOME OF SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION IN JAPAN

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Introduction: Some studies have shown the protective actions of estrogen on dopaminergic neurons and a gender difference in the prevalence of Parkinson's disease (PD). In western countries, men have been shown to have 1.49 times greater risk of PD than women. Conversely, the prevalence rate of PD is high among women in Asian countries. Particularly in Japan, the prevalence rate of PD is 1.8 times higher in women than in men. Hence, whether the gender difference reflects the outcome of STN-DBS is an intriguing issue.

Materials/Methods: We designed a retrospective, single-center, observational study. The subjects were 57 patients (men, 29; women, 28) who underwent electrode implantation for STN-DBS in our institute. The gender difference in outcome was studied on the basis of Unified Parkinson's Disease Rating Scale (UPDRS) score and score improvement rate in the short (1month) and long terms (5 years).

Results: In the postoperative state, statistically significant gender differences were noted in the improvement rates of UPDRS total and part III scores during the off-period in the short term. However, statistically significant differences within one month of evaluation disappeared in the fifth year of evaluation. There was no significant gender difference in the long term.

Discussion: The short-term outcome in our study was similar to those in previous studies in Europe, whereas the long-term outcome in our study was essentially in agreement with those in studies in Asia. Furthermore, our five-year long-term results are in agreement with the five-year long-term results of Romito et al. who reported the same outcome in men and women.

Conclusions: This study is the first on the gender difference in the outcome of STN-DBS in Japan. Some significant gender differences were noted in the short term with a higher improvement rate in women.

Objectives: The aim of this study was to clarify the gender difference in the outcome of STN-DBS in Japanese patients. This study is the first on the gender difference in the outcome of STN-DBS in Japan, which has a different gender ratio of the prevalence of PD from western countries

References

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126. INS19-0199

PATHOLOGIC SUBTHALAMIC NUCLEUS ACTIVITY IN FREEZING OF GAIT IN PARKINSON'S DISEASE

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Introduction: Freezing of gait (FOG) is the term used to describe paroxysmal arrest of stepping, like the feet have been frozen to the floor. It can be disabling and can cause falls and serious injury. The neurobiology of freezing of gait is poorly understood. We took opportunity to study FOG during deep brain stimulation (DBS) surgery, during which microelectrodes are used to record neuronal activity from the subthalamic nucleus (STN) of awake patients with Parkinson's disease (PD). Beta oscillations are thought to represent a motor inhibitory signal, and we hypothesised that there would be increased beta oscillatory activity prior to FOG.

Materials/Methods: We used a validated virtual reality (VR) paradigm to simulate walking and FOG during DBS surgery. We analysed foot movement, lower limb EMG, and STN multiunit activity (MUA) during this task. We examined the temporal profile of oscillatory activity in relationship to episodes of FOG.

Results: We identified 19 FOG episodes from 8 individuals. MUA was greater during FOG than volitional stops (13±7 v 8±5, p=0.006). Beta oscillations (13-30Hz) were above the 99th centile of normal walking 0.9s before to 1s after FOG, whereas this threshold was only met at the moment of voluntary stopping. There was a less prominent increase in peri-FOG STN theta (3-8Hz) activity. Lower limb EMG demonstrated the expected 'trembling in place' associated with FOG, predominantly in the theta range. Granger causality analysis suggested that STN beta drove STN theta which drove EMG tremor in place.

Discussion: Oscillatory basal ganglia circuit activity is dynamically involved in the pathophysiology of FOG, and our analysis of STN MUA suggest a causal role for beta oscillations.

Conclusions: Our findings refine the understanding of FOG, and may help further treatment such as early warning alarms or adaptive neuromodulation.

Objectives

Advancing the understanding of the pathophysiology of freezing of gait

Describing the temporal dynamics of STN activity in relation to freezing of gait

References

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Brain: Movement Disorders

127. INS19-0427

FUNCTIONAL CONNECTIVITY DISTRIBUTION WITHIN THE SUBTHALAMIC NUCLEUS AS AN ESSENTIAL TOOL IN DEEP BRAIN STIMULATION FOR PARINSON'S DISEASE

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Introduction: Recent development of modern MR imaging techniques opened the way to visualize functional white matter pathways in movement disorders, thus providing a tool for individualized, patient centric implementations in deep brain stimulation (DBS). The clinical outcome of subthalamic stimulation in Parkinson's disease is undeniable, while the underlying mechanisms are yet to be uncovered.

Materials/Methods: 26 patients who underwent subthalamic nucleus DBS implantation were enrolled in this study. Preoperative MRI acquisitions were completed in two neurosurgical centers on two subgroups using 1.5T GE Signa Excite (14 patients) and 3T Philips Achieva (12 patients) scanners using the following parameters under general anaeshtesia: T1 (1mm isotropic), T2 (1.5T - 0.5x0.5x2mm; 3T - 0.5x0.5x1.5 mm), diffusion tensor imaging (DTI) (1.5T - 64 directions, 0.89x0.89x2.4mm, b=1000; 3T - 32 directions, 1.6x1.6x2mm, b0=1000). Cortical parcellation and DTI analysis has been carried out using tools available in Freesurfer 5.3 and FMRIB Software Library 5.0.9. Tensor reconstruction and probabilistic fiber tracking was completed on a nVidia Titan Xp GPU. Implantation of DBS leads has been carried out according to standard stereotactic principles using intraoperative electrophysiology and macrostimulation, each patient received Medtronic 3389 lead systems. Final active contact locations were identified providing the best achievable clinical outcome after 1 year. Active contact positions and connectivity results obtained during tractography were compared to predict the best location for stimulation after surgery.

Results: Probabilistic fiber tracking was able to identify 7 distinct, but overlapping connectivity regions within the STN in both subgroups (limbic, dorsolateral prefrontal cortex, pre-supplementary motor area, premotor area, supplementary motor area, primary motor, and primary sensory cortex). Statistical analysis determined high and low connectivity tiers comprised of the aforementioned regions. Electrode contacts providing the best clinical outcome were closest to the SMA connections in both subgroups, while in the 3T group favorable outcome was also statistically predicted by M1 connectivity distances.

Discussion: DBS in movement disorders provides indispensable tool in modern functional neurosurgery. In the world of segmented DBS leads, more complicated stimulation fields and parameters developing a tool to predict the best location for directional stimulation is necessary. Interpreting results of DTI and probabilistic tractography, while also comparing these results to clinical outcome can give valuable information for the neurosurgeon and the neurologist.

Conclusions: The described method can provide essential insights during preoperative planning, implantation, and primary programming. It is not only feasible in laboratory settings, but can also be utilized in the daily clinical routine.

Objectives: STN connectivity, DBS, tractography

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128. INS19-0112

DIRECT DBS: A PROSPECTIVE, MULTICENTER, DOUBLE-BLINDED CLINICAL STUDY OF DIRECTIONAL DBS INTRA-VISIT IMPEDANCES UNDER ACUTE STIMULATION CONDITIONS

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Introduction: Recently, Deep Brain Stimulation (DBS) of the subthalamic nucleus (STN) using directional leads has been introduced aiming for more selective stimulation of therapeutically beneficial anatomy via segmented electrodes (contacts). Due to their smaller size, segmented electrodes have higher impedances than conventional ring electrodes. It has been suggested that electrode impedances change over time. Therefore, stimulation accuracy, precision and stability of a directional DBS system might be compromised by changes of individual tissue-contact interface impedances or differences between electrodes. We characterized the impedances of a primary cell, multiple current-source directional DBS system under acute stimulation conditions. Furthermore, the delivered current for single-source DBS systems under the encountered impedance conditions was theoretically modelled.

Materials/Methods: DIRECT-DBS (ClinicalTrials.gov Identifier: NCT02835274) is a prospective, randomized, multi-center, double-blind study with a crossover design. Twelve study participants were implanted with a DBS system (Vercise Cartesia, Boston Scientific) with bilateral directional leads connected to a primary cell pulse generator with independent current sources. Within the study framework, stimulation settings were tested acutely (~15 minutes) and chronically (≥3 weeks). Impedances were measured through all electrodes at various time points throughout course of each visit with acute stimulation settings.

Results: Throughout study visits, ring and segmented electrodes had average impedances of 1240Ω and 2930Ω, respectively. Differences in impedances between segmented electrodes within the same row reached up to 1560Ω. Average impedance variability for electrodes that were actively programmed increased 41.8% and 35.6% for ring and segmented electrodes, respectively. Based on our theoretical model of a single source system, changes in impedance would result in a delivered current, which in 2 cases, would have been above the side effects threshold.

Discussion: Segmented electrodes have higher impedances than conventional ring electrodes and all impedances change over time. Theoretically, these impedances differences and changes could provoke deviations from the intended delivered current for single source systems, which in turn could lead to unintended overstimulation.

Conclusions: Differences in impedance on electrodes within the same segmented row and relationship between these impedances can change over time, theoretically altering the volume of tissue activated if a single source system is being used.

Objectives

1. To characterize impedances of a primary cell, multiple current-source directional DBS system under acute stimulation conditions.

2. To investigate stimulation settings when tested acutely (~15 minutes) and chronically (≥ 3 weeks).

3. To theoretically model delivered current for single-source DBS systems under the encountered impedance conditions.

References

NA

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129. INS19-0052

STN SIZES QUANTIFIED BY MER IN DBS SURGERY

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Introduction: Precise STN targeting is critical in DBS surgery for treating Parkinson's disease and disease modification. 3-D STN sizes of human subjects were quantified using 7 T structural MRI (Keuken et al 2014). Current practice of DBS STN targeting uses 1.5-3 T MRI fused with CT scans for surgical planning, which is then confined by real time intraoperative MER. Current studies define 2-D STN sizes using MER mapping data and its significant versus the anatomical 3-D scan as discussed.

Materials/Methods: Intraoperative MER data from STN surgeries in five centers were pooled to quantify the 2-D STN sizes. The averaged STN coordinates of 11.8-12mm lateral, 1.8-2.6mm posterior, and 4mm below were used. The microelectrodes were immersed in saline for at least one hour before use; such treatment lowers the impedance (0.1-0.5 MΩ) of microelectrodes in order to detect neuronal activities, not axonal, such as internal capsules. The hyperactive segment of "STN" was quantified.

Results: The average AC-PC was 25.47±1.68 mm (average ±STDEV, n=841). The hyperactive segment of MER recorded STN was 5.99±0.72 mm (n=59) for the left and 5.59±0.75 mm (n=56) for the right. The characteristic multi-unit background activity, in contrast to the quiet control baseline (less than 20 Hz), reached 400-1200 Hz. Real time quantifications of HistFreq, RMS, and FFTMRV200 vs. depth were displayed.

Discussion: The 3-D STN sizes by 7T MRI were done using healthy young people (14 F, 16 M, mean age of 24.2). The results showed a LSTN of 52.83 and a RSTN of 59.50mm3. Note that the left STN is smaller than the right STN given that most people are left hemisphere dominant. Our patient data from 2-D quantification using MER STN segment, however, showed a bigger left STN. Although, the dominant hemisphere for most of our patients were documented, the MER data was not discrimitive regarding the dominant side. Nevertheless, given that most patients are right handed, the bigger STN on the left still contrasts with the 7- data, where all subjects were right-handed. We predict that future 7-T scan studies using patients, not healthy volunteers, will have results that parallel our MER data.

Conclusions: Our intraoperative patient MER data shows that the left STN is bigger than the right STN, in contrast to the 7-T 3-D measurement, which used healthy subjects.

Objectives

high resolution MRI
intraoperative MER
real STN sizes

References

Keuken et al 2014

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130. INS19-0409

ALTERATIONS OF STRUCTURAL VOLUMES AND CONNECTIVITY IN ESSENTIAL TREMOR: A GRAPH THEORETICAL ANALYSIS

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Introduction: We aimed to evaluate a brain structural volumes and connectivity using graph theoretical analysis in patients with essential tremor compared to healthy subjects.

Materials/Methods: Ten patients with essential tremor were consecutively recruited in a single tertiary hospital. All of the patients had a normal brain MRI on visual inspection, and did not have any other neurological disorders. We also enrolled age- and sex-matched a control group of 20 healthy subjects. All of the subjects underwent 3D volumetric T1-weighted imaging that was suitable for structural volume analysis. We obtained the absolute structural volumes using the FreeSurfer image analysis, and performed structural global and local connectivity analysis using BRAPH (Brain Analysis using Graph Theory). A p-value of less than 0.001 was considered to indicate statistical significance for all calculations.

Results: The volumes of the left transverse temporal cortex and right lingual cortex were significantly increased in the patients with essential tremor compared to healthy subjects. In addition, in the measures of global structural connectivity, the characteristic path length in the patients with essential tremor was significantly increased than that in the control subjects. Furthermore, in the measures of the local structural connectivity, there was significant hub re-organization in the patients with essential tremor; the closeness centrality of the right entorhinal cortex was increased in the patients with essential tremor compared to the healthy controls.

Discussion: Voxel-based morphometry showed structural white and gray abnormalities in essential tremor patients, which may be related to the pathological substrates associated with the disease. The abnormality in the prefrontal and parietal regions may be associated with non-motor symptoms in essential tremor.

Conclusions: We firstly demonstrate that the structural volumes and connectivity in the patients with essential tremor are significantly different from those in the healthy controls. These alterations are implicated in the pathogenesis of essential tremor, and suggest that essential tremor is a network disease.

Objectives

1. Essential tremor may be suggested a network disease
2. Essential tremor has different structural volume and connectivity compared with healthy controls.
3. Graph theory can provide a theoretical pathophysiology for movement disorder.

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131. INS19-0065

INTERLEAVING STIMULATION MODE CAN IMPROVE BETTER THE HEALTH-RELATED QUALITY OF LIFE IN PRIMARY GENERALIZED OR SEGMENTAL DYSTONIA THAN STANDARD BILATERAL PALLIDAL DEEP BRAIN STIMULATION

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Introduction: For the treatment of drug-refractory dystonia, bilateral pallidal deep brain stimulation (GPi-DBS) is proven to be an efficient option. On average, 40-55% improvement on dystonia rating scales (DRS) could be achieved. However, a considerable portion (10-25%) of patients experience minimal alleviation despite good electrode placement. These patients can be regarded as non-responders to GPi-DBS. In cases series, the interleaving stimulation mode (ILSM) could improve dystonia in patients not responding to standard stimulation techniques. The aim of the present study was to systematically compare the efficacy and side-effect profile of double monopolar stimulation mode (DMSM) to those of ILSM.

Materials/Methods: In this prospective, randomized, double-blind and cross-over study, 34 patients with primary generalized or segmental dystonia were enrolled at the University of Pécs Medical School, Hungary. Patients underwent four visits: (1) preoperative, (2) prestimulation (4 weeks after electrode implantation), (3) 3 months and (4) 6 months stimulation. Based on electrode location, the best two contacts were activated with submaximal amplitude, 120μs, and 130Hz. Patients were randomly assigned to either DMSM»ILSM or ILSM »DMSM sequence. Changes in Burke-Fahn-Marsden DRS, health-related quality of life (SF-36) and side-effects were compared.

Results: Thirty patients completed the study protocol. A linear mixed model analysis was used to compare the efficacy of the two stimulation modes. The dystonia severity (DRS) significantly improved from the preoperative 33 points (median) to 10 points (median) after 6 months of stimulation (p=0.001). There was a trend that ILSM was more efficient (p=0.094). The number of responders was tendentiously higher during the ILSM (p=0.052). The SF-36 improved significantly from the preoperative 49 (median) to 74 (median) after 6 months stimulation (p=0.001). The ILSM was superior to the DMSM (p=0.010). As far as the stimulation-related side-effects were concerned, there were no significant differences between ILSM and DMSM.

Discussion: Although the interleaving stimulation was only tendentiously better at reducing dystonia severity, it was associated with better health-related quality of life measured by the SF-36 Summary Index. Furthermore, interleaving stimulation was not associated with more frequent stimulation-related side-effects than the conventional double monopolar stimulation.

Conclusions: Interleaving stimulation may be an option for improving the benefits of pallidal deep brain stimulation in primary generalized or segmental dystonia without worsening the side-effect profile.

Objectives

ILSM was only tendentiously better at reducing dystonia severity.
ILSM was better improving the health-related quality of life.
ILSM is not associated with increased number of severity side-effects.

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132. INS19-0287

AMELIORATION OF PARKINSONIAN LOCOMOTOR DEFICITS WITH MOTOR CORTICAL STIMULATION

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Introduction: Parkinson's disease (PD) is one of the most common movement disorders. PD is characterized by locomotor deficits such as rigidity and bradykinesia, and increase of burst discharges in the subthalamus (STN) has been implicated to play a key role in the symptomatic pathogenesis. Deep brain stimulation (DBS) at STN has been very successful in ameliorating the locomotor symptoms in both clinical patients and animal models of PD, with decrease in subthalamic burst discharges. In view of the direct connection between motor cortices (MC) and STN via the corticosubthalamic (hyperdirect) pathway, we investigated the effect of stimulation of MC on the locomotor deficits in PD.

Materials/Methods: We made PD rats with lesion of the relevant dopaminergic neurons by 6-hydroxydopamine. Electrical stimulation of MC was applied with implanted intracortical electrodes, with concomitant behavioral studies (open field and treadmill running tests) and electrophysiological recordings.

Results: With passage of constant currents at the most effective level, the moving distance of the PD rats in 5 minutes in an open field increased from 283 $\pm$ 53 (prestimulation) to 666 $\pm$ 72 cm (during stimulation). In comparison, the moving distance was 247 $\pm$ 50 cm with sham stimulation. On the other hand, the moving distance was roughly 500 – 600 cm in the normal rats whether it was the prestimulation, stimulation, or sham stimulation period. The performance in the treadmill test could also be improved with stimulation of MC in the PD rats but was probably adversely affected in the normal rats. Preliminary investigations with epidural electrodes gave roughly similar results. Concomitant electrophysiological recordings in STN revealed either increase or decrease of the total discharges during stimulation of MC, but burst discharges may be slightly decreased. Poststimulation histopathological examination revealed no definite lesions in the MC.

Discussion: Possibly via the direct glutamatergic input from MC to STN via the hyperdirect pathway, MC stimulation may alter the firing pattern of STN and consequently ameliorate the locomotor deficits in PD.

Conclusions: MC potentially could be an alternative site for brain stimulation in the management of PD or even the other movement disorders.

Objectives: Different ways of brain stimulation for PD/The mechanisms underlying brain stimulation therapies and movement disorders/The electrophysiological interactions between MC and STN

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133. INS19-0421

DEEP BRAIN STIMULATION FOR STATUS DYSTONICUS IN CHILDREN: A SINGLE CENTER EXPERIENCE

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Introduction: We present our experience with three cases of refractory status dystonicus (SD) successfully treated either with pallidal or subthalamic deep brain stimulation (DBS). All of three patients in our series (aged 5-12) have acquired dystonia: one presents an heterozygous mutation in GNAO1 gene, associated with involuntary movements and neurodevelopmental delay; two are affected by methylmalonic acidemia (MA), an inborn error of metabolism causing basal ganglia damage and dystonia.

Materials/Methods: The presented data have been obtained through a retrospective review of the clinical records of three pediatric patients who were admitted to ICU for SD and treated with DBS at Padova University Hospital between 2014 and 2015. DBS electrodes were placed bilaterally targeting either globus pallidus internus (one patient with MA and the one with GNAO1 mutation) or subthalamic nucleus (the other MA patient); stimulators were programmed by one neurologist (A.A.). Patients have been followed up ever since. In the patient bearing GNAO1 mutation molecular diagnosis has been obtained with NGS analysis of a panel of genes associated with dystonia in the literature.

Results: After surgery, all three patients experienced resolution of SD (defined as a reduction of involuntary movements allowing weaning from sedation and extubation) within 8-16 days. At last follow-up in 2018, two patients are free from recurrences of SD, while one experienced two more episodes involving the right hemibody.

Discussion: Optimal treatment for status dystonicus, a rare but potentially life-threatening complication, is debated. Accumulating evidence supports the role of neurosurgical intervention with DBS as an effective therapeutic strategy in cases that are refractory to medical management.

Conclusions: We provided additional evidence on the management of status dystonicus in patients affected by GNAO1-related movement disorder and methylmalonic acidemia. DBS is a valid therapeutic solution in the acute phase of a refractory dystonic crisis, and subthalamic nucleus may be an appropriate target when GPi is not suitable. Moreover, our report highlights that GNAO1 mutation should be considered in undiagnosed patients with neurodevelopmental delay showing hyperkinetic movements.

Objectives:
To confirm the efficacy of DBS in status dystonicus
To suggest that STn may be effective for DBS in dystonia
To suggest the indication to DBS for metabolic dystonia

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Brain: Movement Disorders

134. INS19-0206

FEASIBILITY AND SAFETY OF REMOTE DEEP BRAIN STIMULATION PROGRAMMING VIA INTERNET FOR MOVEMENT DISORDERS

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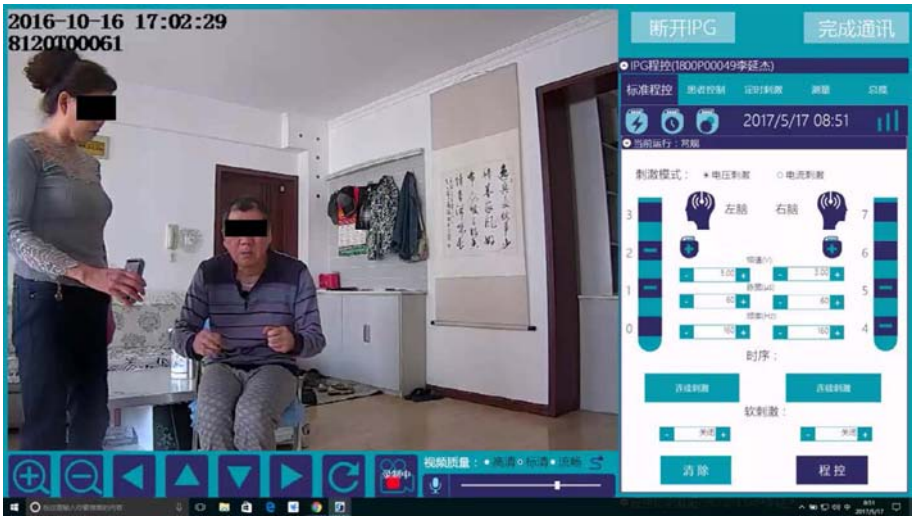
Introduction: Telemedicine has showed promising perspective for the treatment of chronic diseases. A novel deep brain stimulation (DBS) system could be programming via Internet with the supporting hardware. We adjusted the stimulating parameters for patients who stay home by this system, to test the feasibility and safety of remote DBS programming for movement disorders.

Materials/Methods: The patients were included in this study if they were (1) 18 to 75 years old; (2) implanted the novel DBS for movement disorders; (3) accessed to Internet; (4) willing to be programmed remotely



and informed consent was given. All the patients were turned on DBS for the first time in hospital, then they could make appointment for remote or face-to-face programming as they needed. The remote programming process via Internet is like the real-time, synchronous videoconferencing. The patient client hardware at home integrates programmer, camera and microphone, with connection to Internet. The doctor client was a software in PC platform, which could send DBS parameters data to the patient client and pacemaker further. Every time the remote programming was finished, the parameters was verified by the patients' programmer. The patients were asked if they were satisfied with programming this time and if they were willing to continue the remote programming next time. Any side effect was recorded.

Results: From August 2016 to Nov 2018, 22 patients were programmed remotely for 118 times (*Mean*±*SD* 5.36±5.07; *Max* 18; *Min* 1). Successful remote programming was implemented for 114 times (96.7%), as the parameters were verified by patient's programmer. The 4 failed programming were due to terrible unstable Internet connection, and the patients had to make new appointment at other day. The average programming duration is 30.5±16.7 min for doctor, including the disruption and reconnect time. Of all the remote programming process, patients' satisfaction rate was 90.1%, and 97.5% chose to continue remote programming. No medical problem and side effect were found.

Discussion: Deep brain stimulation (DBS) has got great success for movement disorders. After implantation of electrode and pacemaker, the stimulating parameters should be adjusted according to the patients' discomfort over long time. Conventional programming is the face to face process, and the patients must go to clinic although their motor ability might be limited. Remote programming is a promising way to break the limitation.

Conclusions: Remote DBS programming for movement disorders is feasible and safe.

Objectives: To describe how the remote DBS programming works.

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135. INS19-0415

ACUPUNCTURE FOR POSTSTROKE SHOULDER PAIN: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Shoulder pain is the common complaint among patients with stroke. Acupuncture has increasingly been used for shoulder pain treatment after stroke.

Materials/Methods: Five databases were searched without language restrictions. All randomized controlled trials that evaluated the effects of acupuncture for poststroke shoulder pain compared with controls were included. Assessments were performed primarily with the Visual Analogue Scale (VAS), Fugl-Meyer Assessment (FMA), and effective rates.

Results: In all, 201 potentially relevant articles were identified; 12 were randomized controlled trials that met our inclusion criteria. Meta-analysis showed that acupuncture combined with rehabilitation treatment appeared to be more effective than rehabilitation treatment alone for poststroke shoulder pain, as assessed by VAS (weighted mean difference, 1.87; 95% confidence interval [CI], 1.20-2.54; <0.001); FMA (weighted mean difference, 8.70; 95% CI, 6.58-10.82; $P < 0.001$); and effective rate (RR, 1.31; 95% CI, 1.18-1.47; $P < 0.001$).

Discussion: Our systematic review and meta-analysis suggested evidence for the effectiveness of acupuncture in treating poststroke shoulder pain. All 12 studies were RCTs and all showed favorable results for combined acupuncture and rehabilitation treatment compared with rehabilitation alone. Pain relief and improvement of upper-limb motor function are important treatment aspects in stroke rehabilitation.

Conclusions: Our results suggest that acupuncture may be effective for treating shoulder pain after stroke. However, further studies with more subjects and a rigorous study design are needed to confirm the role of acupuncture in the treatment of poststroke shoulder pain.

Objectives: The aim of the present study was to summarize and evaluate evidence for the effectiveness of acupuncture in relieving poststroke shoulder pain.

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136. INS19-0086

EFFECT OF TRANSCRANIAL DIRECT CURRENT STIMULATION COMBINED WITH NEUROMUSCULAR ELECTRICAL STIMULATION ON MOTOR RECOVERY OF UPPER EXTREMITY IN PATIENTS WITH CHRONIC STROKE

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Introduction: Previous studies have shown transcranial direct current stimulation (tDCS) and neuromuscular electrical stimulation (NMES) have been effective for promoting motor recovery of stroke patients. However, the effects of tDCS combined with NMES on upper extremity (UE) motor recovery in patients with stroke have not been investigated.

Materials/Methods: A randomized, double-blinded and sham-stimulation study was conducted. Twenty-two participants with chronic stroke (onset > 6 months) were assigned into one of three groups (tDCS combined with NMES, tDCS combined with sham NMES, or sham tDCS combined with sham NMES) by block randomization. In addition to conventional rehabilitation, all subjects received an additional protocol with a total of 15 sessions for 3 weeks (5 times per week, 30 minutes daily). The UE subscale of Fugl-Meyer assessment (UE-FMA) and Action Research Arm Test (ARAT) as primary outcome measures were assessed at beginning of the intervention, 3-week post-treatment and one-month follow-up.

Results: Most of the participants had mild to moderate disability in activity of daily living. No significant differences in the primary outcome measures at post-treatment and one-month follow-up were found among the tDCS combined with NMES group (n=8), tDCS combined with sham NMES group (n=7), and the sham tDCS combined with sham NMES group (n=7). However, significant score changes in UE-FMA (from baseline to post-treatment, p= 0.02) and ARAT (from baseline to post-treatment, p= 0.04) were found for the tDCS combined with NMES group.

Discussion: The results of this study will help to clarify the treatment effects of tDCS combined with NMES therapy on facilitating motor and function recovery in patients with chronic stroke.

Conclusions: This preliminary study reveals that the tDCS combined with NMES appears to be beneficial to UE motor recovery after stroke but is not superior to the tDCS alone. Future study recruited more sample is warranted.

Objectives

To investigate the effects of the combination treatment strategy.

To learn the randomized, double-blinded and sham-stimulation study.

To learn the outcome measures assessment.

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Brain: Movement Disorders

137. INS19-0376

DEEP BRAIN STIMULATION AND COGNITIVE OUTCOMES AMONG PATIENTS WITH PARKINSON'S DISEASE: A HISTORICAL COHORT STUDY

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Introduction: Parkinson's disease (PD) is a neurodegenerative disease. PD manifests with both motor and non-motor symptoms including resting tremor, rigidity, bradykinesia, stooped posture, neurobehavioral disorders, cognitive impairment, and autonomic dysfunction {1}. Current treatments for PD include pharmacotherapy, non-pharmacological alternatives, and deep brain stimulation (DBS). The aim of this study is to build upon this literature and add to it more specific cognitive data regarding the effect of both GPi and STN DBS on cognitive outcomes.

Materials/Methods: This historical cohort study included 32 PD patients; 13 patients underwent bilateral GPi DBS and 19 patients underwent bilateral STN DBS by a single surgeon (MKL). The inclusion criteria were a diagnosis of PD and available neuropsychological testing at baseline and 6 months post-DBS (follow-up).

Patients completed a neuropsychological test battery before undergoing DBS and 6 months post DBS. Four neuropsychological tests were used in this study to assess cognitive domains: 1) Language: (Boston Naming Test and Wechsler Adult Intelligence Scale); 2) Attention/ concentration: (Wechsler Adult Intelligence Scale; and 3) Processing speed: (Wechsler Adult Intelligence Scale).

Results: There was no significant difference between patients in the GPi and the STN DBS groups in terms of age, sex, disease duration, time between surgery and follow-up tests, or baseline scores on any of the four tests. Among GPi DBS patients, there was no significant difference between baseline and follow-up scores on any of the neuropsychological tests. STN DBS patients had significantly lower scores at 6-month follow-up as compared to baseline.

Discussion: Our findings are in line with few other studies that also reported a cognitive decline in STN DBS as compared to GPi DBS patients. For example, a multicenter study group observed a more pronounced decline on a task measuring processing speed and working memory in patients who underwent STN DBS as compared to GPi DBS [14].

Conclusions: Patients with STN DBS performed significantly worse on follow-up on a test measuring processing speed. In addition, when compared to GPi DBS patients, STN DBS patients had lower mean scores on cognitive tests measuring language, attention/concentration, and processing speed at 6 months post-DBS as compared to baseline.

Objectives

Learn potential differences in cognitive outcomes in PD patients undergoing GPi vs STN DBS

Compare results in postoperative cognition results from different DBS centers.

Learn neurocognitive domains of importance in PD patients undergoing DBS

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138. INS19-0191

TWO-YEAR FOLLOW-UP OF A PROSPECTIVE, DOUBLE-BLINDED, MULTI-CENTER RANDOMIZED CONTROLLED TRIAL EVALUATING DBS WITH A NEW MULTIPLE-SOURCE, CONSTANT-CURRENT RECHARGEABLE SYSTEM FOR PARKINSON'S DISEASE (INTREPID)

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Introduction: Deep Brain Stimulation (DBS) is a surgical therapy used for treatment of motor signs and fluctuations associated with Parkinson's disease (PD). Its efficacy has been substantiated by several randomized controlled trials. Moreover, motor improvement following DBS may be sustained for up to 10 years (1). The INTREPID clinical trial assessed improvement in motor function and quality of life in patients with advanced, levodopa responsive Parkinson's disease (PD) following bilateral subthalamic nucleus (STN) DBS using a new device equipped with multiple current sources. In this report, 2-year follow-up data will be described.

Materials/Methods: INTREPID (ClinicalTrials.gov Identifier: NCT01839396) is a multi-center, prospective, double-blinded, randomized controlled trial (RCT) sponsored by Boston Scientific. Subjects with advanced PD were implanted bilaterally in the STN with a multiple-source, constant current DBS System (Vercise, Boston Scientific). One hundred and sixty subjects were randomized to either receive active vs. control settings for 12-week blinded period. Subjects were blinded to treatment assignment and study assessments were administered by a clinician blinded to treatment condition. Motor improvement was evaluated using several assessments including subject motor diaries, UPDRS scores, etc. Assessments for quality of life (e.g. PDQ39) were also administered.

Results: The study met the primary endpoint demonstrated by mean difference of 3.03 $\pm$ 4.52 hrs. ($p < 0.001$) between active and control groups in ON time without troublesome dyskinesia, with no increase in antiparkinsonian medication, from post-implant baseline to 12-weeks post-randomization. At 1-year compared to pre-surgery screening, a 49.2% improvement in UPDRS III scores was reported, and overall improvement in quality of life was maintained. Reporting of 2-year follow-up data is planned.

Discussion: The INTREPID RCT successfully met the primary endpoint and several secondary endpoints based on outcomes of the blinded period (12 weeks). This analysis will describe outcomes derived from subjects assessed out to 2-years follow-up.

Conclusions: Results of the INTREPID RCT demonstrate that use of a multiple-source, constant-current DBS system is safe and effective for treatment of Parkinson's disease symptoms.

Objectives

1. To report UPDRS III outcomes out to 2-years post-implant from the INTREPID randomized controlled trial.

2. To report quality of life outcomes out to 2-years post-implant from the INTREPID randomized controlled trial.

3. To report ON time without troublesome dyskinesia, with no increase in antiparkinsonian medication out to 2-years post-implant from the INTREPID randomized controlled trial.

References

NA

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139. INS19-0370

PREDICTIVE FACTORS FOR LONG-TERM CLINICAL OUTCOMES OF DEEP BRAIN STIMULATION IN THE TREATMENT OF PRIMARY MEIGE SYNDROME

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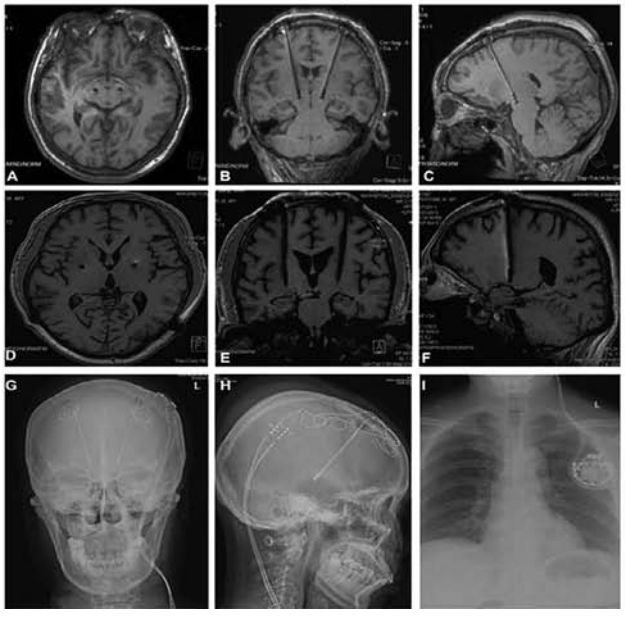
Table Comparisons of the Clinical Factors between the Two Groups

		Good-results Group (N=9)	Poor-results Group (N=11)	*P* value
X1	Age at Surgery (yrs)	59.56±4.19(52-64)	60.55±9.03(43-71)	0.237*
X2	Age at Onset (yrs)	54.00±5.57(45-61)	56.82±8.24(43-66)	0.394†
X3	Gender(M/F)	3/6	7/4	0.370‡
X4	Disease Duration(yrs)	5.59±4.99(0.25-17)	3.72±3.94(0.33-14)	0.252*
X5	Targets (STN/GPi)	9/0	6/5	0.038‡
X6	Electrode(M/P)	3/6	5/6	0.670‡
X7	Mul onset sites (Y/N)	0/9	6/5	0.014‡
X8	BFMDRS-M total sco	11.16±6.66(3-26)	15.73±5.91(8-25)	0.122†
X9	BFMDRS-D total sco	1.78±3.35(0-10)	1.45±1.57(0-4)	0.714*
X10	Eyes sco	14.89±3.33(6-16)	13.55±3.56(8-16)	0.294*
X11	Mouth sco	3.56±4.92(0-12)	10.55±5.77(0-16)	0.014*
X12	SS sco	1.89±4.01(0-12)	3.64±3.61(0-9)	0.128*
X13	Syms in neck (Y/N)	1/8	1/10	1.000‡
X14	Dyspnea (Y/N)	3/6	2/9	0.617‡
X15	FU months	10.67±6.80(3-23)	24.36±12.89(8-52)	0.010†

yrs=years; M=Medtronic; P=PINS; Mul=Multiple; sco=scores; Syms=Symptoms; FU=Follow-up; SS=Speech and Swallowing; STN= subthalamic nucleus; GPi= globus pallidus internus
* For comparisons of variables with non-normality distributions; Mann-Whitney test
† For comparisons of variables with normality distributions; two-sample t tests
‡ For comparisons of binary variables; Fisher's exact tests

Figures.

Fig.1 (A-C) Location of microelectrodes in the STN **(D-F)** Location of microelectrodes in the GPi **(G-I)** Sites of microelectrode, leading wires and IPG.



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Introduction: DBS is recognized as an effective therapy for patients with Primary Meige syndrome, but previous studies on this matter have focused on the clinical effects. This study explored the predictors of clinical outcome in patients with Meige syndrome who underwent DBS.

Materials/Methods: Twenty patients who underwent DBS targeting the bilateral STN or GPi were enrolled. Their clinical outcomes were evaluated using the BFMDRS scores; patients were accordingly divided into Good and Poor-outcome group. Putative influential factors were examined separately, and the factors with statistical significance were subjected to logistic regression analysis to identify predictors.

Results: Four factors showed significant differences between the Good and Poor outcome groups: the DBS target (STN vs. GPi); whether symptoms first appeared at multiple sites or at a single site; the subitem scores of the mouth at baseline; and the follow-up period ($P < 0.05$). Binary logistic regression analysis revealed that initial involvement of multiple sites and the mouth score were the only significant predictors of the clinical outcome.

Discussion: In the study, 15 patients with STN DBS and 5 patients with GPi stimulation were enrolled, constituting a larger number of cases from a single center than have been studied in the previous literature. Good outcomes were defined as an improvement of more than 30% after DBS to allow evaluation of predictive factors and exploration of the types of patients who are more likely to benefit from DBS. The LR analysis indicated that multiple sites of onset and a high mouth score in the BFMDRS were the only 2 factors independently and significantly predicting a poor clinical outcome.

Conclusions: Thus, the severity of the disease in the initial stage and pre-surgical period were the only independent predictive factors of the clinical outcomes of DBS for the treatment of patients with Meige syndrome.

Objectives

1. Conservative therapies are ineffective in many Meige patients. In these cases, DBS has been proposed as an effective surgical therapy.

2. This study offered a method for analyzing predictive factors of the outcomes of DBS.

3. STN-DBS produced better results in these patients, but the strongest predictor of outcome was the severity of the disease at baseline.

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140. INS19-0239

EFFECTS OF PEDUNCULOPONTINE NUCLEUS (PPN) DEEP BRAIN STIMULATION (DBS) IN REDUCING FALLS, IMPROVING GAIT AND POSTURAL CONTROL IN PARKINSON'S DISEASE (PD): 5-YEARS FOLLOW-UP

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Introduction: In recent years, PPN-DBS has been explored to address the axial motor symptoms of gait freezing and loss of postural control (adding to tremor, rigidity and bradykinesia as drivers of disease burden in advanced PD). However, the role of PPN-DBS remains unclear. The purpose of this study was to determine the advantage of bilateral PPN-DBS in reducing falls, improving gait and postural control in patients with advanced PD.

Materials/Methods: A prospective, four-phase, within-subject crossover, double-blinded study where bilateral STN (Med. 3389) and PPN-DBS (Med. 3387) electrodes were implanted in six-patients with advanced PD and axial motor symptoms while on optimal medical therapy. The primary endpoint was the reduction in falls and improvement in gait. Performance was recorded on optimal medical therapy only (open-label phase), bilateral subthalamic nucleus (STN) or PPN-DBS and simultaneous bilateral STN & PPN-DBS (ALL neurostimulation in conjunction with optimal medical therapy; 6- months each). The study received local ethics approval and informed written consent was obtained from all patients.

Results: There was an 89%, 92% and 100% decrease (Wilcoxon signed-ranks test; $p < 0.05$) in ICNG Index (falls/1000 steps) with bilateral STN-DBS (at 2.6 $\pm$ 0.2 V, 140 Hz, 60 μs), bilateral PPN-DBS (at 1.5 $\pm$ 0.2 V, 20 Hz, 60 μs) and simultaneous bilateral STN & PPN-DBS in conjunction with optimal medical therapy, respectively, compared to optimal medical therapy only. PPN-DBS was generally well tolerated and only induced momentary ipsilateral oscillopsia at commencement on ≥ 2.0 V with rapid habituation, consistent with previous findings. No other complications were reported with PPN-DBS.

Discussion: In appropriately selected patients, simultaneous bilateral STN & PPN- DBS, in conjunction with optimal medical therapy, targeting the mid-lower PPN with the aid of DWI/DTI scans with PDT analysis and resultant saccadic modulation coupled with performance changes in the relevant axial motor segments, offers the possibility of ameliorating both the axial motor symptoms as well as the limb motor symptoms of advanced PD.

Conclusions: Simultaneous bilateral STN & PPN-DBS offers the possibility of ameliorating both the axial motor symptoms as well as the limb motor symptoms of advanced PD.

Objectives

Explore brainstem anatomy in relation to PD

Define efficacy of PPN-DBS in treating axial symptoms of advanced PD

Investigate effects of PPN-DBS on saccades/gaze displacement of advanced PD

References

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141. INS19-0219

OPTIMAL INCISION FOR DBS IMPLANTATION

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Introduction: Deep brain stimulation (DBS) is being increasingly utilised for treatment of various medically refractive conditions such as movement disorders. There is no consensus on the type of burr hole incision (x2 linear parasagittal/linear coronal/curvilinear coronal – either separate or combined for bilateral implantation) for this procedure and there is limited published literature on complication rate stratified by the different choice of incisions (Constantoyannis et al., 2005 & Solmaz et al., 2014).

Materials/Methods: Subjective and objective review of all DBS cases performed in Cambridge, UK over a period of two-years.

Results: Overall, wound complications from DBS procedures remained acceptably low. There was no statistically significant difference in wound infection or dehiscence/erosion of implant through skin associated with the different choice of incisions. Subjectively, greater incidence of incision site hypoesthesia was reported with combined curvilinear coronal incisions.

Discussion: Linear parasagittal burr hole incision(s) may afford the most optimal balance for preserving the neurovascular anatomy of the scalp thus reducing wound associated complications from DBS procedures including incision site hypoesthesia. Combined with better tolerability during awake procedures, linear parasagittal burr hole incision(s) may prove to be the optimal choice for DBS procedures. This finding may be corroborated with the establishment of an neuromodulation implant registry and long term follow-up.

Conclusions: Incision site hypoesthesia may be preventable with linear parasagittal burr hole incision(s) for DBS implantation without an increase in other wound associated complications such as infection or dehiscence/erosion of implant through skin. Linear parasagittal burr hole incision(s) are also the best tolerated during awake procedures.

Objectives

Neuro-vascular anatomy of the scalp

Optimal burr hole incision(s) for DBS procedures

Advantages of an registry/audit for post-op complications of DBS procedures

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142. INS19-0321

DEEP BRAIN STIMULATION FOR PEDIATRIC DYSTONIA

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Introduction: Dystonia is a debilitating movement disorder with a variety of underlying etiologies. When rehabilitation and/or medications fail to relieve painful, dystonic muscle contractions, surgery is considered. Deep brain stimulation (DBS) of the globus pallidus internus (GPi) is a neuromodulatory intervention that should be weighed as a viable treatment option. The authors describe DBS outcomes for patients with primary and secondary dystonia.

Materials/Methods: Our Interdisciplinary Movement Disorders group prospectively reviewed cases of DBS performed at our institution for dystonia (IRB 3799). Demographics and DBS outcomes were analyzed.

Results: DBS of the GPi was performed on eight subjects (3 females, 5 males) by COO at CNMC. In all but two cases, bilateral leads were placed. In one case, Clearpoint navigation was used. Underlying etiologies were anoxic brain injury (n=2), traumatic brain injury (TBI, n=2), *DYT1* primary dystonia (n=1), glutaric acidemia type I (n=1), pantothenate kinase-associated neurodegeneration (PKAN, n=1), and undetermined (n=1). Average age at first DBS stimulation and length of follow-up were 15.6 years (range 9.2-24.8) and 28.7 months (range: 3.1-59.3) respectively. The average percentage changes in Barry-Albright Dystonia (BAD) and Burke-Fahn-Marsden Disability Rating (BFMDR) scores relative to pre-op scores were 22.9% (range: -12.5-100) and 28.4% (range: 2.1-100) respectively. There were no post-operative infections.

Discussion: Patients with longer follow-up generally experienced greater outcome score improvements than those with shorter stimulation lengths. This is consistent with the literature that suggest DBS benefits are compounded over time.1 In seven cases, dystonia scores either remained stable or improved. For one patient, however, BAD score increased 12.5%, while BFMDR score decreased 23.3% at most recent clinical follow-up relative to pre-operative scores. This subject had the longest stimulation history of our cohort (59.3 months), but was also the oldest at time of surgery (24.8 years), with a nearly 24-year history of progressive dystonia. A major limitation of our analysis was small cohort size.

Conclusions: DBS is a safe and effective neuromodulatory intervention for pediatric dystonia, especially that which is refractory to less invasive alternatives. Further studies are necessary for elucidating which cohorts may experience the greatest improvements.

Objectives

1. Pediatric dystonia is a severely disabling condition with diverse underlying etiologies.

2. The safety of pediatric GPi DBS has been demonstrated.

3. The effectiveness of DBS may vary with respect to primary vs. secondary disorder and the underlying diagnosis.

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143. INS19-0390

MOTOR PLASTICITY EFFECTS INDUCED BY CORTICAL ELECTRICAL STIMULATION IN TRAUMATIC BRAIN INJURED RATS

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Introduction: *Traumatic brain injury (TBI) is a global scenario with high mortality and disability, which does not have an effectual and approved therapy till now. Electrophysiologic methods, and in particular, transcranial magnetic stimulation (TMS) or cortical electrical stimulation (CES), have been demonstrated to provide prognostic value in several neurological disorders. However, no study has been reported to quantify the electrophysiological changes by using CES method following TBI. This study investigated corticomotor excitability and inhibition in TBI rat model.*

Materials/Methods: *Cortical excitability was studied in 20 TBI and in 20 normal rats using paired pulses CES. The parameters of testing included resting motor threshold (RMT), recruitment curve (REC) of motor evoked potential (MEP) and long-interval cortical inhibition (LICI) at long intervals (10, 50, 100, 200, and 300 ms). Furthermore, the changes of motor plasticity induced by intermittent theta burst stimulation (iTBS) were also tested in in normal and TBI animals.*

Results: *In results, the TBI group overall revealed a significant lower RMT and narrower recruitment curves compared to normal rats. The alterations in LICI were significant in TBI rats. In addition, MEPs significantly increases immediately after iTBS in normal rats for 30 minutes. In TBI rats, MEPs maintained the same level after iTBS without obvious change.*

Discussion: *These results showed that TBI rats had less response to iTBS and revealed that motor plasticity was reduced in TBI rats.*

Conclusions: *In Conclusion, this study was the first to demonstrate differences in motor plasticity and intracortical inhibition in TBI animal model. Based on our results, brain injury may alter the neural activity in electrophysiological performance. Longitudinal studies in individuals with TBI would be valuable to identify this hypothesis further, which might provide prognostic biomarkers and suggest novel therapeutic strategies.*

Objectives: *This study provided the information of the resting motor threshold, corticomotor excitability, and corticomotor inhibition in TBI rat model.*

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144. INS19-0225

A PALM-WORN DEVICE TO MONITOR RIGIDITY IN PARKINSON'S DISEASE

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Introduction: Parkinsonian rigidity is identified on clinical examination as resistance to passive movement. Rigidity is commonly measured using ordinal rating scales (MDS-UPDRS[1]); however instrumented measures may provide greater insights. We present a palm-worn instrument to quantify rigidity on a continuous scale and aim to: determine congruence with the MDS-UPDRS; investigate the impact of deep brain stimulation (DBS) and contralateral movement; make comparisons with healthy individuals.

Materials/Methods: The device employs a miniature motor to flex the third digit of the hand about the metacarpophalangeal joint whilst transducers record flexion/extension forces. Eight participants with Parkinson's disease underwent evaluation during conditions: on/off DBS, and with and without contralateral limb movement to activate rigidity. During each DBS condition, wash-in/out effects were tracked using both our instrument and two blinded clinical raters. Sixteen healthy volunteers served as controls.

Results: Rigidity measured using our instrument had moderate agreement with the MDS-UPDRS ($R = 0.676$, stepwise linear regression). Post-hoc tests revealed that our instrument can differentiate therapy (on vs. off DBS, $p < 0.001$) and cohorts (disease vs. healthy, $p < 0.001$). Moreover, the instrument has sufficient sensitivity to detect activation maneuvers in both Parkinson's ($p = 0.021$) and healthy volunteers ($p = 0.014$). Rigidity gradually worsened over a one-hour period after DBS cessation, but improved rapidly with DBS resumption.

Discussion: Our findings support the notion that an instrumented rigidity measure offers advantages over conventional clinical ratings. It may be used to guide DBS surgery and assess intraoperative effects of stimulation[2], determine optimum therapeutic windows[3], and provide insight into mechanism of therapeutic action[4]. Importantly, instrumented methods allow continuous monitoring, delivering insight into temporal characteristics of symptom changes[5].

Conclusions: Given its ability to track changes in rigidity due to therapeutic intervention, our technique could have applications where continuous measurement is required or where a suitably qualified rater is absent.

Objectives

1. Rigidity in Parkinson's disease
2. Objective symptom monitoring
3. Transient effects of DBS

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145. INS19-0252

1.5T VS. 3T FMRI BOLD ACTIVATION ARE COMPARABLE IN MEASUREMENT OF DBS EFFECTS

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Introduction: It has been established that fMRI at 3T has higher sensitivity in detecting brain activation than at 1.5T. Performing fMRI at 3T in patients with deep brain stimulation (DBS) implants, however, poses additional challenges, as the FDA has only approved imaging of DBS patients at 1.5T with their stimulation ON (provided the devices meet specific characteristics). 3T studies require additional, site specific safety tests and IRB approvals. The goal of this study was to compare activation levels in BOLD levels in a cohort of DBS patients scanned at both field strengths to determine if differences occurred in reproducibility.

Materials/Methods: Patients with Parkinson's disease (n=5, mean age 65.4 (range 55-71), 5 men) treated with DBS underwent fMRI studies at both 1.5T and 3T. DBS was cycled for 30 seconds ON and 30 seconds OFF for 5 minutes at 3T and 8 minutes at 1.5T. The longer acquisition time for 1.5T compensated for the lower signal to noise ratio relative to 3T. Activation maps were obtained for each patient and at each field strength. A region of interest (ROI) analysis was performed at each field strength, and evidence of group differences was sought in the primary somatosensory cortex (S1), primary motor cortex (M1), thalamus, and cerebellum.

Results: There was no statistically significant difference in activation levels between 1.5T and 3T for S1 (p=0.23), M1 (p=0.68), thalamus (p=0.40) or cerebellum (p=0.47). Compared to 1.5T images, 3T images demonstrated an improved signal-to-noise ratio.

Discussion: The results demonstrate that no significant activation/deactivation detected by 3T is lost with 1.5T fMRI studies in DBS patients. Given the wider availability of 1.5T scanners, and the fact that scanning of DBS patients with specific hardware types is already approved at 1.5T, these results suggest that although data collected at 3T has improved signal to noise ratio and necessitates a shorter acquisition time than 1.5T for an equivalent signal, data collected at 1.5T is reliable and comparable to 3T data.

Conclusions: Data collected at 1.5T is reliable and comparable to 3T data.

Objectives: To determine if data collected at 1.5T is comparable to data collected at 3T.

References

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146. INS19-0218

FRAMELESS ROBOT-ASSISTED GPI DEEP BRAIN STIMULATION FOR PARKINSON'S DISEASE

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Introduction: Frame-based implantation of deep brain stimulation electrodes remains the "gold standard" due to its reported submillimeter accuracy, but image-guided frameless techniques with acceptable accuracy are becoming more popular. Frameless robot-assisted methods are popular in Europe but have only been reported for STN placement in the US. We present the case of a 73 year-old female referred for DBS for Parkinson's disease with increased motor fluctuations. Because of anxiety and a fixed cervicothoracic kyphosis, awake frame-based implantation technique was not possible. Therefore, a frameless, robot-assisted asleep procedure was performed.

Materials/Methods: The patient underwent bilateral GPi electrode implantation under general anesthesia using 3 Tesla MRI planning imaging processed through a robotic stereotactic navigation system. Skull fiducials and intraoperative CT were used for registration and then image fusion to the patient's MRI with pre-planned trajectories was completed. Bilateral intracranial leads were advanced using robotic stereotactic guidance. macrostimulation testing was performed with serial escalation in amplitude while observing for any signs of facial contraction. Post-implantation intraoperative CT was obtained to verify lead location using image fusion to the planning MRI. The right lead position was satisfactory, but the left lead was 8mm deep to target. It was withdrawn, and the appropriate GPi location was then confirmed with additional CT imaging. The patient returned a week later for standard extension and generator placement.

Results: The vector error for the left lead was 3.28mm and 2.63mm for the right. Both were to the left and shallow of target, but less than 1mm error in A-P dimension. Despite greater than average reported vector error, the patient had 41% reduction in UPDRS-III motor score.

Discussion: Asleep robot-assisted, frameless DBS has similar vector errors and outcomes to other frameless techniques. We believe there is a steep learning curve to robot-assisted placement of leads and believe vector errors will improve with increasing use.

Conclusions: Frameless robot-assisted DBS deep brain stimulation has accomplished comparable outcomes and vector error as conventional methods. The use of intraoperative CT allowed for immediate repositioning of a lead with a Z coordinate error. For patients with extenuating circumstances preventing conventional methods of targeting, frameless robot-assisted DBS with intraoperative image confirmation is an option.

Objectives

1. Show how to calculate vector error.
2. Present a case of asleep robot-assisted frameless DBS.
3. Discuss utility of intraoperative verification imaging.

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147. INS19-0352

TARGET MATTERS: RETROSPECTIVE VECTOR ERROR ANALYSIS OF 258 DEEP BRAIN STIMULATION ELECTRODES AT SINGLE INSTITUTION

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Introduction: A recent survey highlighted the immense variation in strategies for deep brain stimulation.1 It is important to assess the accuracy of these strategies to ensure patient safety. We present our case series utilizing Leksell frame placement with MRI in frame, direct image-guided targeting, awake bilateral implantation with macrostimulation through the lead for physiologic confirmation with fluoroscopic confirmation of electrode at target followed by post-operative MRI in frame.

Materials/Methods: A retrospective review of our DBS database was used to identify 139 patients between 2010 and 2016 for a total of 258 leads. Using our pre-operative planning software we identified the intended x, y, and z coordinates for each lead as well as the post-operative location of contact 1. The vector error was calculated for each lead.

Results: Of our 139 patients, 96 patients were treated for Parkinson's Disease, 36 for essential tremor, 5 for dystonia, 1 for obsessive-compulsive disorder, and 1 for Tourette's Syndrome. STN was targeted in 55 patients (98 leads), GPI in 40 patients (77 leads), VIM in 40 patients (75 leads), ZI in 2 patients (4 leads), and VC/VS in 2 patients (4 leads). We found our average vector error to be 2.65. There was not a significant difference in vector error by laterality when performing bilateral lead placement (left=2.70, right 2.60). We averaged submillimeter accuracy in any single dimension (x=0.31, y=0.56, z=0.46). The largest average vector error was with targeting VC/VS (3.12) compared to ZI (2.83), VIM (2.71), STN (2.66).

Discussion: When performing deep brain stimulation it is important to be both accurate and precise. Our vector errors are comparable to other centers (1.2-2.71).2-9 Though we did not find statistical difference in error based on laterality, target did appear to matter. The most likely reason for this difference is the small sample size of certain targets, but familiarity with target and imaging quality may play a role. We plan to further investigate the clinical efficacy of our targeting and how this relates to accuracy.

Conclusions: Awake bilateral implantation using frame-based, direct, image-guided targeting with physiologic (macrostimulation) as well as fluoroscopic and MRI post-implantation confirmation of lead location provides similar accuracy to other reported methods of deep brain stimulation. Laterality does not appear to affect error but target does.

Objectives

1. How to calculate vector error.
2. Review literature on accuracy with DBS.
3. Discuss sources of vector error.

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148. INS19-0353

UTILITY OF AWAKE DEEP BRAIN STIMULATION WHEN TARGETING GLOBUS PALLIDUS INTERNUS

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Introduction: Globus pallidus internus (GPi) is a popular target for the treatment of Parkinson's Disease and dystonia. There is an ongoing debate over awake versus asleep deep brain stimulation and the importance of patient comfort versus physiologic confirmation of target. We present our outcomes with awake deep brain stimulation targeting GPi and the utility of physiologic confirmation.

Materials/Methods: A retrospective analysis of our deep brain stimulation database found 40 patients (77 leads) who underwent GPi stimulation. Using our pre-operative planning software, we identified the intended and actual x, y, and z coordinates for each lead and calculated the vector error. For patients with Parkinson's Disease, chart reviews were performed to obtain patient's preoperative and 1 year postoperative UPDRS-III scores. Stimulation parameters at 1 year were also recorded. Statistical analysis was performed to determine if laterality or order of placement affected error and if there was a correlation between error and clinical outcomes.

Results: The average vector error over 77 leads was 2.55. Laterality and order of placement did not significantly effect vector error (p-0.64, p=0.97). There was a significant difference in z error compared to x or y (p=0.009; p=0.002). Preoperative and postoperative UPDRS-III scores were recorded for 14 of 35 patients. The average UPDRS-III improvement was 50% (-29% to 85%) at 1 year. Simple programming parameters were used in 81% of patients. The lead was moved intraoperatively due to capsular effects with macrostimulation in 14 of 40 patients. There was no significant correlation between accuracy and improvement in UPDRS-III scores (p=0.65).

Discussion: Asleep implantation of deep brain stimulation has gained popularity with increasing visibility in targets due to advances in imaging. However, no one has been able to show a clear correlation between radiologic accuracy and clinical outcomes.1 We have found that often being within 2mm of the intended target still gives capsular effects with macrostimulation prompting moving the electrode to a more lateral or superficial location. We believe this leads to better outcomes with simple stimulation parameters minimizing side effects for the patient.

Conclusions: Globus pallidus internus stimulation often is limited by capsular side effects when programming. There is no significant correlation between accuracy and clinical outcomes; therefore, we believe physiologic confirmation with macrostimulation can minimize these side effects leading to improved clinical outcomes with simple stimulation parameters.

Objectives

1. Calculate vector error for electrodes.
2. Compare accuracy to clinical outcomes.
3. Provide supporting evidence for awake deep brain stimulation.

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Brain: Movement Disorders

149. INS19-0236

CAN NON-INVASIVE BRAIN STIMULATION ENHANCE DUAL-TASK PERFORMANCE IN PARKINSON'S DISEASE?

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Introduction: Parkinson's disease (PD) is a degenerative disease of the central nervous system. Motor dysfunction is a primary feature of PD, with postural instability, one of the key features that leads to an increased likelihood of falls. When asked to perform concurrent motor and cognitive tasks, (e.g. standing while counting numbers), postural control can deteriorate further. Transcranial Direct Current Stimulation (tDCS) can be used to safely modulate cortical excitability without serious adverse effects. It has been employed to promote executive function, attention and working memory in healthy older people and has shown potential benefits to people with PD.

The purpose of this study is to investigate the effects of tDCS on dual task performance in people with PD.

Materials/Methods: Three groups of participants (healthy young, healthy older people and people with PD) will complete the following tasks in a randomised order. Under both real and sham stimulation conditions participants will stand on stable and unstable surfaces on a force plate. Performance under the single task (quiet stance only) and dual task (quiet stance + serial subtraction task) conditions will be assessed on both surfaces prior, during and after stimulation. Sham condition will consist of 15s of stimulation at the beginning and the end of intervention period only.

Results: It is anticipated that when compared with sham tDCS, real tDCS will reduce the cost of secondary cognitive task on postural control. Participants will have greater enhancement of postural control on unstable surface (foam) when compared to the stable surface (firm). Furthermore, it is expected that when compared with healthy participants, people with PD will have greater benefits from non-invasive brain stimulation, and show greater improvements on both postural and cognitive performance after real tDCS.

Discussion: Discussion will not be included in this study protocol.

Conclusions: The efficacy of tDCS for improving cognitive performance and promoting balance in people with PD will be determined. The effects of current stimulation over left DLPFC on dual task in different populations will be ascertained.

Objectives: Use of tDCS may provide an effective and safe strategy for treatment of motor and cognitive dysfunction of people with PD. It will also provide better understanding of the relationship between cognition and balance in PD.

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150. INS19-0038

A STUDY ON NEUROMODULATION FOR OPTIMIZING SUBTHALAMIC-NUCLEI STIMULATING EFFECT OF VARIED FREQUENCY PARAMETERS TO ENHANCE THE GAIT WITH DUAL TASKING IN PARKINSON'S DISEASE

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Introduction: Gait disturbances and freezing-episodes are broad in advanced idiopathic Parkinson's disease (PD) and they worsen with dual (also multi) tasking. In PD, though, subthalamic-nuclei deep brain stimulation (STN-DBS) is an effective-restorative-therapeutic option for enhancing motor, freezing-of-gait (FoG) and other axial-symptoms, albeit, its impact on gait-disturbances is hazy. Studies [1] suggest that low frequencies can augment gait-parameters provided frequency-parameters (including stimulation-intensity and pulse-width) are changed.

Materials/Methods: 40Parkinson's post STN-DBS patients with gait-disturbances were included in the study. All patients were on constant neurostimulation-parameters and dopaminergic-medication for a month prior to assessment. Gait-parameters were analyzed during-medication 'on' and DBS 'on' state, at 4 classes-of-frequencies 180Hz,130Hz,90Hz, and at 60Hz and DBS 'off' medication 'on' state. Gait was analyzed using stand-walk-sit (SWS) test and freezing-of-gait (FoG) scales. Total elapsed-times, number of steps/freezing episodes were analyzed in SWS test. Effect of dual-tasking on gait was analyzed using FoG score. While analyzing-parameters at different-frequencies, Wilcoxon signed rank-test was employed.

Results: 40Parkinson's on neuromodulation were studied, out of which 29 were male. Average mean-age was 55.45+10.76 years. Mean-duration of disease at the onset was 13.13+6.41 years. Post-surgery mean-duration was 3.58+2.4 years. 38Parkinson's showed significant-improvement in gait at a single-frequency, which was singular for each patient while 2patients showed optimal-response at two frequencies. In SWS-test, 17patients (42.5%) had good-response at 180Hz, 6(15%) at 130Hz,14(46.7%) at 90Hz,5 (12.5%) at 60Hz. [Table 1] Total FoG-scores and sub-scores based on dual-task also improved at similar frequencies.

Discussion: Statistically-significant-improvement in all gait-parameters including dual-tasking at best-frequency in comparison to DBS 'off' and 130Hz, with $\chi 2 = 9.2857$ with 2 degree-of-freedom, highly-significant at 5% (*<0.0001)*. [Table 2] Optimal-frequency was independent of any demographic parameters, disease-severity or duration or other stimulation parameters [Fig 1]. There is a significant-effect of varying stimulation-frequency-parameters. The frequency-modulation certainly help PD patients with FoG and also axial-symptoms (particularly in case of bilateral STN-DBS).

Conclusions: Optimization of frequency-parameter-setting for each Parkinson can recover gait yet with a cognitive-load. High and low-frequencies may be of use and needs to be individualized. We also suggest that bilateral STN-stimulation enhances in case of the majority of axial-symptoms of Parkinson's and that a synergistic-result can be attained when DBS is used in concurrence with L-dopa.

Objectives: To compute the effect of varied frequency-parameter-settings of STN-DBS in Parkinson's gait without and with dual tasking.

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151. INS19-0039

MICROELECTRODE RECORDING ANALYSIS OF SUBTHALAMIC-NUCLEI DEEP BRAIN STIMULATON IN PARKINSON'S – A STUDY OF 46 PD PATIENTS ON NEUROMODULATION

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Introduction: Microelectrode-recording (MER) is a tool targets STN-neurons accurately in Parkinson's. 270patients have undergone-DBS at our NIMS tertiary-care hospital in South-India. Five Channel Lead-Point MER is done in all PDs. MER data of 46patients were analyzed.

Materials/Methods: Patients characteristics: Mean age was 58.1 +9.1 years, Mean disease-duration(8.8+3.64yrs), mean-UPDRS-score in 'off'/'on' state was ('52.7+10.6'/'13.4+5.0'). 5Channel-Medtronic LeadPoint MER is done in all PD-patients.

Results: Mean number of 5 multiple-channels in which STN-MER was detected right-side(hemisphere)=3.5+1.1, left-(side) hemisphere =3.6+1.04. The 92sides were computed and concordance-rate with the finer-signal and maximum-width of signal-recording were and combination were analyzed. Final-channel selected were Central in 39/92-42.3% (0.042), Anterior in 31/92-33.7%,Medial in 15/92-16.3%, Posterior in 4/92-4.3%, and Lateral in 3/92-3.2%. Concordance with the (chosen-track) highest-recording was seen in 58.7%, Mean-maximum length-of-recording was 5.3+1.3 mm, Maximum length-of-STN was in the chosen track in 48%, and Concordance with either highest-recording or maximum-length was noted in 64%. In 28patients, final-tract did not correspond either to the tract with highest-recording or maximum-width-of-MER. 13had central-tract, 8had anterior, 7had medial-tract as final-tract, Mean-length of MER-recording in these channels was 2.3+1.8mm.

Discussion: MER-confirms the presence-of-abnormal STN neurons. Effective MER-data can ease us to study behavior-of-disease, offers new therapies, and its prediction and control, but also in the early prognostic-diagnosis, regardless of the system-information, the symptom is only considered as the output. It increases our knowledge of the disorders behavior and disease-symptoms. MER data consider the involved structures in the symptoms appearance as well as the final-disease-symptoms. This can save us the time and cost of the researchers effectively and help them select appropriate treatment-mechanisms among all possible options.

Conclusions: 93.48% of patients showed STN-recording in the final-channel chosen. Absence of any recording from STN in the final-tract selected was noted in 6/92-6.52% (0.0652). Out of 6-patients, one-patient had no MER-recording in any of the five-channels and lead was placed in central-channel. 2patients had medial, 2anterior and 2central channels as their final tract. This was selected based on macrostimulation. In our study, we find that MER gives proof of correct-positioning-of-electrode, ensures accurate-detection of STN precincts its exact-coordinates in a more objective-way.

Objectives: To analyze microelectrode-recording (MER) with subthalamic-nuclei (STN) deep-brain-stimulation (DBS) in Parkinson's disease (PD)

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Brain: Movement Disorders

152. INS19-0372

ANALYSIS OF BILATERAL SUBTHALAMIC-NUECLEUS DEEP BRAIN STIMULATION (STN-DBS) THROUGH MICROELECTRODE RECORDING (MER) SIGNALS IN PARKINSON'S DISEASED PATIENTS

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Introduction: Numerous-scientists researched on open-loop-DBS-systems with intraoperative microelectrodes/presented their results towards subjective-analysis-clinically[1],[2]. However, not much of the work done on the prognostic-diagnosis of STN-neurons objectively, data-gathered during-stimulations of STNs with DBS microelectrode-recordings (MER). In this study intraoperative-MER was done with STN-DBS in 52advanced idiopathic Parkinson's disease (PD) patients prognostically. Parkinson's disease is a motor-infirmity progress-slowly involves problems-with-movement, affecting dopamineproducing-neurons accountable for body-movements. In PD, dopamineproducing nerves of the brain die-slowly. When dopamine-levels decrease, the symptoms of PD develop thence movement-frails. The exact cause-of-PD unclear, some risk-factors (environment, age, and genetics) have been identified. Genetics play a role, as do certain environmental-triggers such as the exposure-to-toxins.

Materials/Methods: Intraoperative microelectrode-recordings were acquired from 52advanced-idiopathic PD-patients underwent DBS in bilateral-STN and intra-operative LFP-recording while DBS on, at rest and during-movements. Images were reconstructed/visualized in three-dimensional-space for determining coordinates-of-contact. Resting-spectral-power and movement-related power-modulation of LFP-oscillations were estimated.

Results: STN-LFP activities-gathered-recorded at rest and its modulation-by-movement. Spatial-distribution of alpha-band-activity and modulation was significantly-different to that in beta-band. Also, there were significant-differences in the time-scale of movement-related-modulation across frequency-bands.

Discussion: The field-potentials acquired with DBS-electrodes in the STN are a rich-source-of-information that could prove-useful in better-refining surgical-targeting, contact-selection and DBS-therapy. The following study gives an interesting insight into pathophysiology if electrical stimulation. All this year's Dr Louis Benabid in his experiment stressed that continuous stimulation does not damage the membrane-cells. Hence DBS has no side effect. The above study-emphasizes that continuous-stimulation-reactivates cells and prevents-apoptosis. Hence it has potential-benefits of altering the disease-process. This has been observed-clinically/diagnostically in our patient population. Patients who underwent DBS had a longer-survival and better-quality-of-life(BQoL) compared to their counterparts who had medical-management in only.

Conclusions: This finding suggests that STN-electrophysiological signal-characteristics are sturdily-correlated to the extent of motor-behavior-improvement observed in STN-DBS. STN-LFP activities within specific frequency bands can be distinguished by spatial-topography and signature—pattern of movement-related-modulation.

Objectives: The long term clinical and/or diagnostic studies have so far botched to prove that high-frequency(*hf*) DBS-stimulations have been able to measure along the progress-of-disease. In MPTP treated monkeys *hf* stimulation of the STN could guard neurons in the substantia-nigra (SN) [2]. To test this hypothesis in PD-patients, we performed STN stimulations and data gathered with MER of STN-DBS and analyzed in Mat-lab and

framelink-software. The current study aimed to examine whether electrical stimulation could prevent apoptotic neuronal cell death during treatment.

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153. INS19-0201

CHARACTERIZING THE SUBTHALAMIC-NUCLEI DEEP BRAIN STIMULATION LOCAL FIELD POTENTIAL OSCILLATIONS IN PARKINSON'S DISEASE BY UING INTRAOPERATIVELY MICROELECTRODE RECORDING

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Introduction: There is a growing interest in the nature of local-field-potentials (LFP) behavior gathered from the microelectrode-recordings (MER) of subthalamic-nuclei (STN) with deep brain stimulations (DBS) of advanced idiopathic Parkinson's disease (PD) patients underwent DBS-stereotactic-functional-neurosurgery. This is energized by the data that oscillatory-activity in the beta-band-frequency is unduly synchronized and sturdy in these patients and that these link to lack-of-dopamine in basal-ganglia (BG) parallel-circuit. Hence, power of beta-activity is correlated with the motor-impairment in PDs and the changes in motoric-symptoms rigidity and Bradykinesia, etc. The origin of these activities in STN area has been explored using microelectrode-recording intra-operatively. We focus and explore the spatial-topography and movement-related-reactivity of spectral-features recorded directly from bilateral STN-DBS electrodes in 46 patients with advanced idiopathic Parkinson's disease.

Materials/Methods: Preoperative and intraoperative functional Magnetic Resonance Imaging (fMRI) were recorded from advanced idiopathic Parkinson's disease (PD) patients who underwent DBS in the STN-LFP acquisition with MER at rest and during cued-movements. Signatures were reconstructed and visualized in three dimensions using the effectiveness of lead point with DBS to establish the coordinates of contact. The resting spectral power and movement-related power modulation of LFP-oscillations were estimated.

Results: Results Both STN-LFP activities acquired - recorded at rest and its modulation by movement had focal maxima in the alpha (α) beta (β) and gamma (γ)-bands. The spatial-distribution of α-band activity and its modulation was significantly different due to that in β-band. Also, there were significant differences in the scale and timing of movement related modulation across frequency band.

Discussion: We showed that both subthalamic-nuclei-LFP activities gathered at rest and its modulation by movement have focal maxima in the β-band. The coordinates of these maxima communicate to STN. The image/signal was somewhat more complicated in α and γ-bands though. In the α-band, the peak-power at rest was extensively dispersed and extensive to include the zona-incerta bordering the dorsal-STN. However, upon movement-reactivity in this band became more focal. The converse was seen in the gamma-band, which was focal-at-rest, but became less clustered-during-movement, when reactivity extended to include the zona-incerta.

Conclusions: STN-LFP activities within specific-frequency-bands can be distinguished by spatial-topography and pattern-of-movement related-modulation. Significance-evaluation of the frequency, focality and pattern-movement related-modulation of STN-LFP discloses heterogeneity of neural-population-activity (NPA) in this area. Potentially this could be leveraged to intraoperative targeting finesse—skill and postoperative contact-choice (CC).

Objectives: This study aims to use the behavioral activities acquired from deep brain stimulation (DBS) microelectrode-recordings (MER) to address the focality and distinct nature of the STN-LFP activities at different frequencies.

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154. INS19-0412

EFFECTIVENESS OF LEAD-POINT WITH MICROELECTRODE SIGNAL RECORDING IN DETERMINING SUBTHALAMIC-NUCLEUS DEEP BRAIN STIMULATING ELECTRODE-IMPLANTATION IN PARKINSON'S DISEASE (MER SIGNAL ANALYSIS WITH STN-DBS IN PD)

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Introduction: Parkinson's disease (PD) or Parkinsonism is the long-term complex neurodegenerative disorder-of-brain that causes-tremors in elders, which is characterised by the convolution of four-classes of cardinal-motoric-symptoms (tremor, rigidity, Bradykinesia and postural-instability). Deep-brain-stimulation of bilateral-subthalamic-nucleus (DBS-STN) is an effective-therapy in patients with idiopathic-Parkinson's disease (PD). Accurate-targeting and implanting-microelectrodes are paramount-importance for optimal-results after STN-DBS. Stereotactic-assessment, intra-operative microelectrode-recording and intra-operative stimulation-effects have all been employed in targeting STN, albeit individual role-of-each-modality is still not-known.

Materials/Methods: 52subjects with PD were included in the study. Subjects with advanced PD of >5 years with good response to levodopa and H and Y score of less-than 4 with normal-cognition were eligible for surgery. Surgery was planned using a Cosmon-Roberts-Wells frame (CRW) frame which has a luminant MR localizer with MRI-protocol using Stereo-Calc Framelink-software with 5channels (Medtronic). Microelectrode-recording was carried out in all subjects below the 10mm STN. Final-tar-get-selection was based on the effects and side-effects of macrostimulation and confirmed by post op MRI.

Results: 52subjects with PD with their mean-age of 58.1±9.1years, mean-disease-duration of 8.8±3.64 years were-included. Prior-to-implanta-tion, mean-UPDRS-score in 'DBS-OFF' state was 52.7±10.6 and in 'DBS-ON' state was 13.4±5.0. STN-MER were detected in a mean of 3.5±1.1 chan-nels on right-side (RH:Right-Hemisphere) and 3.6±1.04 on left-side(LS:Left-Hemishpere). Final-channel selected were most commonly central seen in 42.3% followed by anterior in 33.7%. Concordance of final-track with the channel-having the highest-recording was58.7%, with the channel-show-ing-maximum depth-of-recording was48% and with either was64%. Absence-of-any-recording in the final-tract-chosen was seen in6.52%, in these subjects the tract was chosen based-on-stimulation-results. The depth-of-microelectrodes was identified by microelectrode-recording in75.6%.

Discussion: Parkinson disease quite often presents with a tremor, but in approximately one fourth of all patients it never develops at all. In patients who do display tremor, it often reduces in amplitude as the disease pro-gresses, with increasing bradykinesia (slowness of movement). Tremor in PD is a resting tremor made up of agonist antagonist activation tuned precisely.

Conclusions: Microelectrode-recording is useful to identify and confirm the tract in which DBS electrodes are implanted and is most useful in determining the depth-of-electrodes-placement but has to be taken in consideration with effects seen on macrostimulation.

Objectives: To study the effectiveness of microelectrode-recording in determining the final-tract for implanting DBS-electrode and correlation of

MER with the final-tract chosen during bilateral STN-DBS performed at a specialized centre in South India.

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155. INS19-0152

X-LINKED DYSTONIA-PARKINSONISM IS A RARE GENETIC ENDEMIC MOVEMENT DISORDER IN THE PHILIPPINES. BILATERAL DDBS OF THE INTERNAL GLOBUS PALLIDUM IN A COHORT STUDY IS PRESENTED

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Introduction: Generally, deep brain stimulation (DBS) of specific target areas is performed as a standard procedure for chronic movement disorders, predominant Parkinsonism or dystonia. X-linked Dystonia-Parkinsonism (XDP) is a rare endemic genetic movement disorder in the Philippines. Mostly, the disease starts with symptoms of dystonia and, over time, symptoms of Parkinsonism are seen. Invasive treatment with DBS of the Globus pallidum internum (GPi) is considered in the dystonic stadium if pharmacological therapy is inefficient. A prospective observational cohort of 16 patients including the postoperative follow-up course is presented.

Materials/Methods: DBS was offered to 16 male patients (age: 30-52 years) with severe dystonia. The procedure was performed in Germany and in general anaesthesia in 13 out of 16 patients. In 3 patients the clinical condition made it possible to perform surgery in local anaesthesia. In all patients a stereotactic 3D-MRI data set with gadolinium contrast was used to achieve stereotactic transformation. Bilateral target coordinates were calculated with respect to the mid-point of the intercommissural line: 20 mm lateral, 2 mm anterior and 2 mm inferior. Sequential microelectrode recordings were performed to identify the internal pallidum. Prior to implantation of the stimulation device a stereotactic MRI-scan was performed to check the lead position and rule out intracerebral complications.

Results: Bilateral GPi lead implantation was successfully performed in all patients and a stimulation device implanted. Malposition of two leads was detected by control MRI and replacement was performed. Immediate postoperative and during the follow-up course up to five years an improvement of the movement disorder and quality of life, measured with the BFM- or UPDRS-scores, were evaluated in all patients. Battery replacements were performed in 9 patients.

Discussion: Patient selection for DBS in XDP-syndrome is most important in cases refractory to pharmacological therapy. Indication for the procedure should be stated in the early dystonic stadium.

Conclusions: In patients with XDP bilateral DBS of the GPi is an effective procedure and may lead to an significant improvement of the dystonic symptoms and remarkable increase of quality of life.

Objectives

Bilateral DBS of the GPi in XDP-syndrome is safe and efficient.

In selected XDP-patients DBS should be offered even in the early stage of the disease.

Clinical follow-up examinations are recommended in experienced centers for functional neurosurgery.

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156. INS19-0386

DBS OF THE STN IS A STANDARD PROCEDURE TO IMPROVE SYMPTOMS IN PARKINSON´S DISEASE. PRELIMINARY DATA WITH EVALUATION OF BODY MASS FOLLOWING STN-DBS ARE PRESENTED.

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Introduction: Generally, deep brain stimulation (DBS) of specific target areas is performed as a standard procedure for chronic movement disorders, predominant Parkinson's disease (PD) or dystonia. The subthalamic nucleus (STN) is the standard target area for DBS in most patients with PD. Certain side effects of the therapeutic DBS are known, as dysphonia or dysarthria. Preliminary data of an ongoing prospective observational cohort with respect to the body mass are presented.

Materials/Methods: Bilateral DBS of the STN was performed in 7 patients with PD. Body mass and body mass index were evaluated at time of surgery and during the follow-up course after 3, 6, 12 months and thereafter.

Results: During the time course after DBS-surgery an increase in body mass and body mass index was detected in all patients. Three months after surgery and with active DBS a mean increase of 3.3 kg (d=0.69) and after six months of 3.9 kg (d=0.21) was measured. After 12 months body mass gain was 6.4 kg (d=0.72) and thereafter 6.1 kg (d=1.02).

Discussion: In this prospective case study of a small patient sample, a significant increase of body mass was detected in PD and bilateral DBS of the STN. Due to this ongoing trial one must await the final results. Different mechanisms for these findings need to be considered and discussed, like changes in eating behaviour, hormonal regulation and improvement of motor symptoms.

Conclusions: In the light of obesity and negative side effects of weight gain we recommend the information and mentoring of patients, including an adapted dietary therapy, in the follow-up course with STN-DBS.

Objectives

STN-DBS is a standard procedure for PD.

Body mass gain is a side effect of STN-DBS.

Information of the patients and dietary therapy is recommended.

References

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Poster Presentations - May 27 - May 30
Brain: Movement Disorders

157. INS19-0040

MOTOR EVOKED POTENTIALS RECORDED FROM SEGMENTED DBS LEADS: RELATIONSHIP OF DISTANCE TO THE CORTICOSPINAL TRACT

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Introduction: One adverse effect of deep brain stimulation (DBS) in the sub-thalamic nucleus (STN) is inadvertent stimulation of the corticospinal tract (CST) thus causing unwanted muscle contractions. Segmented leads are supposed to help alleviate this issue by focusing stimulation energy away from the CST. This study investigates the relationship of each segmented contact relative to the CST by the use of motor evoked potentials (MEPs).

Materials/Methods: MEPs from each DBS lead are recorded by using a short train stimulus at individual DBS contacts to activate the CST. Stimulus parameters are as follows: ISI=0.2 mSec, PW=500 uSec and amplitudes from 0.1 to 5 mA. The lowest threshold activation of individual muscles are noted for each lead. obicularis oris/occuli, deltoid, bicep/tricep, forearm flexor/extensor, APB/ADM, and FDI muscles were monitored. The specific lead used had three segmented contacts placed on the two middle rings of a 4 ring DBS lead. Correlation to the post-operative contacts used for therapeutic stimulation was then performed.

Results: 10 patients and 20 sides have been evaluated. There is a pattern of response with associated contacts (eg 2a,3a) having lower thresholds than other pairs. In some patients the "a" contacts correspond to the lowest threshold while in other patients it is the "b" or "c" contacts that correspond to the lowest threshold. In all but two patients there is a strong correlation between the associated contact pairs and the thresholds. Thresholds vary from 0.9 mA up through 4.8 mA. Each individual patient showed the lowest threshold in a specific muscle, but there was variation in the muscle with the lowest threshold in different patients.

Discussion: Modeling has shown that focused stimulation is possible from segmented DBS leads. To date there has been no physiologic study to prove focused stimulation of DBS leads can effect the threshold response to motor activity in the area surrounding the DBS lead, specifically the CST. The data presented in this study demonstrates equivocally that there is a physiologic focusing of the DBS stimulation field from the segmented leads.

Conclusions: Segmented DBS contacts do focus the stimulation energy away or towards different structures surrounding the STN. This focusing can allow for a better therapeutic outcome that when using a full ring stimulation.

Objectives

1. Discuss the activation of the CST MEPs using short train stimulation
2. Discuss the relationship of segmented contacts in relation to MEP activation
3. Discuss the anatomy of the STN area in relation to physiologic stimulation

Results:

References

None.

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158. INS19-0231

SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION MODULATES EVOKED RESONANT NEURAL ACTIVITY

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Introduction: Subthalamic nucleus deep brain stimulation (STN-DBS) is an established treatment for Parkinson's disease; however, a robust biomarker is needed to optimise therapy. Recently, we reported that STN-DBS evokes a neural response resembling a decaying oscillation[1], termed evoked resonant neural activity (ERNA). Crucially, ERNA is localisable to the most efficacious stimulation sites and has much greater amplitude than spontaneous neural activity. However, whether ERNA is modulated by therapeutic STN-DBS and its relationship to spontaneous activity are unknown.

Materials/Methods: ERNA and spontaneous neural activity were recorded from STN-DBS electrodes implanted in 10 Parkinson's disease subjects (19 STN) undergoing awake implantation surgery. Three stimuli were applied: 1) clinical 130Hz DBS at 0.67, 1, 1.5, 2.25, and 3.38mA, 2) bursts of 10 pulses per second (130Hz, 3.38mA), and 3) 2.25mA 20Hz DBS. Limb bradykinesia and rigidity were assessed using the Unified Parkinson's Disease Rating Scale. ERNA frequency and amplitude were compared to spontaneous beta (13-30Hz) and high frequency oscillation (200-400Hz) measures derived from spectral estimates. Statistical analyses were performed using Friedman Repeated Measures ANOVA on Ranks and Wilcoxon Signed Rank tests.

Results: ERNA frequency and amplitude varied with clinical 130Hz stimulation level ($p < 0.001$ respectively). These effects coincided with improvement of clinical signs ($p < 0.001$) and spontaneous beta band suppression ($p < 0.001$), and were observed to wash out after clinical DBS was stopped. ERNA modulation also coincided with changes in spontaneous high frequency oscillations, with the frequency of both decreasing to around 260Hz - twice the stimulation rate - with therapy. Non-therapeutic 20Hz DBS elicited ERNA, but did not modulate it over time (frequency: $p = 0.7$; amplitude: $p = 0.34$).

Discussion: These results suggest that STN-DBS modulates the high-frequency oscillatory state of the underlying neural circuits, as reflected in ERNA. Both the frequency and amplitude of ERNA contain clinically relevant information that could potentially be used to optimise therapy. The relationship between ERNA and high frequency oscillations suggests they could arise from the same or associated circuits and be mechanistically related.

Conclusions: ERNA is modulated by therapeutic STN-DBS and has potential as a dynamic feedback signal for optimising therapy and providing insight into brain function.

Objectives

1. To investigate the effects of STN-DBS on ERNA
2. To investigate the relationship between ERNA and spontaneous neural activity
3. To provide insight into the mechanisms of action of DBS

References

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Brain: Movement Disorders

159. INS19-0197

ACCURACY OF DEEP BRAIN STIMULATION (DBS) ELECTRODE PLACEMENT USING O-ARM INTRAOPERATIVE COMPUTED TOMOGRAPHY (ICT) DURING IMAGE-GUIDED, FRAME-BASED, ASLEEP DBS FOR MOVEMENT DISORDERS

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Introduction: Intraoperative imaging allows near-real-time assessment of stereotactic accuracy during implantation of deep brain stimulation (DBS) electrodes. We investigated the accuracy of DBS electrode placement using intraoperative O-arm iCT during image-guided, asleep DBS.

Materials/Methods: stereotactic accuracy for asleep DBS was investigated in 23 patients (14 patients with PD and 9 with dystonia). Electrode implant locations were the globus pallidus internus (GPI) and subthalamic nucleus (STN) in 16 and 7 patients, respectively.

Results: Forty-two electrodes in 23 patients were examined. The average radial error was 1.28 $\pm$ 0.27 (n=42). There was no difference in radial error and Euclidean error between the STN and GPI (1.25 $\pm$ 0.57 and 1.29 $\pm$ 0.28; radial error, 1.58 $\pm$ 0.44 and 1.48 $\pm$ 0.64; Euclidean error, $p>0.05$). The coronal approach angle to STN and the distance to the lateral ventricle were significantly greater in GPI targeting ($p<0.05$). Although no difference was evident in the radial and Euclidean errors in the coronal approach angle and distance to lateral ventricle between the right and left STN, there was tendency in medial placement in the right STN asleep DBS (1.529 $\pm$ 0.36 and 0.93 $\pm$ 0.63, respectively. $p=0.057$). In the both sides of the GPI implantation, no difference in the radial and Euclidean errors, coronal angle, distance to lateral ventricle was found ($p>0.05$).

The motor and disability scales of the Burke-Fahn-Marsden dystonia rating scale (BFMDRS) improved 65.2% and 58.6%, respectively, at postoperative 6 month. At a median follow-up of 6 months, there was a mean improvement in off-medication, motor part of Unified Parkinson's Disease Rating Scale (UPDRS III) of 27.7 points equivalent to a mean improvement of 52% ($p<0.001$).

Discussion: Our initial results indicate the procedure of image-guided, asleep DBS is safe, with accuracy comparable to those using microelectrode recording under local anesthesia.

Conclusions: Image-guided, asleep DBS can lead to substantial improvement in motor disability of movement disorders with low morbidity.

Objectives: To investigate the accuracy of DBS electrode placement using intraoperative O-arm iCT during image-guided, asleep DBS.

References

Manuscript in surmission

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160. INS19-0110

DIRECT DBS: A PROSPECTIVE, MULTICENTER, DOUBLE-BLINDED CLINICAL STUDY OF DIRECTIONAL DBS ENERGY CONSUMPTION AND ESTIMATED BATTERY LONGEVITY FOR CHRONIC STIMULATION

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Introduction: Deep Brain Stimulation (DBS) of the subthalamic nucleus (STN) has proven to be effective in treating motor symptoms in Parkinson's Disease (PD) patients. Recently, directional leads have been introduced aiming for more selective stimulation of therapeutically beneficial anatomy via segmented electrodes (i.e., contacts). Segmented electrodes are smaller than conventional ring electrodes, thus having generally higher impedances. Because energy consumption of DBS systems is directly proportional to the stimulation's amplitude and electrode-tissue interface's impedance, the higher impedance of segmental electrodes might lead to greater energy consumption and compromise longevity of non-rechargeable DBS systems. For this report, we characterized energy consumption and battery longevity of a primary cell, multiple current-source directional DBS system.

Materials/Methods: DIRECT-DBS (ClinicalTrials.gov Identifier: NCT02835274) is a prospective, randomized, multi-center, double-blind study with a crossover design. Twelve study participants were implanted with a DBS system (Vercise Cartesia, Boston Scientific) with bilateral directional leads connected to a primary cell pulse generator with independent current sources. Within the study framework, stimulation settings were tested acutely (~15 minutes) and chronically (≥3 weeks). Clinical outcomes, as well as impedance and stimulation settings data from each DBS system have been collected at four study related programming visits in periods of 3-5 weeks and 6-8 months.

Results: Compared to baseline, UPDRS III scores for stimulation settings tested in periods of 3-5 weeks (n=12) and 6-8 months (n=8) improved in average 29.3% and 32.7%, respectively. In 92.2% of stimulation settings applied chronically, more than one electrode was activated. Mean current amplitude for segmented and ring electrodes was 0.76mA and 1.56mA, respectively, whereas their mean impedance was 2.8kΩ and 1.4kΩ, respectively. Stimulation settings led to energy consumption averaging 0.47mW, resulting in an average estimated longevity of 5 years for the analyzed pulse generator.

Discussion: The results show that effective DBS therapy was achieved and that in most cases, several electrodes on the same lead were activated, which generally did not compromise the estimated pulse generator's longevity.

Conclusions: Directional DBS can provide effective therapy for PD patients, where single cell pulse generators have a theoretical lifespan of several years. Larger patient cohorts are needed to confirm these results.

Objectives

1. To report energy consumption using a primary cell, multiple current-source directional DBS system.
2. To report battery longevity using a primary cell, multiple current-source directional DBS system.
3. To report impedance and stimulation settings using a primary cell, multiple current-source directional DBS system.

References

NA

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Brain: Movement Disorders

161. INS19-0114

DIRECT DBS: A PROSPECTIVE, MULTI-CENTER, DOUBLE-BLINDED CLINICAL STUDY OF A DIRECTIONAL DEEP BRAIN STIMULATION LEAD -- THERAPEUTIC WINDOWS WITH DIRECTIONAL STIMULATION

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Introduction: Deep Brain Stimulation (DBS) of the subthalamic nucleus (STN) is effective in treating motor symptoms of Parkinson's Disease (PD). Historically, DBS systems have delivered stimulation using cylindrical electrodes, which may stimulate neurons around the circumference of the lead. Recently introduced directional DBS leads aim for more selective stimulation of therapeutically beneficial anatomy via segmented electrodes. For this report, we evaluated whether acute changes in stimulation direction influences the therapeutic window.

Materials/Methods: DIRECT-DBS (ClinicalTrials.gov Identifier: NCT02835274) is a prospective, randomized, multicenter, double-blind study with a crossover design. Twelve study participants were implanted with a DBS system (Vercise Cartesia, Boston Scientific) with bilateral directional leads connected to a primary cell pulse generator with independent current sources. Stimulation settings were tested acutely (~15 minutes) and chronically (≥ 3 weeks). In one visit, various horizontal stimulation directions (orthogonal to lead) were tested unilaterally and acutely at the longitudinal level (along lead) that rendered highest side effect amplitude thresholds. Stimulation directions were tested in random order, first in 90° increments, and then 30° increments. At each setting, therapeutic window was calculated based on minimum amplitude giving full rigidity control and minimum amplitude eliciting a limiting side effect.

Results: In 6 of 12 study subjects, activation of two or more adjacent segmented electrodes led to the highest side effect thresholds. Moreover, in 5 of these subjects, adjacent electrodes were unequally activated (i.e., different current). Collected data shows significant differences in therapeutic windows in response to changes of 90° and 30° in the stimulation's direction (0.60mA and 0.41mA on average, respectively).

Discussion: Use of a directional DBS system that incorporates independent sources for each of the lead's electrodes, the directed stimulation field could be rotated in angles of 90° and 30°. Differences in therapeutic window where found even for small steps of 30°. Moreover, results show that when two or more segmented electrodes needed to be activated to achieve high side effect amplitude thresholds, the blinded examiner decided mostly for an unequal current distribution through these contacts.

Conclusions: Based on results, directional stimulation might help widening the therapeutic windows by rotating the stimulation field activating more than one segmented electrode.

Objectives

1. To evaluate whether acute changes in stimulation direction influence therapeutic window.
2. To assess stimulation settings tested acutely (~15 minutes) and chronically (≥3 weeks).
3. To investigate various horizontal stimulation directions (orthogonal to lead) tested unilaterally and acutely at longitudinal level (along lead) that renders highest side-effect amplitude thresholds.

References

NA

Poster Presentations - May 27 - May 30
Brain: Movement Disorders

162. INS19-0115

DIRECT DBS: A PROSPECTIVE, MULTI-CENTER, DOUBLE-BLINDED CLINICAL STUDY OF DIRECTIONAL DEEP BRAIN STIMULATION -- INTER-VISIT IMPEDANCES AND THEIR POSSIBLE EFFECTS ON DELIVERED THERAPEUTIC CURRENT

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Introduction: Deep Brain Stimulation (DBS) of the subthalamic nucleus (STN) is effective in treating motor symptoms in Parkinson's Disease (PD). Recently introduced directional leads aim for more selective stimulation of therapeutically beneficial anatomy via segmented electrodes. Activation of tissue depends on the current amplitude applied, which depends on impedance of the tissue-contact interface. It has been suggested that electrode impedances change over time. Therefore, stimulation accuracy, precision and stability of a directional DBS system might be compromised by changes of individual tissue-contact interface impedances or differences between electrodes. We characterized impedances of a primary cell, multiple current-source directional DBS system used for chronic stimulation. Furthermore, the delivered current for single source DBS systems under the encountered impedance conditions was theoretically modelled.

Materials/Methods: DIRECT-DBS (ClinicalTrials.gov Identifier: NCT02835274) is a prospective, randomized, multi-center, double-blind study with a crossover design. Twelve study participants were implanted with a DBS system (Vercise Cartesia, Boston Scientific) with bilateral directional leads connected to a primary cell pulse generator with independent current sources. Within the study framework, stimulation settings were tested acutely (~15 minutes) and chronically (≥3 weeks). Impedance and stimulation settings data from each DBS system have been collected at each of the seven study related programming visits in 1-day, 3-5 weeks and 6-8 months periods.

Results: Compared to ring electrodes, segmented electrodes have in average higher impedances (1323Ω and 2993Ω, respectively). Substantial impedance changes over time for ring, and especially segmented electrodes (7.6% and 10% average impedance change, respectively) were observed. Based on our theoretical model, these would result in deviations from the intended delivered current of up to 25% and 77.9%, respectively, if single source current and voltage-controlled DBS systems would be used.

Discussion: The results show that for directional leads, segmented electrodes have higher impedances than conventional ring electrodes, and that impedances change over time. Theoretically, these impedance differences and changes can provoke deviations from the intended delivered current for single source systems.

Conclusions: Based on obtained results, the effect of impedance differences and changes of directional leads electrodes could be theoretically minimized if each electrode has its own independent current source. The clinical relevance of these findings must be further investigated.

Objectives

1. To characterize impedances of a primary cell, multiple current-source directional DBS system under chronic stimulation conditions.
2. To investigate stimulation settings when tested acutely (~15 minutes) and chronically (≥3 weeks).
3. To theoretically model delivered current for single-source DBS systems under the encountered impedance conditions.

References

NA

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163. INS19-0397

BETA POWER IN THE PRIMARY SENSORIMOTOR CORTEX CORRELATES WITH BRADYKINESIA IN PARKINSONIAN PATIENTS TREATED WITH BILATERAL SUBTHALAMIC DEEP BRAIN STIMULATION

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Introduction: Beta power in the subthalamic nucleus (STN) was shown to be associated with different kinetic states in Parkinson's disease; the prospects rose of utilizing it as a biomarker for closed-loop deep brain stimulation (DBS). We hypothesize that suitable symptom-related biomarkers could also be originated from the primary sensorimotor cortex for a closed-loop system.

Materials/Methods: We recruited 20 Parkinsonian patients treated with bilateral STN stimulation. In the first part of the measurements, bradykinesia of the most affected hand was measured with the Kinesia motion sensor system (Great Lakes NeuroTechnologies) in medication withdrawal; and four levels of contralateral stimulation (1: OFF, 2-4: decreasing symptoms to ON state) was individually selected. In the second part of the work, we performed 64-channel electroencephalography (EEG) measurement simultaneously with motion detection during a resting state, finger tapping, hand grasping tasks and pronation-supination of the arm, with the aforementioned four levels of stimulation settings. We stimulated the usually used contacts during the whole study, and the ipsilateral stimulation remained ON and unchanged. We compared spectral power at the low (13-20Hz) and high (21-30Hz) beta frequency bands at the sensorimotor cortical region both contralateral and ipsilateral to the examined hand using a beamformer algorithm called the Dynamic Imaging of Coherent Sources. The 2 minutes long EEG segments were pre-processed by in-house algorithms[1] for cleaning the data from DBS artifacts. We performed line-noise removal; eye blinks and muscle artifacts were eliminated using ICA analyses. Speed, amplitude and rhythm of hand movements were calculated from the 3D motion data of the gyroscope.

The Medical Research Council in Hungary provided ethical approval. (080958/2015/OTIG).

The support of Medtronic Inc. for this project is gratefully acknowledged.

Results: High and low-frequency beta power measured contralateral to the hand movement significantly ($p<0.05$) correlated with the speed of motion in each task. Amplitude, rhythm, and decrement of these parameters showed individual variability. In the stimulated ipsilateral hemisphere, beta power remained consistently low.

Discussion: Our study confirms that STN-DBS decreases the beta power in the ipsilateral primary sensorimotor cortex. Beta power decrease evoked by different stimulation settings represents the improvement of the contralateral movement speed.

Conclusions: Beta power in the sensorimotor cortex could be a potential biomarker for closed-loop DBS.

Objectives

Cortical beta power represents the level of bradykinesia

Biomarker can be detected by EEG

STN stimulation reduces cortical beta activity

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164. INS19-0124

STN—DBS HAVE BEEN IMPROVING SLEEP CONDITION OF PARKINSON'S DISEASE PATIENTS

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Introduction: Parkinson's disease (PD) exhibits a sleep disorder as non-motor symptoms in many cases. The prevalence of sleep disorders is 42-98%. Sleep disorders would decrease an arousal level and would give an adverse effect on motor symptoms. We would believe that the successful of the treatment for PD is important to improve the sleep disorders. We have experienced that STN-DBS in PD could improve Motor symptoms and Sleep disorders at the same time. We investigated whether STN-DBS improved sleep disorders in PD.

Materials/Methods: We studied ten patients undergoing STN-DBS at our facility. We observed the results of Polysomnography before and after STN- DBS.

Results: Total Sleep Time (TST) extended in nine cases. Nocturnal awaking time (NAT) shortened in eight cases. Arousal index (AI) improved in seven patients. Sleep efficiency was improved in nine cases. STN-DBS could increase N I and II of sleep stage.

Discussion: Electrical stimulation of STN-DBS can be transmitted to the PPN (Pedunculopontine nucleus), and activate the dorsal pathway of ascending reticular activating system. Therefore, this secondary stimulation for PPN could improve the balance of sleep and arousal. STN-DBS have decreased REM sleep and increased non-REM sleep in our study. We believe that improvement of sleep quality could modulate the motor function.

Conclusions: STN-DBS could improve the sleep condition of PD patients

Objectives

STN-DBS improve sleep disorder of Parkinson's disease.

STN-DBS can increase non-REM sleep.

We suspect that secondary electrical stimulation of PPN through STN may improve the sleep disorder.

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165. INS19-0283

DOES ENERGY CONSUMPTION CHANGE AFTER SWITCHING OR REPLACING DEEP BRAIN STIMULATION SYSTEMS?

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Introduction: In this ongoing study, we observed energy consumption between a group that had a CV to CV – (Group I), a group with CC systems (Group II) and a group that had a CV to CC (Group III) in patients implanted with a deep brain stimulation (DBS) system at 5 years post implant. We also analysed data taken from those with a CC system (Group IV) and a replacement of a CV into a CV driven system at 7 years follow-up.

Materials/Methods: We assume a constant impedance for calculations as changes are only seen in the acute period after implantation and to avoid mistakes by using impedance measurement from different systems [1]. At 5 and 7 years we compare groups starting with the formula presented by Koss et al [2] and applying Ohm's Law.

Results: Thus far we analysed total energy delivered by deriving electrophysiological parameters from a total of 31 patients (CV: 19, CC: 6 and CV to CC: 6) at the 5-year mark. Data was collected for both electrodes to ensure we didn't encounter statistical differences between both sides. The total energy delivered by the systems didn't show any statistical differences between Group I, Group II and Group III ($p = 0.567$) at the 5 years. Comparing results in 13 subjects for Groups IIII ($n = 5$) and Group IV ($n = 8$) corresponding at 7 years follow-up we didn't find any statistical differences either ($p = 0.739$).

Discussion: Energy consumption is an important factor to plan for replacements ahead of full battery drainage in order to avoid possible rebound effects. Nowadays it is possible to mix systems and the question raised whether this would change or not energy consumption and thus IPG battery duration, which then would result in device management-, clinical- and health economic consequences.

Conclusions: No significant differences in energy consumption were observed between de groups of patients that had a CV to CC replacement and those that remained with a similar energy driven system.

Objectives

a) Discuss long-term energy consumption of CC and CV DBS.

b) Identify differences/similarities between CC and CV DBS.

c) Identify mixed systems' energy consumption.

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Brain: Movement Disorders

166. INS19-0295

CONSTANT CURRENT AND CONSTANT VOLTAGE DEEP BRAIN STIMULATION: LONG-TERM CLINICAL EFFICACY

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Introduction: Compare the long-term efficacy of constant voltage (CV) versus constant current (CC) deep brain stimulation (DBS) systems in Parkinson's Disease (PD).

Materials/Methods: We are analysing clinical data of patients with advanced PD and severe motor symptoms, eligible for DBS between 2005 and March 2019. Only patients with a long-term follow-up period of at least 4 years are included. Apart from demographic characteristics, we collect data using the Unified Parkinson's Disease Rating Scale (UPDRS), Hoehn and Yahr, ON and OFF hours, hours of dyskinesia and dystonia, and levodopa intake, at baseline and post-implant.

Results: Preliminary data evaluation showed the following outcomes, but will be updated for the congress: 44 PD patients (male: 19 (43.2%), female: 25 (56.8%) implanted with either a DBS CV (n = 28, 63.6%) or a CC system (n = 16, 36.4%). Implant target was as follows: 41 (93.2%) subthalamic, 2 (4.5%) nucleus pallidus and 1 (2.3%) ventral intermediate (VIM) nucleus of the thalamus. Average disease duration before implantation was 11.6 years. Intergroup analysis didn't show statistically significant differences in absolute values between both groups for the higher mentioned variables. nor in outcomes compared to baseline on the higher mentioned data collections. Analysis of changes of the variables in % compared to baseline, revealed only a statistically significant difference in UPDRS III On in favour of CC.

Discussion: Long-term (4 years) comparative clinical efficacy differences weren't observed in this study, apart from % increase in UPDRS III On, which didn't translate in an increase in HY outcome. This confirms previous reports, proving both waveforms can be safely and effectively applied in DBS [1,2].

Conclusions: Long-term follow-up of 4-years comparative analysis of patients implanted with a CC- or a CV DBS system revealed clinical outcomes are independent of the type of system applied.

Objectives

a) Discuss long-term clinical outcomes of CC and CV DBS.
b) Identify differences/similarities between CC and CV DBS.
c) Discuss impedance relevance in DBS.

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167. INS19-0342

14 YEARS OF EXPERIENCE WITH MIXED IMPLANTS FOR MOVEMENT DISORDERS

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Introduction: A recent study showed replacing constant voltage (CV) with constant current (CC) IPGs is a safe and effective procedure [1]. In another study looking at CC versus CV in Parkinson's disease (PD) patients no significant differences could be identified for equivalent motor efficacy, nor for non-motor evaluations [2]. We compare the long-term clinical efficacy and management of CV and CC DBS IPGs over the course of 14 years.

Materials/Methods: In this ongoing observational study (since 2005), to date 103 PD patients who received DBS therapy are monitored. We compare clinical efficacy using different measures, as well as postoperative clinical management. Data was collected at 3, 6, 12, 24, 36 and 48 months.

Results: Preliminary results revealed, 205 leads (102 bilateral, 1 unilateral) were implanted in 103 PD patients (male: 57, female: 46). Average age at implantation was 61.4 years. 41 patients were implanted with a CV device and 62 with a CC IPG. Average disease duration before implantation was 11.3 years. At 3M we saw a significant difference in the increment of % On hours in the CV group ($p < 0.05$). Independent sample tests didn't reveal significant differences for clinical outcomes at 1, 2, 3 and 4 years between both groups. A statistical difference ($p < 0.05$) was observed at 24M for number of visits, number of visits per month. No differences in changing parameters could be found, although a trend was seen ($p = 0.07$) at 6 months in accumulated and accumulated per month changes, which disappeared afterwards.

Discussion: Long-term clinical efficacy differences weren't observed in this study confirming previous reports, proving both waveforms can be safely and effectively applied in DBS [3,4]. Programming and parameter changing didn't reveal much of a difference. The fact that patients in the CC group were younger, may be explained by a change in attitude and actitude toward interventional therapy for movement disorders in our unit, thus including younger patients and patients with less evolved disease states.

Conclusions: Long-term follow-up comparative analysis of patients implanted with a CC- or a CV DBS system revealed clinical outcomes are independent of the type of system applied.

Objectives

a) Discuss long-term clinical outcomes of CC and CV DBS.
b) Discuss postoperative therapy management.
c) Discuss safety and effectiveness of DBS.

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168. INS19-0434

TECHNICAL ACCURACY OF FRAMELESS DBS WITH INTRAOPERATIVE 2D/3D CONE-BEAM CT WITHOUT FIDUCIAL-MARKERS

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Introduction: The aim of our study was to investigate the accuracy of targeting using intraoperative cone-beam CT during frameless deep brain stimulation (DBS) surgery without bone fiducials

Materials/Methods: Twelve patients with advance Parkinson Disease (PD) were implanted bilaterally with 24 deep brain stimulation leads using a modified frameless stereotaxy methods. Implantation of the leads were performed using a frameless Nexframe system without the use of skull fiducial and coregistration of the system in an intraoperative O-arm2 intraoperative imaging system acquired volumetric studies. Preoperative MRI based plan were compared with post-procedure intraoperative location of the lead on O-arm 2 acquired volumetric images. All implanted leads euclidean localization error (vector error, VE) was calculated by the root mean square sum formula: [x2 + y2 + z2]1/2 the relative standard deviation, as well the error of each side

Results: The mean euclidean localization error for all 24 leads was 2.09mm +/- 0.71, whether the mean VE for the right sided implanted leads was 2.31mm +/- 0.47 and for the left sided implants 1.87mm +/- 0.86.

Discussion: The accuracy of this new framless method when compared with previous using bone fiducials or frame based doesn't differ significantly.

Conclusions: The new described approach in our early experience suggest advantages in term of patient compliance and decreased operating time. This features impact positively outcome and procedural satisfaction in patient with advance PD.

Objectives

Improve surgical technique

Improve comfort for patients

Application of new technology

References

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169. INS19-0126

DBS IN DYSTONIA

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Introduction: Dystonia is a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures or both.

• Treatment can be classified into oral medications, chemodenervation, and surgical intervention.

• In 2003, deep brain stimulation (DBS) received a humanitarian exemption by the FDA for use in dystonia

• Since this time, it has emerged as first-line surgical therapy for dystonia.

Materials/Methods: We have reported the results of our Dystonia cases (15) who underwent DBS and discuss the problems during and after DBS

•Patients were assessed preoperatively and at defined follow-up examinations postoperatively, using the Burke-Fahn-Marsden dystonia rating scale (BFMDRS) for movement and functional disability assessment.

Results: •12 bilateral GPI •3 unilateral GPI •

9 cases under general anesthesia •6 awake •No intraoperatif complication

•Generally 3 microelectrodes driven •Center is the most common finale electrode location (10 case) 3 case Anterior 2 case Lateral

Discussion: Microelectrode recording is still safe and most reliable methods for DBS cases.

Conclusions: •Dystonia complex problem for surgery •

Gpi is still the best target for dystonia We believe that new target points and stimulation parameters will be tried in the near future in the treatment of dystonia and that combined treatment options will increase

Objectives

Microelectrode recording is still safe and most reliable methods for DBS cases.

Best Surgical Treatment of dystonia is DBS still.

Gpoi is the most common target for dystonia

References

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170. INS19-0053

DYNAMIC CHANGE OF THE CUTANEOUS SILENT PERIOD IN PATIENTS WITH PARKINSON DISEASE

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Introduction: The cutaneous silent period (CuSP) is defined as a transient brief pause of voluntary muscle contraction triggered by electrical stimulation of a cutaneous nerve, and it may be one of the defense mechanisms using spinal interneuron inhibition of alpha motoneurons (α-MN). Several studies have been conducted comparing the CuSP of patients with Parkinson disease (PD) to normal controls, or evaluating the effect of medication on the CuSP in PD. Because the dynamic change of the CuSP in individual cases has, however, yet to be clarified, we evaluated whether the CuSP could be validated as an electrophysiological indicator during PD therapy.

Materials/Methods: The CuSP was recorded in 8 PD patients before and after the intake of anti-PD medication as a pre-DBS (deep brain stimulation) examination (4 cases), as well as in the "on" and 30 minutes after the "off" states of subthalamic nucleus DBS during hospitalization for the change of the implantable pulse generator (4 cases). The CuSP was elicited by electrical stimulation of the index finger with a strength of 2, 4, and 15 times the sensory threshold (ST), and was recorded from the abductor pollicis brevis muscle. The correlation between changes in the CuSP and in clinical symptoms was evaluated.

Results: The CuSP became clearly identifiable after the intake of anti-PD medication in cases with improvement of hand rigidity. Moderate appearance of dyskinesia after medication did not influence the appearance of the CuSP, but the CuSP tended to be suppressed or disappeared in one case showing severe drug-induced dyskinesia. When the DBS switch was turned off, the CuSP became unclear in one case with deterioration of hand rigidity, and in one case without change of clinical symptoms. In cases with preserved CuSP in both conditions of low (2 or 4 ST) and high (15 ST) strength stimulations, the change of the CuSP by the "on/off" state of medication or DBS appears to be simple to detect under low strength stimuli.

Discussion: The CuSP tended to become apparent when the rigidity or dyskinesia subsided through medication and/or DBS. Low strength stimulation might be a sensitive parameter to capture the change of inhibitory activity to spinalα-MN in PD.

Conclusions: The CuSP could be a useful electrophysiological indicator to objectively evaluate the patient's clinical state during PD therapy.

Objectives: Electrophysiological indicator, Parkinson disease, Spinal inhibitory interneuron

References

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171. INS19-0340

AN EXPERIENCE ANALYSIS OF USING UNI- AND MULTITRACK MICRORECORDING IN DEEP BRAIN STIMULATION

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Introduction: Determine the precision of the therapeutic target calculation and the relation of the precision of the different processes. Secondly, determine the utility of multitrack use and the number of unnecessary processes in deep brain stimulation (DBS), as well as comparing the safety profile of both techniques.

Materials/Methods: Select the three simultaneous trajectories, with apart from the central tract the remaining two depending on the most frequently realized corrections during the period a unique trajectory is realized. We applied also a qualitative evaluation of the accuracy. Deviation with respect to the AC-PC line were calculated in the form of the angle in the XY – YZ and XZ planes. Furthermore, we also did sub-analyses to compare both techniques with other variables, and looked at possible safety issues linked to either one.

Results: 139 patients with an average age of 60.7 years (range: 19-79) were included in the study augmenting to 273 trajectories (right: 135, 49.5%/left: 138, 50.5%). Further baseline demographics can be found in table 2. Average number of tracts per target (and side) was found to be 2.98 $\pm$ 1.279. The distribution of the trajectories can be found in table 3. Average AC-PC distance was 24.5 $\pm$ 1.06mm. Average deviation of the target in the XY plane was 1.40 $\pm$ 1.25°, 4.3 $\pm$ 2.83° in YZ and 1.29 $\pm$ 1.06°in the XZ plane. In 99 cases (36.3%) the BQES-DIA (Barcelona Qualitative Evaluation Scale of DBS Implantation Accuracy) was found to be 0, in 102 cases (37.4%) 1, in 29 cases (10.6%) it was 2 and in 43 cases (15.7%) it was 3. No differences were observed in complication rates peri- and postoperative: haemorrhages and infections.

Discussion: We found that in 73.6% of the trajectories that the initial calculation was optimal when using multitrack system and in 84.2% the marker didn't need to be moved. As for clinical outcomes related to the technique there were, apart from the HY On for the first three months, no significant differences at 12 months were observed between both techniques.

Conclusions: In our series, the multi-trajectory technique permitted us to implant with clinical efficacy, 82.5% of the cases without additional trajectories. 88.5% of the implants didn't need a repositioning of the stereotactic marker when applying multitrack. No adverse event differences were observed between applying either techniques.

Objectives

a) Look at effectiveness of different MER techniques.
b) Look at clinical outcomes related to MER.
c) Identify safety profile of MER techniques.

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172. INS19-0095

OUTCOMES OF A PROSPECTIVE, MULTICENTER INTERNATIONAL REGISTRY OF DEEP BRAIN STIMULATION FOR PARKINSON'S DISEASE

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Introduction: The effectiveness of Deep Brain Stimulation (DBS) for reducing motor complications of Parkinson's disease (PD) has been substantiated by randomized controlled trials (Schuepbach et al.,2013). Additionally, motor improvement is sustained for up to 10 years (Deuschl et al. 2013). Large patient data registries may facilitate insights regarding real world, clinical use of DBS. Furthermore, no registry database currently exists for a multiple-source, constant current DBS system. The objective this report is to describe collected outcomes from a large scale registry of a Deep Brain Stimulation (DBS) system capable of Multiple Independent Current Source Control (MICC) in the management of symptoms of levodopa-responsive PD.

Materials/Methods: The Vercise DBS Registry (ClinicalTrials.gov Identifier: NCT02071134) is a prospective, on-label, multi-center, international registry sponsored by Boston Scientific Corporation. The Vercise DBS system (Boston Scientific) is a multiple-source, constant-current system. Subjects were followed up to 3 years post-implantation where their overall improvement in quality of life and PD motor symptoms was evaluated. Clinical endpoints evaluated at baseline and during study follow included Unified Parkinson's disease Rating Scale (UPDRS), MDS-UPDRS, Parkinson's disease Questionnaire (PDQ-39), and Global Impression of Change.

Results: To date, 290 patients have been enrolled in the registry and this report will provide an overview of the data collected so far from implanted patients within this cohort. At 1-year post-implant, 36.2% improvement in MDS-UPDRS III scores (stim on/meds off) compared with baseline was reported. This improvement in motor function was supported by an improvement in quality of life as assessed by PDQ39 Summary Index (5.6 point improvement, n =146) at 1 year. Roughly 90% of patients and clinicians reported improvement as compared with Baseline.

Discussion: This DBS registry represents the first comprehensive, large scale collection of real-world outcomes and evaluation of safety and effectiveness of a multiple-source, constant-current DBS system.

Conclusions: This DBS registry represents the first comprehensive, large scale collection of real-world outcomes and evaluation of safety and effectiveness of a multiple-source, constant-current DBS system.

Objectives

The aim of this large scale registry is to collect outcomes associated with a Deep Brain Stimulation (DBS) system capable of Multiple Independent Current Source Control (MICC) in the management of symptoms of levodopa-responsive PD, specifically the following:

1) Unified Parkinson's disease Rating Scale (UPDRS)
2) MDS-UPDRS
3) Parkinson's disease Questionnaire (PDQ-39)
4) Global Impression of Change

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173. INS19-0100

REAL-WORLD OUTCOMES USING A NOVEL DIRECTIONAL LEAD FROM A DEEP BRAIN STIMULATION REGISTRY FOR PARKINSON'S DISEASE

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Introduction: Deep Brain Stimulation (DBS) systems have historically used ring-shaped electrodes that produce stimulation fields with limited control over field shape and volume of tissue activated. Directional current steering may permit a more personalized DBS approach with respect to individualized shape and pattern of electrical field and corresponding volume of tissue activated. Here we report initial real-world outcomes using a directional lead with a DBS system capable of multiple independent current source control (MICC) for use in managing symptoms of levodopa-responsive Parkinson's disease (PD).

Materials/Methods: The Vercise DBS Registry (ClinicalTrials.gov Identifier: NCT02071134) is a prospective, on-label, multi-center, international registry sponsored by Boston Scientific Corporation. Subjects in this cohort were implanted with a directional lead included as part of a multiple-source, constant-current directional DBS system (Vercise Cartesia, Boston Scientific). Subjects were followed up to 3 years post-implantation where their overall improvement in quality of life and PD motor symptoms was evaluated. Clinical endpoints evaluated at baseline and during study follow included Unified Parkinson's disease Rating Scale (UPDRS), MDS-UPDRS, Parkinson's disease Questionnaire (PDQ-39), and Global Impression of Change. Adverse events are also collected.

Results: A total of over 100 subjects have been enrolled in this specific cohort. A 6.1 $\pm$ 12.11 (n = 73) point improvement was noted in the PDQ-39 Summary Index at the 6-month interval compared with Baseline and this improvement continued up to 1-year post-implant. Subjects, clinicians, and caregivers reported over 90% improvement in the symptoms at 6 months post-lead implant as compared with Baseline and this was maintained up to the 12-month interval. Additional data is to be presented.

Discussion: Enabling fractionalization of current using MICC can permit the application of a well-defined, shaped, electrical field. Use of a directional lead allows for the steering of current in horizontal directions by combining segmented leads and MICC.

Conclusions: This DBS registry represents the first comprehensive, large scale collection of real-world outcomes and evaluation of safety and effectiveness of a multiple-source, constant-current directional DBS system.

Objectives: The aim of this large scale registry is to collect outcomes associated with a directional Deep Brain Stimulation (DBS) system capable of Multiple Independent Current Source Control (MICC) in the management of symptoms of levodopa-responsive PD, specifically the following: 1) Unified Parkinson's disease Rating Scale (UPDRS) 2) MDS-UPDRS 3) Parkinson's disease Questionnaire (PDQ-39) 4) Global Impression of Change

References

NA

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174. INS19-0144

ESTABLISHING THE OPTIMUM TDCS APPLICATION ON DUAL TASK GAIT PERFORMANCE -EXPLORATION OF PEOPLE WITH CHRONIC STROKE

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Introduction: Gait dysfunction influences activities of daily living in individuals with stroke. Although gait dysfunction can be improved by exercise, some dysfunction still exists especially challenged by a secondary task during walking (dual task gait) in stroke patients even at the chronic stage. Such dysfunction may be due to impaired modulation from central nervous system. Transcranial direct current stimulation (tDCS) is noninvasive and is possibly able to alter and modulate cortical excitation. However, the best montage for gait performance in patients with chronic stroke needs to be established.

Materials/Methods: This was a randomized controlled trial with pre- and post-measurement study. A total of 44 participants meeting the criteria were recruited and assigned to one of the four groups: anodal stimulation to affected hemisphere, cathodal stimulation to unaffected hemisphere, bi-hemisphere stimulation, and sham control. Participants in each group received 20 mins of tDCS stimulation, except the sham group. Gait performance was measured by GaitRite system, including speed, cadence, stride time, and stride length during single walking, cognitive dual task walking, and motor dual task walking conditions. Two-way analysis of variance with repeated measures with Tukey post hoc test was used to determine the effects of different interventions on the outcomes. Statistical significance was set at $p<.05$.

Results: Participants increased the gait speed and decreased the stride time of both legs during motor and cognitive dual task walking after receiving 20-min of cathodal stimulation to the unaffected hemisphere. Furthermore, the decreased stride time of both legs during motor dual task walking were significantly more than the anodal stimulation and the sham control. Participants received bi-hemisphere stimulation increased the gait speed during cognitive dual task walking.

Discussion: tDCS is able to improve gait performance in patients with chronic stroke. Participants received cathodal tDCS is effective in improving motor and cognitive dual task walking.

Conclusions: According to our results, cathodal tDCS to the unaffected hemisphere seems to be more effective in improving dual task walking performance in people with chronic stroke.

Objectives: The purpose of this study is to establish the optimum stimulation by comparing the effect of different tDCS electrode placement (anodal, cathodal, bilateral, or sham) on gait performance and cortical activities in individuals with chronic stroke.

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175. INS19-0426

DOUBLE-TARGET DBS VIA SAME LEAD FOR ESSENTIAL TREMOR (PSA AND VIM STIMULATED BY SAME LEAD - DIFFERENT CONTACTS)

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Introduction: Essential tremor (ET), is one of the most common neurological disorders, affecting up to 5% of individuals aged over 65 years (1). Surgical treatment strategies such as Thalamotomy or Bilateral Thalamic Vim Deep Brain Stimulation (DBS) are reserved for selected patients who are unable to adequately respond to medical therapy (2). In such cases the side effects and tolerance development may limit the treatment effect. More recently the posterior subthalamic area (PSA) has been suggested as an alternative target for treatment of ET. We aimed to bilateral implantation of 8-contact leads aligning the Vim and the PSA in the same trajectory, to compare the stimulation effects and the side effects on same patient for two different targets.

Materials/Methods: A 52 years old woman diagnosed with ET 6 years ago, admitted to our outpatient clinic with severe action tremor. Bilateral DBS surgery under local anesthesia with the guidance of micro-electrode recording was performed. eight contact leads (Boston Scientific Inc., Valencia, CA) was preferred to achieve the double target stimulation. The double targeting of Vim and the PSA on the same alignment was achieved by the stereotactic planning software (Integra Radionics). After the lead implantation the Macrostimulation was performed and all contacts was evaluated for the efficiency and the side effects one by one.

Results: The stimulator was activated one week later. The tremor was evaluated by the TremorSense mobile software Evident improvement was obtained both on Vim and PSA contacts, but the PSA and double stimulation was found superior on control of tremor (Tremor scores were found as 96 when stimulation off, 15 when Vim stimulation on, 5 when PSA stimulation on and 3 when Vim+PSA stimulation on.)

Discussion: Although the Vim target have a satisfactory results in ET the PSA target have better results with less side effects. The uses of the both targets could have more advantages in deal with severe tremor.

Conclusions: Eight contact leads has great advantage for double targeting in ET, PSA can more effective then Vim and we can achieve better result by double target stimulation.

Objectives

PSA and Vim can stimulate with same electrode.
Eight contact lead has great advantages in double target.
PSA more effective than Vim on ET.

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176. INS19-0429

INVESTIGATING THE EFFECT OF STN-DBS ON VOICE QUALITY

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Introduction: Deep brain stimulation (DBS) is a standard surgical treatment method which is generally applied to subthalamic nucleus in Parkinson's patients in cases where medical treatment is insufficient in treating the motor symptoms (4). It is known that Subthalamic Nucleus Deep brain stimulation (STN DBS) treats many motor symptoms. However, the results of studies on speech and voice vary. The aim of the study is analyzing the effect of STN-DBS on the characteristics of voice.

Materials/Methods: A total of 12 patients, (8 male - 4 female) with an age average of 58.8 $\pm$ 9.6, who have been applied DBS surgery on STN included in the study. The voice recordings of the patients have been done prior to surgery and 6 months after the surgery. The evaluation of voice has been carried out through the instrumental method. The patients' voice recordings of the /a/, /e/, /i/, /o/ vowels have been done (Picture1). The obtained recordings were evaluated by the Praat program and the effects on jitter, shimmer, fundamental frequency (F0) and noise harmonic rate (NHR) were analyzed.

Results: Numerical values of F0 of all female participants have been decreased for all of the vowels postoperatively. In the females; jhitter and fraction parameters were found to be significantly different (0.056 and 0.017, perspectively) for the vowel /e/. In addition, p values in the shimmer for vowels /e,i/ were thought to be clinically significant (0.087, 0.079 and 0.076) respectively. All these changes in second measurements were found to indicate worsening vocal quality after the DBS in females. In males, there is not any significant difference observed between two measures in any of the parameters of any vowels.

Discussion: DBS is an accepted therapy on PD but its effects on voice is remains controversial. Different studies have different results.

Conclusions: The present study indicates that voice quality deteriates after DBS stimulation; which is more prominent in females.

Objectives

STN-DBS has an effect on voice quality.

Voice quality could be deteriorated after STN-DBS stimulation.

The deterioration is more obvious In females.

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Poster Presentations - May 27 - May 30
Brain: Movement Disorders

177. INS19-0433

DOES SUBTHALAMIC NUCLEUS DEEP BRAIN STIMULATION EFFECT THE STATIC BALANCE AT DIFFERENT FREQUENCIES?

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Introduction: Balance and gait disorders are the major source of motor disabilities in different terms of Parkinson's disease (PD) (1). With the development of science; subthalamic nucleus deep brain stimulation (STN-DBS) become a surgical intervention aimed at ameliorating the effects of symptoms associated with PD. The present study aimed at investigating the effects of bilateral STN-DBS at different stimulation frequencies on static balance scores.

Materials/Methods: Twenty patients diagnosed with idiopathic PD who underwent STN-DBS surgery (15 male, 5 female) were recruited for the study. The balance assessments of the patients were performed by the Techno Body Rehabilitation System at four different frequencies including 230, 130, 90, and 60 Hz and off-stimulation. 15 min were allowed for habituation to the new stimulator setting prior to testing, to clearly see the effects of each frequency. The tests were performed on the stability easy platform, using the test mode stabilometry test in an instable position. In stabiliometric assessment with eye-opened and eye-closed bipedal and monopedal parameters (Ellipse area, perimeter, front/back and mediolateral standard deviation) during 30 seconds for static balances.

Results: There was no difference between the results of static balance tests at any frequency ($p>0.05$). stabilometric perimeter and left foot perimeter elips area results were significantly better in female than male ($p<0.05$).

Discussion: Although DBS is known to be effective on motor symptoms of Parkinson's Disease [2], its effects on balance remains controversial.

Conclusions: Static balance is important for falling risk and daily living activities. Unlike some studies in literature, this study shows STN-DBS didn't effect the static balance negatively.

Objectives

STN-DBS didn't effect the balance negatively.

There is no any differences in term of static balance on different frequencies.

STN-DBS doesn't have negative effect on daily living activities in term of static postural balance.

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Poster Presentations - May 27 - May 30
Brain: Psychiatric Disorders

178. INS19-0307

TARGETING THE HUMAN NUCLEUS ACCUMBENS TO MODULATE LOSS OF CONTROL

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Introduction: Loss of control (LOC) is pervasive in several brain disorders. Improved neurological understanding has propelled our first-in-human, feasibility trial of on-demand, responsive neurostimulation (RNS) of the nucleus accumbens (NAc) for LOC over eating. We had previously pioneered RNS of the NAc shell (NAcSh) in mice guided by delta-band power fluctuations that predict such impulsive behavior. The NAcSh has monosynaptic connections to the lateral hypothalamus (LH), Brodmann's area 25 (BA25), insula, hippocampus, and amygdala, which are critically involved in feeding, impulse control, and motivated behavior. Although this supports the NAcSh as the RNS target for LOC, this subregion is undetectable on conventional human MRI. Hereby, we use tractography to leverage these well-described connections to define the target for our clinical trial.

Materials/Methods: Following previous work using whole-brain tractography to subdivide the NAc, we used diffusion MRI (dMRI) data from 40 healthy subjects to assess whether we can use probabilistic tractography to define the NAc subregion with biased connections to the LH, BA25, insula, hippocampus, and amygdala. Every NAc voxel was used as seeds, and each region of interest (ROI) as targets. Two NAc subregions with similar streamline probability for each ROI were generated using k-means.

Results: The feasibility of using dMRI probabilistic tractography to target known NAc connections was demonstrated. Ventromedial and dorsolateral subregions were visualized within the human NAc according to its streamline probability to either the LH, BA25, insula, hippocampus or amygdala. The presumed NAcSh (ventromedial) subregion presented higher streamline probability to these ROIs. The individual NAc subregions were averaged and reproduced an MRI atlas of the human NAc.

Discussion: We have applied advanced dMRI techniques to target specific neural connections within the NAc to treat LOC in humans. These known connections confirmed our previously defined NAc subdivision, consistent with histochemically-defined NAc core and shell. Our connection-based target could then be load on clinical software for stereotactic planning. We are further working on validating these connectivity findings within the human NAc using brain-clearing 3D histology.

Conclusions: Probabilistic tractography defined the presumed NAcSh as the target for our trial of RNS for LOC over eating. This represents a paradigm shift in the treatment of severe pathological mental states.

Objectives: To leverage known NAc connections, to perform a circuitry-based NAc segmentation, and to identify the RNS target for LOC over eating.

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Poster Presentations - May 27 - May 30
Brain: Psychiatric Disorders

179. INS19-0285

COMBINING COGNITIVE MODIFICATION BIAS INTERVENTION WITH TRANSCRANIAL DIRECT CURRENT STIMULATION INCREASES CRAVING FOR FOOD

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Introduction: Active bilateral tDCS over the Dorsolateral Prefrontal Cortex (DLPFC) has already been shown to decrease craving for food. From a cognitive standpoint, it is thought that craving for unhealthy/addictive food is reinforced by an implicit cognitive biased process. The objective of this experiment was to test if active bilateral tDCS combined with an approach avoidance task for chocolate (CBM) was effective in reducing chocolate craving on implicit (i.e. implicit association task - IAT) and explicit measures (visual analogue scale – VAS).

Materials/Methods: Fifty one-college healthy and normal weight range (BMI >18.5 and <25) volunteers (38 females; mean age: 22.12 $\pm$ 3.38) were enrolled. Participants were randomized to receive CBM training based on the Approach Avoidance task along with either Sham, Right anodal-Left cathodal (RALC), or Left anodal-Right cathodal (LARC) tDCS (2mA; 20 min) to the DLPFC.

Results: Participants receiving CBM + LARC tDCS explicitly self-reported more craving for chocolate than those receiving RALC tDCS ($p = .023$). This effect was also observed on the implicit measure [$F(2,46) = 4.168$, $p = .022$]. Also, LARC tDCS + CMB significantly increased the implicit preference for chocolate when compared to both RALC ($p=0.009$) and Sham tDCS ($p=0.034$).

Discussion: Increase in chocolate craving, induced by the combination of CBM and LARC tDCS, may be the result of the temporal and spatial summation of several underlying cognitive processes. The right cathode may have decreased the activity on the PFC with the corresponding increase in approach behaviour(1). The anode over the left PFC confirms facilitation effects during cue-induced craving(2).

Conclusions: Previous studies showed that RALC tDCS over PFC were able to effectively decrease craving for food (3). However, we did not replicate those effects, suggesting, on the contrary, that LARC tDCS can actually increase preference for chocolate. This result is compatible with recent models of brain laterality, with a left/right dissociations for cue craving/approach behaviour.

Objectives

Understand:

1. Brain mechanisms associated with food craving
2. The role of cognitive modification bias in food craving
3. The effects of tDCS in food craving

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Poster Presentations - May 27 - May 30
Brain: Psychiatric Disorders

180. INS19-0305

DEEP BRAIN STIMULATION FOR TOURETTE'S SYNDROME: FROM SUICIDAL TO THRIVING

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Introduction: Deep brain stimulation (DBS) has been commercially available for treatment of movement disorders since the 1980s, and its efficacy has been well established. Here we present application of DBS for malignant Tourette's syndrome.

Materials/Methods: A 15-year-old boy diagnosed Tourette's at age 10 persisted in having suicidal ideation and severe motor tics resulting in diffuse myelopathy. He required use of a wheelchair and had constant urinary dribbling. Given his progressive weakness, an appeal to the hospital's institutional review board for a humanitarian device off-label use of DBS was granted. The bilateral anteromedial globus pallidus interna (Gpi) were selected as targets. He underwent an awake procedure with microelectrode recording.

Results: During left microelectrode macrostimulation, the patient reported amelioration of his tic urge at 5 mm above target at 2 volts with no adverse effects. The same phenomenon was appreciated on lead macrostimulation. On the right side, the patient again reported complete resolution of symptoms with stimulation at 2 volts. Since undergoing programming, the patient has reported a 75% improvement in his tic urgency and obsessive-compulsive behaviors with persistent benefit after four years. Though he had dropped out of high school prior to surgery, he has now been able to complete his GED. He endorses complete resolution of his suicidal ideation. He is able to walk independently again, although he still has some intermittent urinary dribbling.

Discussion: Multiple targets for DBS, including the Gpi, anterior cingulate gyrus, thalamus, and cerebellum, have been described for Tourette's with varying degrees of success.(1,2,3,5,6) Anteromedial Gpi was selected for this case considering the patient's progressive myelopathy, and subsequently additional studies have suggested that Gpi is the preferred target for Tourette's.(7) A previous study demonstrated improvement with Gpi DBS in a similar scenario but presented only short-term follow-up.(4)

Conclusions: Anteromedial Gpi DBS has proven effective over four-year-follow-up in our patient with malignant Tourette's syndrome. More patients ought to be evaluated, but clinicians should be aware of the potential therapy for appropriate patients.

Objectives

-Identify applications for DBS beyond movement disorders
-Identify candidates for neuromodulation with Tourette's
-Discuss possible targets for neuromodulation of Tourette's

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Poster Presentations - May 27 - May 30
Brain: Psychiatric Disorders

181. INS19-0035

ELECTROPHYSIOLOGICAL AND IMAGING EVIDENCE OF SUSTAINED INHIBITION IN LIMBIC AND FRONTAL NETWORKS FOLLOWING DEEP BRAIN STIMULATION FOR TREATMENT-REFRACTORY OBSESSIVE COMPULSIVE DISORDER

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Introduction: Obsessive-compulsive disorder (OCD) is a neuropsychiatric disorder that arises from a complex interaction of environmental and genetic factors. Despite numerous pharmacological and behavioral interventions, approximately 10 % of patients remain refractory. High-frequency deep brain stimulation (HF-DBS) has shown promising results for treatment-refractory OCD. We report the follow-up result of up to 6 years of 4 treatment-refractory OCD patients treated by HF-DBS.

Materials/Methods: The patients underwent microelectrode (MER)-guided HF-DBS implantation in single institution. Targets of stimulation were the anterior limb of the internal capsule (ALIC) in two cases, and the nucleus accumbens (NAc) in the remaining cohort. The clinical profiles were quantified by the Yale-Brown obsessive-compulsive scale (Y-BOCS).

Results: Highly significant reductions in Y-BOCS scores were obtained from all patients during the follow-up period. A greater that 90 % reduction in Y-BOCS, observed in the most successful case, was achieved with NAc HF-DBS. Y-BOCS scores in the other patients consistently achieved over 50 % reductions in OCD symptoms. FDG-PET imaging indicated post-surgical reductions in metabolism, in not only targeted limbic networks, but also other frontal cortical and subcortical regions, suggesting that large-scale network modulation and inhibitions are associated with functional recovery in OCD.

Discussion: HF-DBS for OCD shows favorable outcome in terms of YBOCS reduction from (50–93) %. The therapeutic mechanism of HF-DBS for OCD is related to a reduction of synaptic hyperconnectivity identified with FDG-PET, with an increase in striatal dopamine and improvement of reward processing. In our experience, HF-DBS for treatment-refractory OCD has shown adequate effect on clinical symptoms, and acceptable safety. HF-DBS may be an effective treatment for refractory OCD.

Conclusions: This study demonstrates that HF-DBS targeted to the ALIC and NAc is a safe and effective method for ameliorating intractable, treatment-refractory OCD symptoms. The NAc appeared to be the superior target for symptom reduction, and local inhibition of NAc activity and reduced frontal metabolism are key therapeutic indications.

Objectives

HF-DBS targeted to the ALIC and NAc is a safe and effective method for ameliorating intractable, treatment-refractory OCD symptoms.

The NAc appeared to be the superior target for symptom reduction, and local inhibition of NAc activity and reduced frontal metabolism are key therapeutic indications.

Large-scale network modulation and inhibitions are associated with functional recovery in OCD.

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Poster Presentations - May 27 - May 30
Brain: Psychiatric Disorders

182. INS19-0131

EFFECT OF LONG PULSE WIDTH STIMULATION AND ADD-ON COGNITIVE THERAPY IN SUBCALLOSAL CINGULATE DEEP BRAIN STIMULATION FOR TREATMENT RESISTANT DEPRESSION

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Introduction: Stimulation adjustment is required to optimize the clinical outcome of deep brain stimulation (DBS) for treatment resistant depression (TRD), but controlled data on optimal stimulation parameters are limited. We assessed the efficacy and safety of subcallosal cingulate (SCC) DBS for TRD using either long pulse width (LPW) or short pulse width (SPW) stimulation and add-on cognitive behavioral therapy (CBT).

Materials/Methods: This was a double blind randomized controlled parallel and cross over study. Electrodes were implanted bilaterally in the SCC in 22 patients with TRD. Patients were then randomized to receive either LPW or SPW stimulation in the first 6 months. Keeping the frequency (130 Hz) constant, pulse width was increased in LPW group and voltage was increased in SPW group, if the response was inadequate. ≥50% reduction in HRSD from baseline was considered as response and achieving a score of 7 was considered as remission. Non-responders from each group at 6 months were crossed over to other stimulation for additional 6 months. Responders at 6 months and responders and non-responders at 12 months received 12 weeks of CBT.

Results: Both LPW and SPW groups showed significant reduction in HRSD sores at 6 months ($p < 0.001$) but there was no difference between groups in symptom scores ($p=0.61$). In cross over groups there was no significant decrease in HRSD scores within and between groups. Remission (HDRS ≤7) rates were greater in LPW group at 6 months (30%) and cross over to LPW group at 12 months (20%), than SPW group at 6 months (8%) and cross over to SPW group at 12 months (0%). Relapse rates in LPW responders at 12 months (20 %) were lower than in SPW responders (40%). Adverse effects were comparable. The addition of CBT showed improvement in negative attitudes but not in depressive symptoms

Discussion: Both LPW and SPW stimulation are equally effective in relieving depressive symptoms. The clinical response appears stronger with LPW stimulation.

Conclusions: Stimulation algorithm needs to be flexible allowing both pulse width and amplitude adjustments for optimization. Add-on CBT may have a role in the prevention of relapses.

Objectives

1. To learn the efficacy and safety of SCC-DBS in TRD
2. To learn the role of long pulse width adjustments in optimization of SCC-DBS outcome for TRD.
3. To learn whether add-on CBT would improve SCC-DBS outcomes in TRD.

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Poster Presentations - May 27 - May 30
Brain: Psychiatric Disorders

183. INS19-0327

EFFECTS OF CRANIAL ELECTROTHERAPY STIMULATION WITH NOVEL IN-EAR ELECTRODES ON ANXIETY AND RESTING STATE BRAIN ACTIVITY: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

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Introduction: Transcranial alternating current stimulation including Cranial Electrotherapy Stimulation (CES) is a promising non-invasive brain stimulation technique. The miniaturization of CES devices and the possibility of linking them with IT devices make it easy and convenient to improve the degree of symptoms at home. Thus, we aimed to examine the effectiveness of CES with novel in-ear electrodes for anxiety and resting state brain activity.

Materials/Methods: This study was a 3-week, randomized, double-blind, active-controlled design. 69 preclinical subjects who experienced daily stress participated in the study. The device provides alternating current with a frequency of 10 Hz and an intensity of 500μA, linked with smartphone recording treatment logs. Stimulation electrodes were placed resembling the in-ear headphone locations. At baseline, participants are randomly assigned to active and sham groups and each participant was required to treat themselves daily for 50 minutes. In each group, the effectiveness of the device was assessed by changes in anxiety, depression, executive function, and resting state EEG at the end of week 3. All participants signed the informed consent. The study was approved by the IRB of the hospital.

Results: Repeated ANOVA revealed that active group showed a significant improvement in state anxiety after 3 weeks of application (F=4.505, p=.039). However, we found no significant between-group differences in the changes for depression. In the WCST Category Completed, the active group showed improvement at trend level compared with sham group (F=3.694, p=.061). In the quantitative EEG analysis, absolute power for delta (F=6.888, p=.011) and theta (F=4.426, p=.041) band was significantly reduced in active group compared to sham group. In addition, regarding resting EEG coherence, which reflects brain connectivity, the active group exhibited significantly greater frontal EEG coherence increases than the sham group.

Discussion: These results suggest that CES with in-ear electrodes may alleviate state anxiety and has the potential to improve but not be sure of executive function. In particular, CES reduces slow oscillations in brain and increases brain functional connectivity in the frontal region, possibly contributing to emotional regulation and cognitive control.

Conclusions: The study demonstrated the effectiveness of CES with novel in-ear electrodes on relieving anxiety and modulating brain oscillation.

Objectives

Understand neuromodulation technique of CES with novel in-ear electrodes

Learn possible solutions in treating anxiety with non-invasive brain stimulation techniques

Learn challenges in development of novel non-invasive brain stimulation devices

References

Cranial electrotherapy stimulation and transcranial pulsed current stimulation: A computer based high-resolution modeling study. NeuroImage 65 (2013) 280–2

Figure 1 (A). Cranial electrotherapy stimulation (CES) device with novel in-ear electrodes, linked with smartphone for recording treatment logs

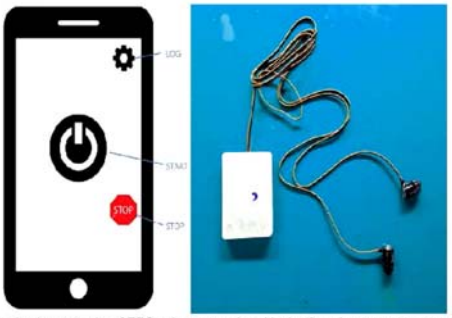
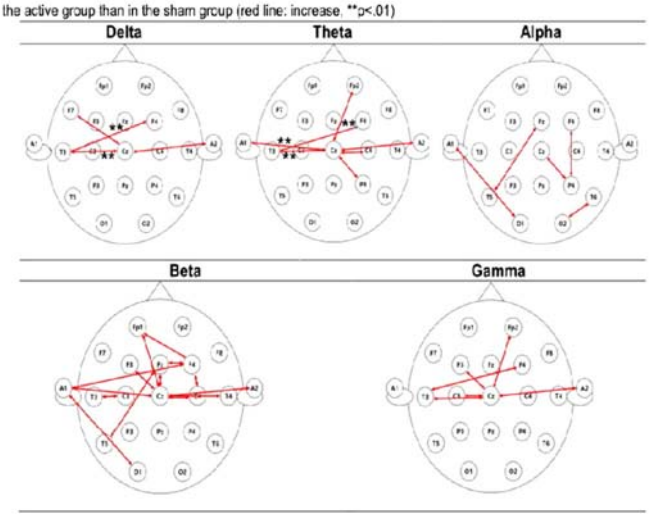


Figure 1 (B). Summarized topography of EEG coherence pairs with significantly greater increases ($p<0.05$) in the active group than in the sham group (red line: increase. **$p<.01$)



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Brain: Psychiatric Disorders

184. INS19-0147

SUPRESSION OF PERIICTAL PSYCHOTIC EPISODES DURING LONG TERM VAGUS NERVE STIMULATION FOR DRUG RESISTANT EPILEPSY

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Introduction: In a minority of patients, periictal psychotic episodes (PPE) can be a side-effect resulting from vagus nerve stimulation (VNS) in drug resistant epilepsy (DRE) patients [1–3]. The objective of this study was to investigate if long-term VNS can suppress PPE.

Materials/Methods: We included all 48 patients treated with VNS during a period from 2006-2016, with a minimum follow-up of 1 year and diagnosed with DRE. Comprehensive presurgical evaluation included: prolonged video-EEG, MRI imaging, neuropsychological and psychiatric evaluation and FDG-PET imaging.

Results: Of the 48 patients, only 4 patients (8.3%) presented with a prior history of PPE. Patient demographics and clinical characteristics can be found in table 1. 2 patients (50%) had undergone previous resective epilepsy surgery. All patients reached >75% seizure reduction and 2 (50%) stopped suffering status or cluster seizures. 3 patients (75%) showed seizure characteristics changes post-implantation (table 2). No patients without PPE prior to implantation suffered psychosis after VNS implantation. All patients with prior PPE, both ictal psychosis (IP) and post-ictal psychosis (PIP) resolved entirely using VNS. Average time to PPE suppression: 8.25 months (range: 6-15 M) (table 3). Pre-VNS FDG-PET results taken from one patient revealed bilateral superior parietal lobe hypo-metabolism and hyper-metabolism in the mesial frontal areas, anterior insulas, and left caudate nucleus (fig. 1). Post-VNS FDG-PET revealed a normalization of the involved areas (fig. 2)

Discussion: Psychosis is considered by some to be an exclusion criteria for epilepsy surgery [4], although more recent studies have shown improvements in PPE [5,6].

Conclusions: We have shown that long term VNS therapy for patients with DRE and a comorbidity of PPE, can achieve an antipsychotic effect, apart from seizure reduction.

Objectives

a) VNS may suppress PPE over time.

b) FDG-PET: different brain structures responsible for PPE.

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Poster Presentations - May 27 - May 30
Brain: Psychiatric Disorders

185. INS19-0217

REPEATED TRANSCRANIAL DIRECT CURRENT STIMULATION OVER THE PREFRONTAL CORTEX AS ADD-ON TREATMENT IN COCAINE ADDICTION: AN ECOLOGICAL MOMENTARY ASSESSMENT STUDY

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Introduction: Repeated transcranial Direct Current Stimulation (tDCS) over the dorsolateral prefrontal cortex (DLPFC) has been shown to decrease craving in various substance use disorders, and seemed to reduce relapse rates in alcohol addiction. The few studies that have explored tDCS in cocaine addiction found that tDCS may reduce craving, but little is known about the effects of tDCS on relapse rates. The current study explored whether repeated sessions of tDCS over the DLPFC as add-on treatment could affect relapse to cocaine use for three months. In addition, measures of cognitive control were taken into account to get a better understanding of the working mechanism.

Materials/Methods: The current study had a between subject, double-blind, randomized, sham-controlled design (https://clinicaltrials.gov/ct2/show/NCT03025321). Recently abstinent cocaine addicted patients were randomly allocated to either active tDCS (n = 29) or sham tDCS (n = 27) two-times daily for five consecutive days. The primary outcome was number of relapse days after three months, as measured by mobile Ecological momentary assessments (EMA) and verified by urine screens. In addition, they kept track of their craving and affect with EMA. Before and after the intervention week, and at three months follow-up participants performed computerised tasks to measure cognitive control.

Results: All participants for the current study are included, and data collection for the follow-up stage will be completed in March 2019. It is expected that relapse rates for the active tDCS group will be lower compared to sham tDCS. We expect the effect of tDCS on relapse rates to be modulated by craving and cognitive control.

Discussion: A recent study found that repeated tDCS had no effect on relapse in Crack-Cocaine Users (Klauss et al., 2018). If our hypotheses are confirmed, further research is needed to determine the feasibility of tDCS as add-on treatment in cocaine addiction.

Conclusions: Conclusions will be drawn after the data collection has been completed.

Objectives

Future studies need to investigate which modulatory variables can influence the efficacy of repeated tDCS. The use of EMA is recommended to test the efficacy of innovative treatments in addiction research, since it overcomes important issues that are encountered with retrospective self-reports (Jones et al., 2018).

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Poster Presentations - May 27 - May 30
Brain: Psychiatric Disorders

186. INS19-0106

DEEP BRAIN STIMULATION IN PATIENTS WITH ANOREXIA NERVOSA. PRELIMINARY RESULTS OF THE CLINICA TRIAL NCT03168893

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Introduction: Anorexia Nervosa (AN) is a heteregenous disease with high incidence of psychiatric comorbidity that can direct the course of the AN. Subgenual cingulate (SGC) and nucleus accumbens (Nacc) are two key points in the neurobiology of the AN. Patients with AN are being included in a clinical trial where deep brain stimulation (DBS) is performed in the SGC or in the Nacc. The main objective is to assess safety and efficacy. Secondary objectives are to assess the relationship between the response to DBS and clinical /radiological (DTI: difussion tensor image) variables

Materials/Methods: Patients with severe or extreme, chronic and refractory AN have been included to treat with bilateral DBS. Patients with mood disorders were assigned to SGC stimulation; patients with obsessive compulsive disorder or obsessive personality traits were assigned to Nacc stimulation. The evaluation is on a monthly follow-up basis for 1 year. The evaluation implies: weight, psychometric and psychological tests. The main variable is the body mass index (BMI). We consider that the patient responds to DBS if there is: an increase of 10 % in the máximum BMI in the last year prior to surgery (without hospitalization) or if a BMI curve is maintained with a descending curve of BMI since diagnosis. In case of response, the study includes a double blind that takes place 6 months after stimulation, where for 3 months the system is off and the subsequent 3 months on or vice versa

Results: So far we have included 5 patients. 4 Patients have responded to DBS. The improvement found in psychometric scales is in accordance with BMI evolution. We report 1 complication: prosthesis decubitus. No correlation was found between clinical or radiological (DTI) with the response to DBS

Discussion: The treatment with DBS has not shown response in all patients and the degree of effectiveness has been variable. It would be important to know which variables can influence the type of response to DBS.

Conclusions: It seems that DBS in SGC and Nacc can be an effective and safe treatment in some patients with chronic, severe and resistant AN.

Objectives

Deep brain stimulation can be an effective and safe treatment in some patients with severe and resistant AN.

Studies must to investigate which variables can condition the type of response to DBS

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Brain: Psychiatric Disorders

187. INS19-0265

EFFECTIVENESS OF TWICE-DAILY THETA BURST STIMULATION AT PREFRONTAL CORTEX ON METHAMPHETAMINE DEPENDENTS

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Introduction: Craving for substance of abuse acts as one major cause for relapse. Repetitive transcranial magnetic stimulation was employed to treat cue induced craving or drug intake in different types of drug dependents [1]. Theta burst stimulation (TBS) is a new form of stimulation protocol that can be delivered in much shorter time period; however, the clinical effectiveness of intermittent or continuous theta burst stimulation (iTBS/cTBS) for drug craving has not been investigated.

Materials/Methods: In this randomized, single-blinded, pilot study, we allocated 83 methamphetamine dependent subjects in abstinent period for three groups: iTBS or cTBS to the left dorsal-lateral prefrontal cortex (DLPFC), or cTBS to the right DLPFC for 10 times over 5 days. We measured cue induced craving score, sleeping quality, depression and anxiety score, impulsivity changes, and adverse effects as the outcomes.

Results: The results showed that iTBS at left DLPFC and cTBS at right DLPFC reduces craving, but not the cTBS at left DLPFC group. All three groups showed alleviated depression; while iTBS-L and cTBS-L group showed improved sleep quality; only iTBS-L group showed reduced anxiety levels. No changes were found for impulsivity level for the three groups. Self-reported adverse effects were higher in iTBS at left DLPFC groups, when compared to the cTBS at right DLPFC group in the first two sessions.

Discussion: To our knowledge, this is the first randomized trial to systemically compare the effects of different TBS procedures for methamphetamine craving. The present study provided strong evidence that twice daily iTBS-left or cTBS-right DLPFC treatment reduced craving for methamphetamine efficiently and were tolerable for at least 10 sessions, with simultaneously improved sleep quality and mood status. The result is consistent with the previously successes in high frequency rTMS at left DLPFC and low frequency rTMS at right DLPFC for craving modulation [1, 2].

Conclusions: We conclude that TBS can be employed to modulate craving and mood changes in methamphetamine dependents in abstinent period.

Objectives

New protocols with reduced session length would improve the potential cost-effectiveness and accessibility for rTMS in addiction management.

It is still unknown if TBS protocol is effective for methamphetamine abuse patients.

It is much of worth comparing the tolerability and self-reported adverse effects among the three different TBS procedures.

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Poster Presentations - May 27 - May 30
Gastrointestinal and Colorectal Disorders

188. INS19-0193

HUMAN GASTRIC PACING: SLOW-WAVE SPATIOTEMPORAL RESPONSE

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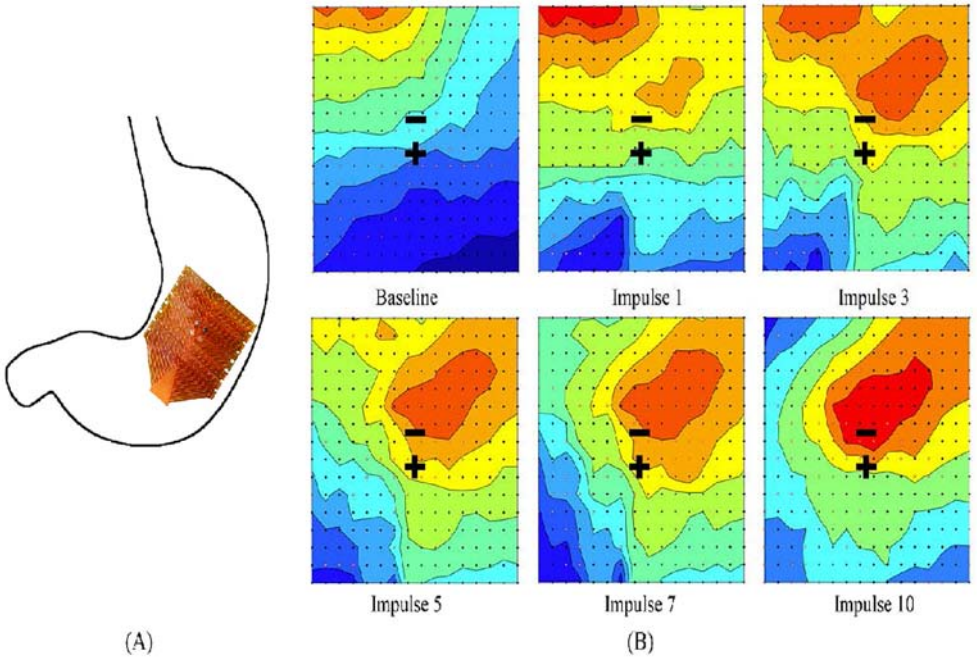

Figure 1: External pacing with HR arrays. (A) Orientation of the recording electrode array and four larger pacing electrodes located in the centre of the array. (B) 6 panes illustrating an isochronal activation profile (red is earliest activation, blue latest activation, colour bands represent 1 s intervals of propagation). The pacing electrodes (positive and negative signs) were located in the middle of the recorded area.

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Introduction: Gastric contractions are, in part, coordinated by bioelectrical slow-waves. Recent studies have shown that subjects with functional motility disorder, such as gastroparesis, have abnormal slow-wave patterns. Gastric pacing has been attempted in a limited number of studies to correct slow-wave abnormalities, but to date there are no established clinical therapies. In this study, we define the spatiotemporal response of slow-wave profiles to external pacing using high-resolution (HR) mapping [1] in human subjects.

Materials/Methods: A custom designed pacemaker device was piloted in seven intra-operative human studies (control cohort undergoing liver surgery) in conjunction with HR mapping (256 electrodes; 6cm × 6cm) to quantify slow-wave spatiotemporal response. HR electrode arrays were placed on the gastric serosa in the corpus region with pacing leads positioned at the center of the arrays to monitor conduction responses in all directions. The average period of recording was 10 minutes comprised of 3 minutes baseline, 5 minutes of pacing, followed by 2 minutes baseline. Pacing was applied with a period of 18 s, amplitude of 2 mA, and pulse width of 100 ms.

Results: Successful onset of pacing was achieved in five of seven cases. Figure 1 shows an example of six frames of propagation patterns of initiated slow-waves. The baseline period of intrinsic slow-waves was 17.6 ± 1.4 s and with pacing onset, an average area of 3.2 cm2 of tissue was excited instantly and a new pacemaker was initiated adjacent to the negative pacing electrode entraining approximately 30% of the mapped area (period of 18 s). Initiated slow-waves propagated anisotropically and gradually entrained the entire mapped area within 10 cycles.

Discussion: HR mapping allowed spatiotemporal quantification of the slow-wave propagation before and after the pacing onset. Due to the presence of the intrinsic slow-wave, there is a narrow excitable gap for external stimulation to excite a large area instantly. However, within 10 cycles, the entire mapped field was entrained.

Conclusions: HR mapping demonstrated rapid entrainment capture using pacing over the mapped region of the stomach. The joint application of pacing and HR mapping is a critical tool for investigating normal human gastric physiology, mechanisms of gastric electrical disorders and potential therapies.

Objectives

- First human pacing study using HR mapping to understand spatiotemporal slow-wave response.
- External impulses can pace gastric slow-wave activity.
- Slow-wave pacing origin is close to negative electrode.

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Gastrointestinal and Colorectal Disorders

189. INS19-0208

SPINAL CORD STIMULATION IN THE TREATMENT OF ISCHEMIC PAIN: MICROCIRCULATION AND TISSUE PERFUSION IMPROVEMENT

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Introduction: Refractory angina pectoris (RAP) and peripheral vascular disease (PVD) is a chronic pain conditions caused by occlusive artery diseases. Since 1976 spinal cord stimulation (SCS) appears to be an effective and safe treatment for these patients - many studies have shown an excellent effect of SCS on pain relief, as illustrated by reduction in the need for oral analgesics and improvement in patients' quality of life. Besides it can improve microcirculatory function.

Materials/Methods: We conducted a prospective analysis of patients with non-reconstructable RAP (n=21) and PVD (n=58) who underwent SCS in our facility between 2012 and 2018. Preoperative and follow-up myocardium perfusion scintigraphy (MPS), transcutaneous oximetry (TCO) and laser-doppler flowmetry (LDF) were performed on admission and in 1 year after procedure. Pain relief was assessed by visual analog scale (VAS) in all patients.

Results: The patients showed 9,37±0,13 marks according VAS before the procedure and pain relief to 1,27±0,09 marks (p<0,01) in 1 year follow-up. All the patients in RAP group demonstrated the rise of tolerance to the physical activity. MPS detected the decrement of perfusion's defect from 13,36±4,16 to 10,14±3,35 units (increase in coronary reserve up to 24%). TCO detected the microcirculatory improvement (n=56): tissue oxygenation increased from 10,5 to 39,5 mm Hg (p=0,045). There were 2 patient (3.4%) who had required postoperative amputation and 1 patient's death from cardiac infarction.

Discussion: The present study has some limitations: the follow-up period was relatively short, leading to limited evaluation of the outcome of SCS. Measurements weren't used to select patients for SCS, since we intended to include this indicator as a factor that could potentially influence the clinical dynamics after this procedure. The approaches to treatment of this diseases need to be optimized to timely use surgical and nonsurgical therapy, including SCS, in order to improve clinical and cost effectiveness.

Conclusions: The duration of clinical manifestations of RAP and PVD is associated with the long-term results of SCS. Our experience confirms that SCS can reduce the pain and improve quality of life with vascular reserve enhancement in patients with ischemic pain syndrome.

Objectives: Upon review of this abstract, specialists in neuromodulation and cardiovascular diseases will be able to discuss efficiency of treatment outcomes for neuromodulation in this patient cohort.

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190. INS19-0245

AUTOMATED ANALYSIS OF HIGH-RESOLUTION COLONIC MANOMETRY OF PATIENTS UNDERGOING NEUROMODULATION FOR FEACAL INCONTINENCE

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Introduction: Faecal Incontinence is defined as the uncontrolled passage of liquid or solid stool. Sacral nerve stimulation (SNS) has emerged as a successful therapy, where high-frequency stimulation is applied to the S3 sacral nerve root. SNS has achieved significant clinical outcomes but the mechanism of action is poorly understood and there remain critical limitations to patient selection and parameter optimisation. Colonic high-resolution manometry (HRM) is an emerging tool enabling accurate elucidation of colonic motor patterns (1,2) to yield new insights into dysmotility (3). We aim to quantify motor patterns during SNS using HRM via automated methods.

Materials/Methods: The colonic activity of 14 FI patients undergoing SNS implantation was mapped using HRM (36 channels at 1cm spacing) before and during stimulation with a meal. An activity index (AI), which was based on the area under the curve of detected events, along with the number of antegrade and retrograde events and percentage of signals in the 2-4 cycles per minute (cpm) frequency range was computed.

Results: The median age of the FI cohort was 61.5, with a mean Faecal Incontinence Severity Index of 39.2. Post neuromodulation with a meal, AI and percentage of 2-4cpm activity increased by 20% and 28%, while the number of antegrade and retrograde events increased by 47% and 73%.

Discussion: The use of HRM to assess colonic motility is under-utilised primarily due to the lack of reliable analysis methods. We have developed and applied novel signal analysis methods to HRM data in FI subjects undergoing SNS. These preliminary results indicate that there are altered distal colonic motor events after SNS, which may represent upregulation of the retrosigmoid brake mechanism.

Conclusions: We have applied rapid automated quantification techniques to analyse HRM recordings. This technology can allow for a detailed understanding of the mechanisms that control bowel function and could enable novel techniques to personalise neuromodulation.

Objectives

-SNS is an emergent therapy for FI.

-Automated HRM analysis methods were used to quantify effects of SNS on FI subjects.

-Increase in colonic activity post stimulation may upregulate brake mechanism.

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191. INS19-0238

FIXING BROKEN PLUMBING WITH BETTER WIRING: ANTI-INFLAMMATORY EFFECTS OF ABDOMINAL VAGUS NERVE STIMULATION IN A RAT MODEL OF INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) is a debilitating, chronic gastrointestinal disease. Electrical stimulation of the cervical vagus nerve is an emerging treatment of IBD (1). However, side effects from cervical vagal nerve stimulation (VNS) are often reported by patients. Here, we hypothesise that stimulating the abdominal vagus nerve, closer to the end organ, will have fewer off-target effects and is an effective therapy of IBD. Specifically, we aimed to: i) demonstrate abdominal VNS had no stimulation-induced off-target effects; ii) record *in vivo* electrically-evoked neural responses, thereby verifying stimulation levels were suprathreshold; iii) demonstrate abdominal VNS reduced chemically-induced intestinal inflammation in rats.

Materials/Methods: An electrode array, designed to stimulate and record neural responses, was developed. VNS off-target experiment: The cervical and abdominal vagus nerves of anaesthetised rats (n=5) were implanted with an electrode array, and stimulation-induced (10 Hz; symmetric biphasic current pulse; 320 nC per phase) changes to heart rate were assessed. VNS efficacy experiment: The abdominal vagus nerve of anaesthetised rats were chronically implanted with an electrode array. After 2 weeks, the intestine was chemically inflamed with TNBS (2.5% 2,4,6-trinitrobenzene sulphonic acid), an established rodent model of IBD. Rats were randomly selected to receive therapeutic VNS (n=7; 10 Hz; symmetric biphasic current pulse; 320 nC per phase; 3 hours/day) or no stimulation (n=8) for 5 days. Stool quality, C-reactive protein (an inflammatory response protein) content in blood and histology of the inflamed intestine were assessed.

Results: VNS off-target experiment: Abdominal VNS had no effect (two-way RM-ANOVA: $P>0.05$) on heart rate, while during cervical VNS heart rate decreased ($P=0.013$). VNS efficacy experiment: During the implantation period, electrically-evoked neural response thresholds were stable (one-way RM-ANOVA: $P = 0.828$), and stayed below 320 nC, confirming that therapeutic stimulation remained suprathreshold. Following TNBS injection, abdominal VNS rats had a decrease in stool quality score (unpaired T-Test: $P=0.002$), C-reactive protein levels in blood (two-way RM ANOVA: $P=0.005$) and resident inflammatory cell populations within intestinal layers (Kruskal-Wallis: $P<0.05$), compared to unstimulated rats.

Discussion: Future studies aim to determine efficacy of abdominal VNS in other models of IBD and determine the minimum stimulation levels required to produce a therapeutic effect.

Conclusions: Abdominal VNS has no off-target effects and is an effective treatment of TNBS-induced intestinal inflammation.

Objectives

i) New therapeutic paradigm; ii) Increasing knowledge base on VNS as a therapy of IBD; iii) Description of the bioengineering challenges and solutions at the neural interface.

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192. INS19-0257

COMPARISON BETWEEEN DIRTECT VAGAL NERVE STIMULATION AND NOINVASIVE AURITCULAR VAGAL NERVE STIMUALTION FOR OPIOID-INDUCED CONSTIPATION

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Introduction: Constipation affects a huge population; the opioid epidemic lead to opioid-induced constipation (OIC) is another major problem. However, treatment options for constipation are limited. Aims of this study were to investigate whether vagal nerve stimulation (VNS) and a noninvasive method of auricular VNS (aVNS) could treat constipation and to compare the performance between the two methods.

Materials/Methods: In acute study, 10 rats implanted with electrodes at vagal nerve as VNS/sham-VNS group and another 10 rats with electrodes at auricular brunch of vagal nerve as aVNS group. All rats implanted with a polyethylene catheter in the proximal colon for assessing whole colon transit by collecting marker at the anus for 100 minutes. For chronic studies, 28 rats were induced OIC then treated with sham-stimulation (N=10, 0mA), VNS (N=10, one hour daily) and aVNS (N=8, one hour daily) with previously optimized parameter for one week. Feces were analyzed daily, distal colon transit time (dCTT) and whole gut transit time (WGTT) were measured before and after the stimulation. Heart rate variability was analyzed to evaluate autonomic functions. Colon tissues were collected. The protein expressions of ChAT, nNOS, GDNF, p-Akt were assessed by western blot.

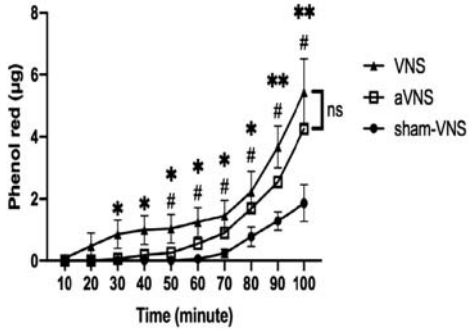

Fig.1: Whole colon transit. *: P<0.05; **: P<0.001, VNS group vs. sham-VNS; #: P<0.05, aVNS group and sham-VNS.

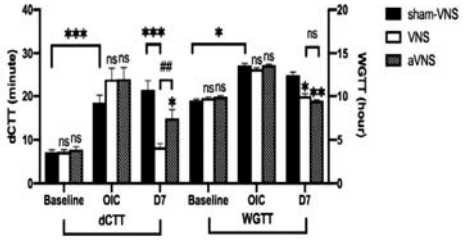

Fig.2 Distal Conlon Transit Time (dCTT) and Whole Gut Transit Time (WGTT). *: P<0.05, **: P<0.01, ***: P<0.001, vs. sham-VNS; ##: P<0.01, VNS vs. aVNS

Results: 1) Both VNS and aVNS accelerated the whole colon transit (Fig.1). 2) One-week VNS increased the total number of fecal pellets (261 vs. 219, P<0.01, vs. sham-VNS) and water content in feces (23.2±5.8% vs. 16.5±5.2%, P<0.02). aVNS showed similar effects. 3) Both chronic VNS and aVNS shortened WGTT and dCTT (Fig.2). VNS was more potent than aVNS for dCTT but not WGTT. 4) Both VNS and aVNS decreased sympathovagal ratio (64.6%, P<0.05 and 49.2%, P<0.05 vs. sham-VNS), increased vagal activity (54.5%, P<0.05 and 47.8%, P<0.05 vs. sham-VNS). 5) VNS increased the protein expression of ChAT by 21.7% (P<0.02, vs sham-VNS) and GDNF by 50.6% (P<0.01) but decreased the protein expression of nNOS by 28.3% (P=0.01) and p-Akt by 31.6% (P=0.08).

Discussion: VNS and aVNS can both improve constipation. The aVNS seems to be a more attractive therapy for constipation since it has similar effects on OIC as VNS but can be implemented noninvasively.

Conclusions: Both VNS and aVNS improve constipation by enhancing colon motility mediated by balancing autonomic functions.

Objectives

1) To assess the effect of VNS and noninvasive VNS in treating constipation. 2) To analyze the mechanism of VNS and aVNS in both acute and chronic status. 3) To compare the performance of the noninvasive aVNS with direct invasive VNS.

References

No reference.

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Genitourinary Disorders

193. INS19-0127

LONG-TERM OUTCOMES FOR THE TREATMENT OF OVERACTIVE BLADDER WITH A MINIATURIZED, RECHARGEABLE SACRAL NEUROMODULATION SYSTEM

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Introduction: Sacral neuromodulation (SNM) is a treatment for overactive bladder (OAB). Historically, only a non-rechargeable SNM system with a lifespan of 3-6 years was available. This system requires replacement surgeries, resulting in increased surgical risks and health-care costs. The miniaturized, rechargeable SNM system is designed for a 15-year lifespan and approved in Europe, Canada and Australia. RELAX-OAB is a post-market clinical study to test the safety and efficacy. 18-month follow-up results are presented.

Materials/Methods: This prospective study treated 51 OAB patients across 7 centers. Subjects were implanted with a tined lead and IPG in a single-stage procedure. Efficacy data was collected using a 3-day bladder diary, quality of life (ICIQ-OABqol) questionnaire, and subject satisfaction questionnaire. Responders were identified as patients with ≥50% reduction in voids and/or incontinence episodes compared to baseline or with reduction to less than 8 voids per day. Primary analyses were performed on Test Responders, defined as subjects that were responders at 2-week or 1-month post-implant.

Results: At baseline, subjects had an average of 14.6 ± 6.1 voids per day and 9.6 ± 5.1 incontinence episodes per day. 34 of 51 (71%) subjects were Test Responders. At 18-months, 89% of the Test Responders continued to be therapy responders. Voids reduced to 7.5 ± 1.8 per day, and incontinence episodes reduced to 1.9 ± 2.3 per day ($p<0.001$). Compared to Baseline, Test Responders experienced a 28.2 point improvement on their ICIQ-OABqol score, which was statistically and clinically significant (minimally important difference 10 points; 1). 93% of the Test Responders were satisfied with their rechargeable SNM therapy. 91% of all implanted subjects responded that it was easy to recharge their device and 97% responded the charging frequency and duration was acceptable. No serious device-related adverse events have been reported. No charging related adverse events were reported.

Discussion: These results confirm the long-term safety and efficacy of the rechargeable SNM system. A rechargeable SNM system is expected to provide significant cost-savings (2) and long-lived therapeutic benefits.

Conclusions: Patients implanted with the rechargeable SNM system received significant improvements in OAB symptoms and quality of life at 18 months post-implant, and reported that recharging their SNM system is easy and acceptable.

Objectives

To discuss the 18 months effects of a rechargeable sacral neuromodulator.

To discuss endpoints in studies on neuromodulation in overactive bladder.

To discuss the differences between a non-rechargeable and rechargeable sacral neuromodulator.

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Genitourinary Disorders

194. INS19-0120

MID-FIELD POWERED NEUROMODULATION FOR MULTIPLE INDICATIONS: A FIRST-IN-HUMAN EXPERIENCE

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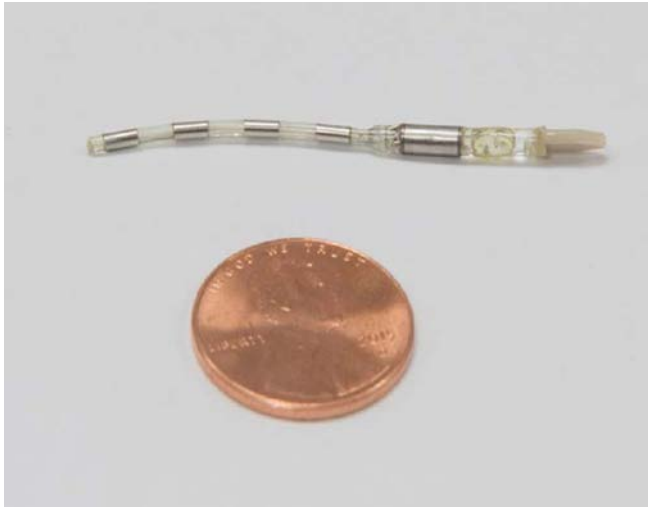
Introduction: Conventional implantable neuromodulation (NM) systems require the placement of a multi-polar lead or array located near the target nerve with the proximal section tunneled subcutaneously to the implantable pulse generator pocket. The treatment of neuropathic pain and movement disorders for some target nerves or nerve structures are not easily addressed with this completely implantable system.

A two-part NM system utilizing a proprietary mid-field powered external device linked to a miniaturized implantable stimulator implanted up to 10 cm in depth has been developed. An acute clinical study was conducted to demonstrate feasibility of this system.

Materials/Methods: The implantable stimulator was developed as a battery-less device. Circuitry for mid-field energy harvesting and stimulation pulse generation were housed in a proximal hermetic enclosure. A set of custom implant tools were developed for first human use. The system was verified with benchtop testing and pre-clinical studies.

A single center acute protocol was developed at MUMC+ in The Netherlands for a study enrolling Overactive Bladder patients. The stimulator was implanted using a modified Seldinger technique. The stimulator was powered by a prototype external mid-field powering unit in a sterile drape.

The primary objective was to verify that energy could be transmitted from the external unit using the mid-field powering method resulting in an observed response to stimulation of the sacral nerve. Fluoroscopy confirmed that the implantable stimulator was correctly placed. The stimulator was explanted after the intraoperative procedure. Safety was assessed during implantation, stimulation and explant.



Results: During the procedure an obvious motor response to stimulation was seen in 4 of the 5 patients. For all patients treated the stimulator was correctly placed and the depth of the implant varied with BMI. The elapsed time was recorded for each procedure step. The complete procedure took on average less than 30 minutes. No adverse events related to the procedure were reported.

Discussion: Figure 1: Implantable Stimulator

Conclusions: The results from this acute clinical study demonstrate the basic feasibility of the mid-field powered neuromodulation system. In addition to SNS for OAB, other neuromodulation indications could be addressed with this system. Future clinical studies will focus on safety and efficacy.

Objectives

1. Describe a novel mid-field powered external device linked to a miniaturized implantable neurostimulator.
2. Describe the implantation technique for a battery-free stimulator lead.
3. Demonstrate the feasibility of stimulating the 3rd sacral root with a mid-field powered system.

References

None

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195. INS19-0396

CHANGES IN ELECTROPHYSIOLOGICAL TEST RESULTS OF THE SOMATIC AND AUTONOMIC NERVOUS SYSTEM FOLLOWING SACRAL NEUROMODULATION

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Introduction: Sacral neuromodulation (SNM) is a well-accepted treatment for non-obstructive urinary retention (NOUR), overactive bladder (OAB) and faecal incontinence. One of the main hypotheses explaining its mechanism of action, is that changed activity in pudendal afferent nerves influences bladder and bowel behavior. However, its impact on other relevant nerves such as pelvic and hypogastric nerves has been largely unexplored. This study evaluates the effect of SNM on the current perception threshold (CPT) in bladder and different locations within the urethra.

Materials/Methods: This prospective study (12/2017-09/2018) evaluates CPT in 10consecutive patients(20-79years) before and at end of their test phase after 3 weeks of continuous subsensory threshold sacral spinal root stimulation with permanent tined lead electrode (pulse width, 210µsec, pulserate,14Hz). CPT testing was done using A 6Fwoven diagnostic electrode Catheter with 10electrodes inter-electrode space 2mm (pict1), which introduced transurethrally. Bladder, filled with 50cc iodine contrast to make standardization of electrode position possible. To determine CPT, current amplitude was slowly increased up to sensory threshold. Square wave pulses were delivered (0.5Hz, 1msec pulseduration, 2msec pulsinterval). The procedure was repeated three times at each site and average was calculated. In the lower urinary tract, trigone (pelvic nerve) was tested, as well the bladder neck /proximal urethra (hypogastric) and distal urethra (pudendal nerve). As reference the CPT of the right forearm was measured. Results before and after three week test stimulation were compared.

Results: Procedure was well tolerated in all patients. 5had OAB, 5NOUR. 7patients had successful testphase (>=50%improvement). CPT on the forearm was not different. CPT's decreased significantly for the trigone from 9.2 +/- 5.4mA to 4.9 +/- 2.9mA(p=0.009) and for distal urethra from 5.1 +/- 1.9mA to 3.6 +/- 1.6mA(p=0.037). No level of significance was reached for bladder neck/posterior urethra, CPT decrease from 8.4 +/- 10.4 to 5.1 +/- 3.7mA(p=0.185).

Discussion: This study shows that continuous subsensory threshold stimulation of sacral spinal nerves decreases CPT in the trigone and distal urethra, suggesting that SNM changes afferent activity not only in pudendal nerve but also the pelvic nerve. In OAB and NOUR a reduction in CPT was noted in these areas, showing an improved sensitivity of these nerves to electrical stimulation. No significant effect was found for bladder neck/posterior urethra, which mainly has hypogastric nerve input, suggesting not such pronounced effect on hypogastric nerve.

Conclusions: SNM affects the sensitivity of autonomic pelvic nerve innervating in lower urinary tract.

Objectives

Sensitivity of autonomic pelvic nerve innervating can be affected by SNM

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196. INS19-0298

CASE SERIES: IMAGING OF SACRAL DORSAL ROOT GANGLION POSITIONS TO GUIDE FLUOROSCOPIC PLACEMENT OF SACRAL NEUROMODULATION LEADS FOR PERINEAL PAIN

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Introduction: Anatomical variability of the nervous system has been demonstrated via cadaver dissection and in vivo with magnetic resonance imaging (MRI) (Moon et al 2010) and ultrasonography (Moriggl 2018) yet little literature exists to describe the position of the sacral dorsal root ganglia.

This case series aims to identify key bony anatomical indicators to guide placement of electrodes to optimally and safely target the sacral dorsal root ganglia (DRG) for those suffering perineal pain and associated bladder, bowel and sexual dysfunction related to pudendal neuropathy.

Materials/Methods: Six patients with clinically diagnosed pudendal neuropathy will be imaged using T1- and T2-based 3D volume MRI protocols to demonstrate the positioning of the sacral DRG. Key bony landmarks will be cross-referenced to guide locations of the DRG based on image intensifier fluoroscopic imaging during the surgical procedure.

Results: Preliminary results suggest the sacral DRG lie within the lateral aspect of the sacral canal.

Discussion: Current practice for DRG stimulation involves the use of small diameter leads in the cervical, thoracic and lumbar spine. The sacral spine differs considerably in that the DRG are more consistently within the sacral canal (intra-spinal)

Conclusions: This case series provides the basis for a larger study to demonstrate the position of the sacral DRG, which is consistently within the lateral aspect of the sacral canal. However, the variability of the relationship of the DRG and the corresponding foramen is greater moving caudally from sacral segments one to five.

Objectives

Guide clinicians in locating sacral DRG's for procedures such as sacral neuromodulation or pulsed radiofrequency.

Improve the safety of interventional pain procedures by clearly visualizing the variability in neuroanatomy in the sacral region

Improve therapeutic outcomes for pudendal neuropathy and related bladder, bowel or sexual dysfunction

References

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197. INS19-0258

EFFECT OF EARLY SACRAL NEUROMODULATION ON BLADDER FUNCTION IN A RAT MODEL OF INCOMPLETE SPINAL CORD INJURY DUE TO FOCAL CONTUSION

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Introduction: Sacral neuromodulation (SNM) has been reported to modulate the micturition reflex to some extent in studies using a completely spinalized rat model, with several possible mechanisms underlying the action of SNM suggested. In actual clinical practice, however, 66% of all patients with spinal cord injury (SCI) are estimated to have incomplete-type of SCI induced by spinal contusion. Nonetheless, most animal studies that have addressed the effect of SNM on bladder function have used rats with spinal transection. Experiments in a rat model of incomplete SCI, which would reflect more relevant conditions of clinical SCI, are scarce. We aimed to evaluate the effect of early SNM on bladder responses in a rat model of incomplete SCI.

Materials/Methods: Altogether, 21 female Sprague-Dawley rats were equally assigned to control (CTR), SCI + sham stimulation (SHAM), and SCI + SNM (SNM) groups. In the SHAM and SNM groups, incomplete SCI was created by producing a moderate contusion with an NYU-MASCIS impactor at the T9-T10 level of the spine, with needle electrodes implanted bilaterally into the S2 or S3 sacral foramen. Only SNM group underwent electrical stimulation for 28 days, beginning on day 7 after SCI. Cystometry was performed 35 days after SCI.

Results: Although the interval between voiding contractions was significantly longer in the SHAM group than the CTR group (25.5 $\pm$ 1.4 vs 12.5 $\pm$ 1.7 min; $P < 0.05$), there were no significant differences between the SNM group (16.5 $\pm$ 1.5 min) and the CTR group. Maximum voiding contraction pressure did not differ among the groups. The SNM group had a significantly lower frequency (3.5 $\pm$ 0.5 vs 14.6 $\pm$ 2.0; $P < 0.05$) and maximum pressure (11.4 $\pm$ 6.2 vs 21.3 $\pm$ 1.8 cmH2O; $P < 0.05$) of nonvoiding contractions than the SHAM group.

Discussion: The present study is the first to evaluate the effect of early SNM treatment on bladder function in an incomplete SCI rat model. The early application of SNM to the rats with incomplete SCI had a significant positive influence on the frequency and pressure of nonvoiding detrusor contractions.

Conclusions: Our results provide experimental evidence that early SNM treatment may prevent or diminish bladder dysfunctions (e.g., detrusor overactivity, abnormal micturition reflex) in a clinical condition of incomplete SCI.

Objectives: To evaluate the effect of early SNM treatment, which is conducted just as soon as detrusor overactivity seems to occur, on bladder responses in a rat model of incomplete SCI.

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198. INS19-0058

RETROGRADE PERCUTANEOUS TECHNIQUE OF LEAD PLACEMENT FOR CHRONIC TIBIAL NERVE STIMULATION: AN OFFICE BASED PROCEDURE

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Introduction: Percutaneous tibial nerve stimulation has been shown to be effective in treating the symptoms of overactive bladder. Limitations of this approach include weekly office visits and intermittent delivery of nerve stimulation. Our goal was to develop a minimally invasive, reproducible and teachable technique to safely place an implantable electrode at the tibial nerve.

Materials/Methods: We performed several cadaver dissections to identify the relevant anatomy of the lower extremity. An antegrade approach had been described in humans to place an electrode the tibial nerve. Using our cadaver model, it became clear this approach was not ideal. We systematically reviewed the anatomy of the tibial nerve and developed a retrograde method to reliably place an implanted electrode at the tibial nerve in the cadaver and translated this to the human.

Results: Using the cadaver model, a retrograde technique (distal to proximal) was developed to place the lead percutaneously along the tibial nerve. The cadaver studies will be reviewed. Retrograde placement of electrodes parallel to the nerve were reliably predicted using bony landmarks and were confirmed with fluoroscopic and ultrasound imaging along with cadaveric dissection. This technique was then translated to the patient where quadripolar leads were implanted along the tibial nerve under local anaesthesia in the office. A site was chosen 1/3 the distance from the medial malleolus to Achilles tendon where a small skin nick was made. The 7 cm lead introducer was advanced to penetrate the fascia of the lower leg to enter the space adjacent to the tibial nerve. The introducer was advanced parallel to the tibia bone and the distal end was stimulated confirming toe flexion and sensory stimulation on the bottom of the foot confirming tibial stimulation. An integrated tined quadripolar lead/receiver was advanced, positioned and tested and deployed (StimGuard, Inc.). Successful tibial nerve stimulation was achieved in all patients.

Discussion: The tibial nerve is comprised of branches from L4, L5, S1-3 and has a role in the management of overactive bladder. This technique allows for permanent implantation of an electrode along the nerve to provide daily, chronic stimulation.

Conclusions: We describe the development and use of a safe retrograde method of percutaneous tibial nerve lead placement that is done is the office under local anesthesia.

Disclosure: Consultant and equity owner in StimGuard, Inc; Consultant Taris; Consultant UroGen

Objectives

1. Understand the tibial anatomy
2. Review approaches to placing an electrode at the tibial nerve
3. Learn office-based technique to implant a lead

References

None

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199. INS19-0059

EARLY EVALUATION OF AN IMPLANTED CHRONIC TIBIAL NERVE STIMULATION DEVICE VERSUS PERCUTANEOUS NERVE STIMULATION FOR THE TREATMENT OF URINARY URGE INCONTINENCE

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Introduction: Tibial nerve stimulation is effective for the treatment of urgency symptoms, yet the weekly 30-minute protocol likely under delivers stimulation and can represent significant patient burden. Implantable tibial nerve technology with wireless energy delivery can provide longer stimulation times at home and more rapid clinical improvement. This prospective study evaluates two office-based treatments for UI; percutaneous tibial nerve stimulation (PTNS) and chronic tibial nerve stimulation (CTNS) via a wireless neuromodulation system.

Materials/Methods: Women reporting bladder symptoms for at least 6 months and experiencing a minimum of 1 UI episode per day were randomized (1:1) to receive 12 weeks of standard PTNS treatments or an implanted CTNS device. CTNS is an investigational office procedure that places a wireless lead parallel to the tibial nerve, patients wear an ankle bracelet and in this study stimulated for 6-8 hours a day. After PTNS women had the option of having the CTNS device placed. Voiding diaries, symptom and QOL questionnaires were completed, and safety was assessed. Descriptive statistics were performed.

Results: Nine women were enrolled; 5 to the CTNS arm and 4 to the PTNS arm. 2 PTNS patients chose to undergo CTNS device implant after

Group PTNS Mean	BASELINE n=4	1 Week n=4	4 Weeks n=4	13 Weeks n=4			
Urge UI episodes/day	4.25	2.25	2.66	2.16			
OAB-q	80.5	67.25	52.5	45.50			
i-QOL	43.47	51.42	61.44	68.75			
CTNS Group Mean	**BASELINE n=7**	**1 Week n=7**	**4 Weeks n=5**	**13 Weeks n=6**	**6 Months n=3**	**9 Months n=3**	**12 Months n=3**
Urge UI episodes/day	3.05	2.57	1.20	1.06	0.89	1.44	0.66
OAB-q	75.86	66	42.20	42.67	49.00	49.67	46.67
i-QOL	54.31	60.97	78.68	83.92	84.09	79.92	77.27

PTNS for a total of 7 CTNS devices implanted. There have been no device explants. All 7 remain active study participants, with 6 completing the 13-week visit, and 3 completing the 12-month visit. All PTNS and CTNS patients reported improvements in UI episodes per day, OAB symptoms and QOL (see table). Most CTNS improvement were observed by 4 weeks vs. PTNS improvement at 13 weeks. Positive treatment effects continued through 12-months post-implant. To date, 5 study-related adverse events (AEs) have been reported, all were minor and have resolved.

Discussion: There is significant scientific interest in developing a safe and reliable implant for the tibial nerve to treat overactive bladder. This will reduce patient burden of frequent office visits for PTNS and will allow daily stimulation that may result in more robust outcomes. An office based procedure can reduce health-care costs.

Conclusions: This is an early evaluation and the sample size is small, but we demonstrate that office based placement of a tibial nerve lead for chronic home-based stimulation is safe and effective in treating UI resulting from OAB. Further work is ongoing.

Disclosure: Consultant/Equity Owner StimGuard LLC

Objectives

1. Understand impact of PTNS on clinical outcomes
2. Learn about the impact of daily stimulation on clinical outcomes
3. Understand lead implant technique and stimulation parameters

References

None

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200. INS19-0162

A NOVEL APPROACH TO MANAGING POST RETROPUBIC VAGINAL SLING PAIN

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Introduction: 50-year-old female had a retropubic TVT® sling done in 2008 for SUI. Postoperatively she noted severe right-sided pain in the deep vagina and behind the pubic bone. This pain never resolved despite multiple procedures to remove the mesh, a hysterectomy and lysis of adhesions, trigger point injections with ropivacaine and Kenalog, and Botox into the levator muscles. Pudendal nerve blocks and TPI done every 8 weeks gave transient improvement in symptoms. Her site of pain was precise, and we elected a novel approach of placing an electrode in the retropubic space at the site of pain.

Materials/Methods: After a successful 1-week test stimulation, a 34-cm tined quadripolar lead with an integrated receiver (StimWave, Inc.) was positioned behind the pubic bone through a tiny skin nick on the lower abdomen. A curved lead introducer was guided behind the pubic bone with a finger in the vagina to the site of her pain. Stimulating this region resulted in an anal wink and CMAP consistent with pudendal nerve (PN) activation (atypical site for a PN branch). The lead was advanced and deployed with fluoroscopic guidance. The receiver end was tunneled through 2 small skin nicks to the right lower abdomen. Post-operatively the device was programmed at 1500 Hz and she stimulated daily using a surface antenna and rechargeable external energy source.

Results: The technique was minimally invasive, took less than 20 minutes and required 3 small skin nicks to deploy and tunnel the lead. The device was programmed at 1500 Hz and the patient activated the lead daily with an external antenna and energy source. The patient had 100% resolution in her pain.

Discussion: Post sling pain is very difficult to manage. This patient underwent multiple treatments over the past decade. The cause of this pain is unknown, but likely due to a nerve injury. Interestingly we had a typical pudendal response by stimulating retropubically, suggesting an aberrant nerve branch. This novel approach led to complete resolution of her pain

Conclusions: Placing an implantable electrode at the site of post-sling pain to stimulate a peripheral nerve branch resulted in complete resolution of the pain. This is the first report of this simple and safe approach to manage pain associated with vaginal mesh placement.

Objectives

1. Understand the management of post-sling pain
2. Learn about the potential of peripheral nerve stimulation to treat post-sling pain
3. Understand that aberrant nerve branches my increase risk of post-surgical pain

References

none

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201. INS19-0057

SACRAL NEUROMODULATION FOR MANAGEMENT OF CHRONIC PELVIC PAIN

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Introduction: Managing Chronic Pelvic Pain (CPP) can be challenging. Often patients go through a multitude of conventional treatments which they may find ineffective. Sacral Nerve Stimulation (SNS) is well-established in the management of urinary and bowel dysfunction. SNS use has expanded to treat bladder pain syndrome. Pilot studies have shown that SNS can also be effective in CPP.

Materials/Methods: We measured changes in pain scores, medication use and improvements in bowel and bladder function in our patients who had SNS implants from January 2007 to December 2016. In all patients the primary goal of treatment trial was pain reduction (rather than functional improvement). In addition to measuring Numerical Rating Scores (NRS) during the routine follow up appointments, further follow-up data was collected using a telephone questionnaire between march and May 2017. The primary outcome was pain levels as measured by NRS. Secondary outcomes consisted of medication use, bladder/bowel and sexual function measured on 11-point numerical Likert scales, and Patient Global Impression of Change (PGIC).

Results: 29 patients with CPP were treated with SNS. Three patients had passed away from unrelated causes, three patients were explanted due to therapeutic failure and four patients were lost to follow-up. Two patients were not able to participate in a phone follow up. N=17 were followed-up ranging 3-113 months after full implant. Average pain relief from baseline NRS at 3-6 months was 38% (8.58 to 5.29) which was maintained at long-term follow-up.

70% reduced analgesics. 80% reported improvement in bladder function while 41% reported improvement in bowel function while 28% reported improvement in sexual function. 88% reported improvement in PGIC scores.

Discussion: This service evaluation has shown SNS is effective in reducing pain in CPP. SNS may be used in a wide variety of chronic pelvic pain diagnoses. SNS may also have a positive impact in reducing medication and improving bladder and bowel function. Overall, most patients were satisfied with their SNS as measured by PGIC.

Conclusions: Based on our evaluation, SNS is beneficial in managing CPP. However more robust studies are warranted to quantify cost-effectiveness.

Objectives

Introduce Sacral neuromodulation to treatment pathways for chronic pelvic pain

Broaden the indications for SNS

Share our experience of long-term outcome of SNS for pelvic pain reduction

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Headache

202. INS19-0154

BURST OCCIPITAL NERVE STIMULATION FOR CHRONIC MIGRAINE AND CHRONIC CLUSTER HEADACHE

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Introduction: Occipital nerve stimulation (ONS) is an established treatment for headache syndromes including chronic cluster headache (CCH)[1,2,3] and chronic migraine (CM)[4]. To date ONS in these conditions has exclusively use tonic waveforms. In spinal cord stimulation there is now overwhelming evidence that paraesthesia is not a prerequisite for effective analgesia. We report here a series of patients treated for CCH and CM using paraesthesia free stimulation.

Materials/Methods: This is a retrospective review of prospectively collected data for 17 patients (5 CCH and 12 CM) treated with burst stimulation of the greater occipital nerves (bONS). Four patients had previously been treated with tonic ONS (tONS). In CCH we recorded the attack frequency and the intensity of headaches on the numeric pain rating scale (NPRS), and in CM we recorded the number of headache days per month and NPRS.

Results: All 5 CCH patients responded well, with at least an 80% reduction in headache frequency (mean reduction 92%, p=0.013, one tailed sign test). There was a mean reduction of 42% in the intensity of residual headaches (p=0.023, one tailed sign test).

Mean reduction in headache days per month in CM was 7.6 (p=0.007, one tailed sign test). Those who preoperatively reported headache every day were less likely to improve with treatment. Mean headache NPRS improved by 16%.

Discussion: The response in CCH appears encouraging when compared to large published case series of tONS where the percentage of patients experiencing a 50% or more reduction in attack frequency was 53-67%. Further studies will be required to see whether these results are borne out in larger groups. While the response in CM also appears good compared to the results of previous trials, our group is small and we had no control group for comparison. Further studies are needed here too.

Conclusions: Early experience suggests that paraesthesia-free bONS may be an effective treatment for severe chronic cluster and chronic migraine headaches.

Objectives: There have been no RCTs in CCH, and although there have been trials in CM, blinding has never been optimal due to the paraesthesia produced by stimulation. Paraesthesia free treatments offer at last the possibility to perform robustly double blind trials of a surgical treatment for pain.

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Poster Presentations - May 27 - May 30
Headache

203. INS19-0428

GASSERIAN GANGLION STIMULATION IN NEUROPATHIC FACIAL PAIN

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Introduction: Neuropathic facial pain is a debilitating disease in its medically intractable form. According to the 3rd Edition of International Classification of Headache Disorders it can be the result of multiple sclerosis, mass effect, or its origin can be associated with posttraumatic, postherpetic nerve injuries. Gasserian ganglion stimulation can provide a reliable tool to decrease neuropathic facial pain.

Materials/Methods: 8 patients suffering from medically intractable neuropathic facial pain were enrolled in this study. Most common indications were of postherpetic, posttraumatic and iatrogenic origin. Each patient was implanted with a custom made Medtronic 3 contact anchored, curved lead, under light sedation and intraoperative trial stimulation. Leads were advanced through the oval foramen under fluoroscopy according to Hartel coordinates, lead extension has been tunneled and externalized on the neck. Each patient underwent an at most 2-week-long postoperative testing period with an external neurostimulator to evaluate the results of stimulation. Visual analogue scale (VAS) scores were obtained three times a day, stimulation parameters were adjusted accordingly.

Results: Of the 8 patients 7 patients completed the trial period successfully. Mean age was 61.14±15.65 years, gender distribution was 50-50%. Mean preoperative VAS 9.29±1,49 decreased to 3.00±2.08 in the first two weeks during testing on an external neurostimulator. At least two months after surgery VAS scores were kept highly significantly in lower ranges - mean VAS 2.5±1.64. One patient became pain free. Stimulation amplitude, frequency and pulse width were inconsistent in the whole group. Each patient required monopolar stimulation, painful areas have been covered with persistent paraesthesia of barely noticeable level. Lead migration due to intra ganglionic anchoring, CSF leakage, infection were not observed.

Discussion: Gasserian ganglion stimulation can be a reliable therapeutic option in medically intractable neuropathic facial pain, but the underlying mechanism is yet to be uncovered. Due to the need of highly variable, patient specific stimulation parameters a short trial period is advised before IPG implantation. The improved anchoring system helps to maintain the therapy but it is still requires further developments.

Conclusions: The described method can reliably decrease neuropathic facial pain in the observed patient population. Enrollment of more patients is necessary to uncover specific parameters that can be tuned to different indications to provide a disease specific guideline for programming.

Objectives: Gasserian ganglion stimulation, implantation technique, anatomical consideration of oval foramen electrode implantation

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Headache

204. INS19-0042

TITLE: ANTICEPHALGIC PHOTOPROTECTIVE PREMEDICATED MASK: A REPORT OF A SUCCESSFUL STUDY OF A TREATMENT FOR MIGRAINE AND/OR TENSION HEADACHES

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Introduction: This study was performed to determine the efficacy of an anticephalgic photoprotective mask in conjunction with a topical medication containing bryonia and rhus toxicodendron in the treatment of migraine and/or tension headache. Many clinicians are seeking headache treatment modalities with improved safety profiles. A premedicated mask would serve not only as a delivery system for benign topical medication, but simultaneously provide photorelief and exert external pressure which may alleviate vascular headaches by collapsing painfully distended extracranial arteries and reducing peripheral sensitization.

Materials/Methods: Thirty-three patients were given masks and tubes of topical medication containing the bryonia and rhus toxicodendron. They were instructed to apply the medication to their frontalis and/or temporalis regions in the event they should suffer a headache and apply a photoprotective mask. Furthermore, they were instructed to take their usual oral or parenteral medications if required for the relief of the headache. They subsequently filled out forms rating the degree of relief which they attributed to the topical medication and the mask using a 0-10 scale.

Results: Thirty out of 33 patients stated the medication and the mask were effective over and above the normal degree of relief they were receiving from their oral and/or parenteral medications. This study demonstrated a significant efficacy rate (91%) in the treatment of migraine and/or tension headache with the anticephalgic mask in conjunction with a topical cream containing bryonia and rhus toxicodendron.

Discussion: This study demonstrated a significant efficacy rate (91%) in the treatment of migraine and/or tension headache with the anticephalgic mask in conjunction with a topical cream containing bryonia and rhus toxicodendron.

Conclusions: Opioid Epidemic. Safe, effective treatment for migraines and/or tension headaches with photosensitivity.

Objectives: This study was performed to determine the efficacy of an anticephalgic photoprotective mask in conjunction with a topical medication containing bryonia and rhus toxicodendron in the treatment of migraine and/or tension headache. Background: Many clinicians are seeking headache treatment modalities with improved safety profiles.

References

Journal of Practical Pain Management March 2008

Poster Presentations - May 27 - May 30
Headache

205. INS19-0036

OCCIPITAL NERVE STIMULATION WITH REFRACTORY OCCIPITAL NEURALGIAS: RESULTS IN 60 PATIENTS OF A SINGLE INSTITUTION STUDY

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Introduction: Objective: Occipital nerve stimulation (ONS) is effective to treat various headache such as Cluster headache, migraine, sunct and hemicrania paroxystic. Many studies focus on migraine and cluster headache. The efficiency of ONS was less evaluated in occipital nevralgia. There is no prospective study in the literature and report of cases do not exceeded 30 cases.

Materials/Methods: Methods: A prospectively collected datas included 60 patients with intractable occipital neuralgias treated with peripheral nerve stimulation (PNS) was performed. Evaluations include Visual Analogic Scale (VAS) before and after PNS implantation, the Medical Quantification Scale (MQS) before and after implantation, failure of medical treatment and multidisciplinary approach of pain. External trials with transcutaneous electric neurostimulation (TENS) were performed to evaluate if the trial is successful. 60 patients were implanted, results at 6 months and 12 months were analyzed.

Results: At the time of follow-up 78 % of patients have 50% of decrease pain on VAS. Mean VAS was 8.4/10 preoperatively compare to 2.85/10 after PNS implantation. Results are quite stables with time even if parameters settings need to be adjusted frequently. Oral pain medication was reduced to about 50%. The MQS was equal to 18 preoperatively and was decreased to 9.9 in postop. Side-effects included 4 patients with infection of the system (6%), and 4 migrations of electrode (6%).

Discussion: The results obtained in our series using occipital stimulation were better than those achieved by surgical ablation and are concordant with those found in the literature. Weiner implanted 13 patients and achieved greater than 50% pain control in 12 patients. Slavin reported that 60 to 90% efficacy of occipital stimulation in 10 of a series of 14 patients. Kapural treated 4 patients with cervicogenic headache, with an efficacy comparable to that of our series (VAS score that changed from 8.6 preoperatively to 2.5 postoperatively). In the series reported by Rodrigo-Royo the 4 patients implanted experienced a significant reduction in pain; in the series reported by Johnstone 5 of 7 patients experienced a reduction in pain.

Conclusions: Occipital nerve stimulation is effective to treat patients with occipital neuralgias.

Objectives

Efficacy of occipital nerve stimulation in occipital neuralgias

Safety and reversibility of the techniques

Selection of patients must be rigorous with multidisciplinary approach

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Poster Presentations - May 27 - May 30
Headache

206. INS19-0276

SPINAL CORD STIMULATION AT 10 KHZ FOR TREATMENT OF CHRONIC HEAD PAIN

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Introduction: Chronic, refractory head pain presents a treatment challenge. Case series show occipital nerve stimulation (ONS) to be efficacious for the treatment of several head pain disorders including migraine headaches, cluster headache, hemicrania continua and occipital neuralgia (1). However, high surgical revision rates and lead migration, reduces the preference for this therapy. The alternative, traditional spinal cord stimulation (SCS) in the cervical region can cause variability in the distribution and intensity of the induced paresthesias and often results in inadequate coverage (2,3). Instead, paresthesia-independent high frequency SCS (HF-SCS) at 10 kHz in the cervical region presents an interesting option for these patients. Here, we present a case series of chronic intractable head pain patients receiving HF-SCS at 10 kHz and reporting on their outcomes.

Materials/Methods: Twenty-seven patients received a HF-SCS implant in the cervical region for the treatment of their predominant head or head and upper body pain, following a successful trial of the system. Each patient was implanted with at least two epidural leads spanning C2-C7 vertebral bodies, with some patients receiving a third lead covering the upper thoracic T1-T3 vertebral bodies to treat the upper body component of pain, if applicable. Programming amplitudes varied between 0.1-2.1mA, depending on the patients. Patients were followed up at an average of 32.1 $\pm$ 21.3 (range: 9-65) months. Results are presented as mean $\pm$ standard deviation. Headache is considered an off-label indication for this therapy.

Results: Patients implanted with a permanent HF-SCS at 10 kHz system reported a significant reduction in their baseline recorded pain when followed up post implant (7.3 $\pm$ 1.4 vs. 2.7 $\pm$ 2.4 on the numerical pain rating scale [NRS]). All but 2 of the 27 patients reported an improvement in their condition. Improved function was observed in 81% of the patients and improved quality of sleep reported by 69% of the patients. Two patients underwent a revision to their leads with good outcomes. No further complications were noted.

Discussion: Early data demonstrates that HF-SCS can offer clinically notable pain relief, whilst overcoming traditional SCS issues such as positional stimulation, and high surgical revisions rates seen with ONS.

Conclusions: Preliminary results from a single clinic using HF-SCS to treat head pain are promising.

Objectives: To investigate the use of cervical HF-SCS as an alternative to occipital nerve stimulation for chronic head pain.

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Poster Presentations - May 27 - May 30

Late-Breaking Research

207. INS19-0354

PLASTICITY MECHANISMS UNDERLYING REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION FOR IMPROVING COGNITION IN BRAIN INJURY

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Introduction: Patients with Traumatic Brain Injuries (TBI) report cognitive problems that may last for months or even years. By using a magnetic pulse to selectively modulate brain networks, Repetitive transcranial magnetic stimulation (rTMS) may promote neural plasticity and lessen TBI symptoms. Brain-Derived Neurotrophic Factor (BDNF) is a key signaling molecule for plasticity and regrowth following injury in the brain. BDNF is encoded by a gene that may contain a methionine (Met) substitution for valine (Val). We report neuroimaging and proteomic/genetic results from our clinical trial to improve cognition in Veterans with TBI enrolled in treatment (n = 17) or sham (n = 16) arm at VA Palo Alto.

Materials/Methods: FDA approved parameters for Major Depressive Disorder (MDD) were utilized (Location: Left Dorsolateral Prefrontal cortex (DLPFC); Pulse frequency: 10 Hz; 20 sessions) with executive function as an outcome measure.

Results: Resting state fMRI analysis revealed a decrease in connectivity between stimulation site (LDLPFC) and cingulo-opercular network (CON) with a standardized beta effect size of -0.81 (p =.036) which was slightly associated with the digit coding task (p=0.046, beta=0.34). At baseline, the Val/Val homozygotes had higher circulating BDNF levels than the met carriers. After 20 sessions of rTMS, there was an overall increase in BDNF, and this pattern continued at 6-month follow-up. The Val/Val individuals also had more proBDNF but overall levels did not change with treatment.

Discussion: Genotype was a significant factor in circulating BDNF levels. In chronic mTBI, rTMS does appear to increase BDNF. Met carriers may be more likely to respond to treatment than the Val/Val homozygotes BDNF is an important factor in recovery from TBI, and genotype may moderate this effect.

Conclusions: These results specifically provide insights into the plasticity mechanisms underlying the relationships between stimulation sites and networks heavily implicated in the TBI population. For instance, these findings pave the way for individualized treatment strategies for TBI. Different cortical stimulation sites other than DLPFC can be compared to see if they result in a difference in levels of BDNF post-rTMS treatment. We leverage this to propose new and innovative study designs for non-invasive therapies that utilize precision medicine tools.

Objectives

1. Learn about rehabilitation treatments that are non-invasive in TBI patients with chronic symptoms.
2. Learn about repetitive transcranial magnetic stimulation
3. Learn about biomarkers and how they change with therapeutic treatments and their interaction with genetics.

References

N/A

Poster Presentations - May 27 - May 30
Late-Breaking Research

208. INS19-0145

ULTRASOUND NEUROMODULATION TO RESTORE FUNCTIONS IN CERVICAL CORD INJURED RATS

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Introduction: Significant research has been carried out in recent years to evaluate the therapeutic impacts of ultrasounds on neurological disorders [1]. However, effects of ultrasound stimulation on spinal cord neurocircuits after a spinal cord injury are still unknown. The purpose of this study was to examine the effects of low-intensity pulsed ultrasound stimulation on forelimb functions in cervical injured rats.

Materials/Methods: Seven adult female Sprague Dawley rats were used in this study. Following 8 weeks of skilled reaching and grasping training, a dorsal funiculus crushed injury at C4 spinal level was done to induce forelimb motor function deficits. The rats were then implanted with a custom ultrasound stimulation probe at cervical level. After recovery, rats were tested to reach and grasp pellets with and without ultrasound stimulation for 6 weeks post-injury. Data were averaged and compared for statistical significance (ANOVA).

Results: There was significance ($p < 0.001$) drop of reaching scores from pre- to post-injury reaching behavior (Fig. 1A). Post-injury, reaching scores were weekly measured pre-, during-, and post-stimulation. Our 6 weeks post-injury data suggest that during- and post-stimulation scores were higher than the pre-stimulation reaching scores (Fig. 1B). However, there is no significant difference was found among three periods.

Fig. 1: A) Pre- and post-injury success rate; B) Post-injury scores at different weeks for pre-, during-, and post-stimulation.

Discussion: Early ultrasound stimulation study on the spinal cord found that the spinal reflex is reversible and depends on the intensity of ultrasound [2, 3]. In the current study, we have demonstrated for the first time that the forelimb reaching and grasping behavior can be modulated during and immediate after ultrasound stimulation to the spinal cord and thus has therapeutic potentials for spinal cord injury rehabilitation.

Conclusions: Ultrasound stimulation has modulatory effects on the spinal cord neurocircuits and may induce neurophysiological changes in the injured spinal cord.

Objectives

To investigate the functional changes mediated by ultrasound stimulation in spinal cord injured rats.

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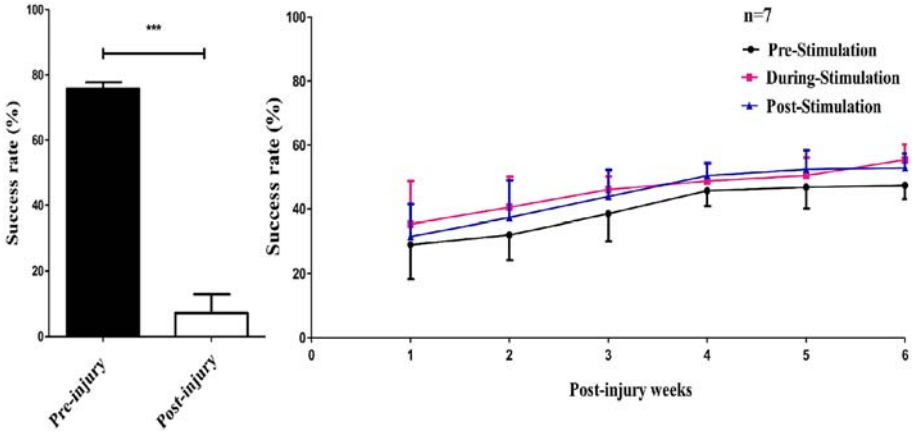

Poster Presentations - May 27 - May 30
Late-Breaking Research

209. INS19-0319

TREATMENT OF NECK AND UPPER LIMB PAIN USING BURSTDR SPINAL CORD STIMULATION

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Introduction: Spinal cord stimulation (SCS) studies have shown that cervical stimulation is effective in relieving pain in the neck and/or the upper extremities (1-3). The Neuromodulation Appropriateness Consensus Committee (NACC) concluded that cervical SCS is as effective and safe as thoracic SCS (4). Nevertheless, the committee also acknowledged that cervical SCS is more vulnerable to changes in paresthesia coverage compared to thoracic SCS, due to the increased mobility of the cervical spine. Burst stimulation is an established waveform that has shown to provide superior back and leg pain relief over traditional tonic SCS, without the requirement of paresthesias. Given this potential benefit of paresthesia-free stimulation, it is crucial to evaluate the therapeutic efficacy Burst stimulation of the cervical spine for the treatment of neck and/or upper extremity pain. Thus, the purpose of this study was to evaluate the safety and therapeutic efficacy of Burst stimulation for the treatment of chronic intractable neck pain with or without radiation down to arm/shoulder/upper back.

Materials/Methods: This ongoing prospective, open label, multicenter feasibility study aimed to evaluate Burst in 30 subjects suffering from chronic neck pain (with or without upper extremity pain) for 1-year, during which they will be evaluated at baseline, after SCS trial, and 3, 6 and 12 months post-permanent implantation. The primary endpoint will evaluate the change in pain intensity from baseline with all follow-up visits using the Visual Analog Scale (VAS) assessments. Similarly, secondary endpoints such as changes in quality of life (EQ-5D), neck disability (ONDI), headache (HIT-6), satisfaction (PGIC), and anxiety and depression (HADS) will be assessed. Pain medication usage and adverse events will also be collected throughout the study.

During implantation, 2 leads will be placed across the C2-C3 vertebral body and three standardized programming parameters will be used. Program 1 will consist of a bipole across the C3-C4 disc junction. Program 2 will be shifted rostrally by one contact from Program 1. Similarly, Program 3 will be shifted caudally by one contact from Program 1.

Results: Data on 50 patients is currently being collected. Primary and secondary endpoints along with medication usage and adverse events will be presented.

Discussion: The results of this prospective open label trial will provide us insight on the effectiveness of Burst stimulation in patients suffering from chronic neck pain with or without upper extremity pain.

Conclusions: Results of this study may suggest the use of Burst for cervical SCS can offer clinically significant paresthesia-free pain relief.

Poster Presentations - May 27 - May 30
Late-Breaking Research

210. INS19-0393

LIMB SURVIVAL AND QUALITY OF LIFE IN PATIENTS WITH CRITICAL LOWER LIMB ISCHEMIA IN PROLONGED PERIOD AFTER IMPLANTATION OF SPINAL CORD STIMULATION SYSTEM

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Introduction: Critical lower limb ischemia (CLLI) is a state with substantially reduced blood flow in lower extremities. Conservative therapy prognosis for CLLI is poor with first-year amputation rate up to 30–55% [1]. In patients unsuitable for surgical revascularization, spinal cord stimulation (SCS) could be used as a pain relief method for which increased limb survival was also demonstrated [2]. However, quality of life (QOL) in patients treated with SCS is studied scarcely, especially for prolonged observation period [3].

Materials/Methods: 44 patients with CLLI underwent SCS system implantation during 2012–2017. QOL was assessed using SF-36 questionnaire before and after the surgery. Mortality and limb survival were also analyzed.

Results: At baseline, median scores for physical functioning (PF), bodily pain (BP), physical (PRF) and emotional role functioning (ERF) were below 20, vitality (VT) and general health (GH) perceptions (35 and 30) were also below Russian population norms [4], social role functioning (SRF) and mental health (MH) were normal (62 and 56). After 12 months of SCS 3 patients died, one underwent below-knee amputation. In remaining 40 patients QOL increased significantly in all scales with PF, BP, PRF and ERF scoring ≥50 points, VT, GH, SRF and MH scored 50, 42, 87 and 76 correspondingly.

2–5 years postimplantation, 5 patients/representatives were unavailable, 15 patients died, 5 underwent below-knee amputation, feet survived in 19 (2 toe amputations). In these 19 patients QOL was still higher than before the surgery in all scales with significant differences for PRF, GH, ERF and SRF. Moreover, PRF, ERF and SRF were significantly higher than in general Russian population. Differences with 12 month follow-up were insignificant.

Discussion: Previously we observed significant augmentation of peripheral perfusion in CLLI patients after 12 months of SCS [5]. Here we demonstrate that this augmetation is manifested in QOL improvement and the latter sustains for a prolonged period.

Conclusions: In CLLI patients SCS significantly raised QOL in 12 months postsurgical. Despite slight decline at the 2–5 years follow-up, QOL indicators in most patients were still higher than before implantation. Limb loss rate was reduced comparing conservative therapy data.

Objectives: Analysis of QOL changes and limb survival after SCS implantation for 12 months and 2–5 years follow-up periods.

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Poster Presentations - May 27 - May 30
Late-Breaking Research

211. INS19-0222

ARE BURSTDR AND HF10 FUNDAMENTALLY THE SAME? A PROSPECTIVE, RANDOMISED, SINGLE BLIND, CROSS OVER EEG-STUDY

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Introduction: Spinal Cord Stimulation (SCS) has seen an expansion in the waveforms in recent years. There is some evidence in use of Electro Encephalogram (EEG) in analysing the brain activation. Studies by De Ridder et al (1) demonstrated that burst stimulation activates the dorsal anterior cingulate and right dorsolateral prefrontal cortex more than tonic and placebo stimulation.

It has been proposed that burst and 10KHz stimulation might both modulate the medial, lateral and descending pain pathways(2).

In order to refute or prove this hypothesis we have completed a study to analyse commonalities and differences in the EEGs of patients undergoing both Burst (5 spikes of 500Hz delivered at 40Hz) and high frequency (10KHz) spinal cord stimulation in patients with failed back surgery syndrome (FBSS)

Materials/Methods:

Patients with FBSS who meet the inclusion criteria were randomised to receive either Burst or 10KHz stimulation by a computer-generated randomisation. A baseline EEG is performed followed by 7-10 days' trial of Burst followed by 10KHz and vice versa. Two electrodes were placed using paraesthesia mapping for BurstDR and anatomical midline to T9/10 for 10 KHz. EEG data was collected with and without active stimulation at the end of the trial period for both treatment paradigms. We also collected data on numerical rating scale (NRS), patient attention vigilance score (PVAQ) and Patient Catastrophising scale (PCS) for the two groups

Results: Seventeen patients with FBSS were recruited, with 11 completed the study. There was an equal preference on the waveform by patients with no correlation to the order of stimulation. The EEG data is still being analysed by a blinded neurophysiologist and will be available for the meeting.

Discussion: This will be the first study looking at EEG changes with Burst and 10KHz stimulation in the same patients, and will demonstrate the commonalities and differences between the two treatments. Patients clearly select one therapy over the other uncorrelated to the randomised order. There is not a huge difference in the waveform preference.

Conclusions: Analysing the results of EEG

Objectives

1. Brain activation pathways
2. EEG in different waveforms
3. Mechanism of action

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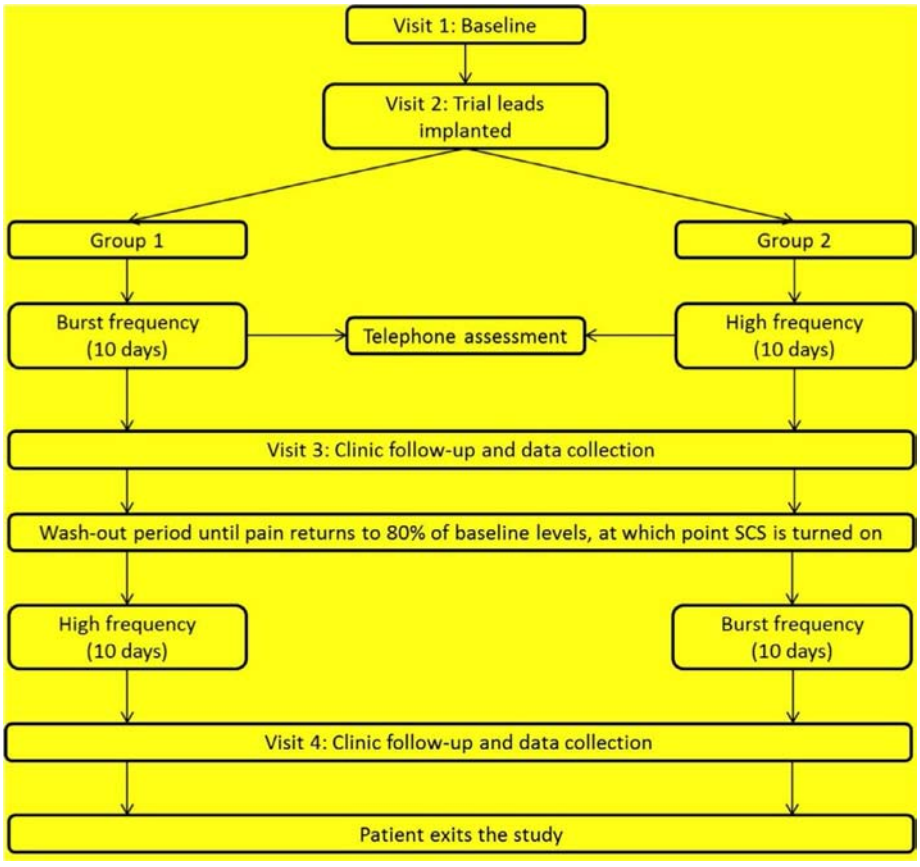

Poster Presentations - May 27 - May 30
Late-Breaking Research

212. INS19-0230

PROSPECTIVE, OPEN LABEL, PILOT STUDY: ONE YEAR RESULTS OF 10KHZ SPINAL CORD STIMULATION (SCS) FOR NEUROPATHIC BACK PAIN IN NON-OPERATED PATIENTS: THE MAIDEN-BACK STUDY

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Introduction: Persistent neuropathic low back pain (LBP) is often difficult to treat, especially when patients have exhausted standard care measures such as physiotherapy and interventional procedures. HF-SCS has been demonstrated to effectively treat chronic neuropathic low back and leg pain (Alkaisy). We present one year follow up results on our prospective Maiden-Back study in moderate to severe chronic neuropathic low back pain patients who are not candidates for spinal surgery.

Materials/Methods: Thirty-five patients enrolled and twenty subjects are active with predominant chronic neuropathic low back pain with or without radiculopathy. Outcomes including visual analog score (VAS), quality of life (EQ-5D-5L) and disability (Oswestry Disability Index - ODI) were captured and will be reported as mean $\pm$ standard deviation. Programming and follow up were carried out independently by site personnel.

Data was also collected on analgesic and anti- neuropathic drugs during this period. A structured questionnaire was used to quantify the pain as neuropathic, nociceptive and mixed. sLANSS, Pain-detect scores along with implantation details such as time taken, radiation time and dosage were collected.

Results: Back and leg pain, QoL and pain-related disability were significantly improved at 6 and 12 months compared to baseline, and medication consumption was reduced at 12 months. Baseline leg pain and health-related QoL significantly predicted change at 12 months: lower baseline scores were related to greater improvements at 12 months. Finally, patients who responded to 12 months of SCS had higher neuropathic pain scores, were in employment and had pain when standing to sitting at baseline.

Discussion: SCS (at a frequency of 10 KHz) was an effective method for improving pain, QoL, medication consumption and pain-related disability in non operated back pain patients with hyperalgesia and allodynia. Better results correlated to higher PainDetect scores and lower ODI. This study is a pilot study and further bigger randomised controlled studies will help in identifying the appropriate back pain patients for neuromodulation.

Conclusions: Our cohort has shown a very good improvement with SCS in non operated back pain selected by skin changes in the back.

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Poster Presentations - May 27 - May 30
Late-Breaking Research

213. INS19-0296

NATIONAL NEUROMODULATION REGISTRY (NNR): UNITED KINGDOM

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Introduction: Neuromodulation is a group of therapeutic modalities indicated in patients with chronic refractory pain. Despite an improving evidence base, there remains a need for long term effectiveness and safety data in the field. The NNR will document the use of neuromodulation techniques in the UK. NNR is a database is owned by NSUKI and developed in collaboration with Northgate Public Services. NNR is not an electronic record of patients. Its main function is a device registry linking with clinical outcomes which will allow for benchmarking and search facility.

Materials/Methods: The current data fields include: Demography, diagnosis, work status, EQ5D-5L, implanted device serial numbers, follow up data (including patient global effect) PGE, drug dosage for ITDD and re-operation data.

SCS, DRG and PNS for pain, Occipital Nerve Stimulation (ONS) for headache and ITDD for spasticity and pain are currently included. NNR will be expanded in the near future to include other modalities such as SNS, DBS, and Gastric stimulation.

Results: NNR is live since February 2018 with data entry from March 2018. 12 of an estimated 39 UK centres have so far entered data. Initial data is entered by clinicians following an operative interaction. Follow up data is collected electronically by a third party directly from patients by email. Currently, more than 650 patients are registered. We will present the data from March 2018 until April 2019. Data will consist of the above outcome measures for a UK national prospective cohort.

Discussion: The recent media interest on devices internationally, clearly highlights the need for device registries. With new devices and technologies being introduced, this is a key development. The Royal College of Surgeons recommended "the Government must act urgently to reform medical device regulations, including a compulsory registry of all new implants in the UK". NSUKI has been advocating the development of a national neuromodulation registry for more than a decade. Recent cross industry funding has made this exciting development possible for the next 3 years.

Conclusions: National registries are key in collecting outcome data and adverse effects both device and patient related. This will help audit the safety and availability of neuromodulation across the UK.

Objectives

National registry
Long term outcome measures
Adverse effect reporting

References

Doctors demand to see evidence on safety of medical devices approved in Europe. BMJ 2018;363:k5105

Poster Presentations - May 27 - May 30
Late-Breaking Research

214. INS19-0374

PEDUNCULPONTINE NUCLEUS STIMULATION: A NOVEL THERAPEUTIC TECHNIQUE IN INTRACTABLE EPILEPSY

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Introduction: The submission is a postulation; therefore, not structured as per required format.

Materials/Methods: The pathogenesis and management of intractable epilepsy (IE) remain a challenge to neuroscientists even today. Electrical stimulation techniques like vagal nerve and deep brain stimulations have assumed significant role as adjunctive therapies. The author postulates pedunculopontine nucleus (PPN), as a novel target for electrical stimulation as an adjunctive therapy in IE, essentially based on the strong anti-epileptic property of rapid eye movement (REM) sleep controlled by acetylcholine neurons (AChN) in the PPN, the stimulation of which is found to induce and enhance REM sleep. Even the severe EEG abnormalities (hypsarrhythmia) in West syndrome (WS) disappear during REM sleep; furthermore, in autopsy examination of cases of WS, the number of AChN in PPN in particular have been found to be reduced with relative preservation of other neurons, suggesting a specific involvement of AChN in epileptogenesis. Adrenocorticotrphic hormone is believed to decrease intractable spasms in WS not only through hypothalamo-hypophyseal-adrenal axis but also through a direct action on the pontine tegmentum probably via REM sleep and the anticonvulsant, lamotrigine, is also found to block alpha4beta2nAChRs-mediated currents. Therefore, PPN stimulation is postulated for inducing and enhancing the genesis of REM sleep throughout the night sleep time that is normally composed mainly of non-rapid eye movement fraction during which the susceptibility to seizure generation and occurrence is known to be enhanced. Involvement and functioning of the PPN in locomotion have already formed the basis of its stimulation in controlling gait impairment in Parkinson's disease.

Results: The submission is a postulation; therefore, not structured as per required format.

Discussion: The submission is a postulation; therefore, not structured as per required format.

Conclusions: The submission is a postulation; therefore, not structured as per required format.

Objectives

To provide:

1. A novel technique to control intractable seizures.
2. A natural anti-epileptic environment in the body.
3. A highly effective and safe therapy.

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Poster Presentations - May 27 - May 30
Late-Breaking Research

215. INS19-0279

NUCLEUS ACCUMBENS SHELL STIMULATION FOR CHRONIC REFRACTORY EPILEPSY AND PSYCHIATRIC COMORBIDITIES: A PROSPECTIVE, OBSERVATIONAL STUDY

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Introduction: We have demonstrated the efficacy and safety in ablating the ventromedial shell of nucleus accumbens (NAc) in drug addiction[1]. Further, we applied diffusion probabilistic tractography to subdivide the NAc into core and shell portions in individual temporal lobe epilepsy patients[2]. Recently, we and others have showed the possible role of NAc in refractory epilepsy. The safety and effect on chronic refractory epilepsy and psychiatric comorbidities of NAc shell deep brain stimulation (NAcS-DBS) were evaluated in this study.

Materials/Methods: In a case series of three patients with chronic refractory epilepsy (1 case bilateral mesio-temporal, 2 cases bilateral frontal and temporal) and psychiatric comorbidities (severe depression and anxiety), a prospective, observational study was performed to get insight into efficacy and safety of 12-month NAc shell stimulation. Seizure frequency, neurocognitive testing, Liverpool Seizure Severity Score, Quality of Life in Epilepsy Inventory, Hamilton Rating Scale for Depression (HAMD), Hamilton Rating Scale for Anxiety (HAMA), Mini-Mental State Examination and Mini International Neuropsychiatric Interview were obtained at every 3-month follow-up.

Results: Under NAc shell stimulation, all three patients had ≥50% reduction in frequency of disabling seizures. Twelve months following initiation of DBS treatment, two patients reached 50% reduction of the HAMD and HAMA. The number of hedonic activities increased significantly. Interestingly, ratings of depression and anxiety were reduced in the whole group but more pronounced in the best seizure responder.

Discussion: Connection abnormalities of the NAc shell portion and the degeneration of the NAc neurons and the aberrant distribution of neuroactive substances have been reported in patients with refractory epilepsy. These changes may be a possible pathophysiological mechanism for the involvement of NAc in epileptogenesis. Furthermore, alterations of the NAc shell may also be involved in neuropsychological change and psychiatric symptoms in patients with refractory epilepsy. Nonetheless, these observations demonstrate the multiple properties of the NAc shell and the complex relationship between the limbic system and refractory epilepsy. The NAc shell can be a new target of DBS to treat refractory epilepsy and psychiatric comorbidities.

Conclusions: We provided initial evidence for safety and feasibility of chronic electrical stimulation of the NAC shell in patients with chronic refractory epilepsy and psychiatric comorbidities, but should be validated in a large and at best randomized double-blinded trial.

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Poster Presentations - May 27 - May 30
Late-Breaking Research

216. INS19-0408

TOWARDS PRECISION PAIN MEDICINE: CHARACTERISING PERSISTENT PAIN AND ITS UNDERLYING GENETICS IN 288,118 ADULTS

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Introduction: Despite wide individual variation in response to interventions for persistent pain (PP), there is little research into genetic factors that may underlie these differences. Here we investigated the genetics of PP in >288K adults using data available in UK Biobank (applic. no. 25331). This work aims to identify novel pain biomarkers to improve the diagnosis, prognosis, prediction and treatment of PP.

Materials/Methods: PP was modelled as a binary trait, ascertained by participants' survey responses to pain occurring in any body region for more than 3 months (controls N=78,691; cases N= 209,426). A genome-wide association (GWA) analysis on this PP phenotype used a linear mixed model (BOLT-LMM) to correct for unobserved confounders and relatedness. Associations were performed while accounting for age (mean=56.38 years, SD=8.12), sex (158,890 female; 129,277 male), genotyping array and the first 10 genetic principal components (to correct for ancestry).

Results: After standard quality control, two novel independent genome-wide significant associations (P<5e-8) were identified, which mapped to genes ADAMTS6 and LEMD2 (Figure 1A). A gene-based test (p<5e-5) also revealed 17 genes associated with PP (Figure 1B).

Discussion: The current GWA study has analysed the largest number of PP cases to date. Among the novel genetic findings, ADAMTS6 also has a risk locus for inguinal hernia [1]. In a large Australian cohort (N=7K with PP [2]), we will also examine the genetics of regional pain (somatotopy), its predictability and genetic correlations with other complex traits (e.g., personality, psychiatric symptoms). This work will inform the design of large collaborative trials to assess the predictive/clinical utility of genetic testing for interventions in PP and other, often-comorbid neuropsychiatric disorders (e.g., depression, migraine, Parkinson's disease [3]).

Conclusions: Choosing a specific drug/dosage regimen and stimulation protocol based on a patient's genome is a new interdisciplinary research area for assessing medication and neuromodulation efficacy. The current

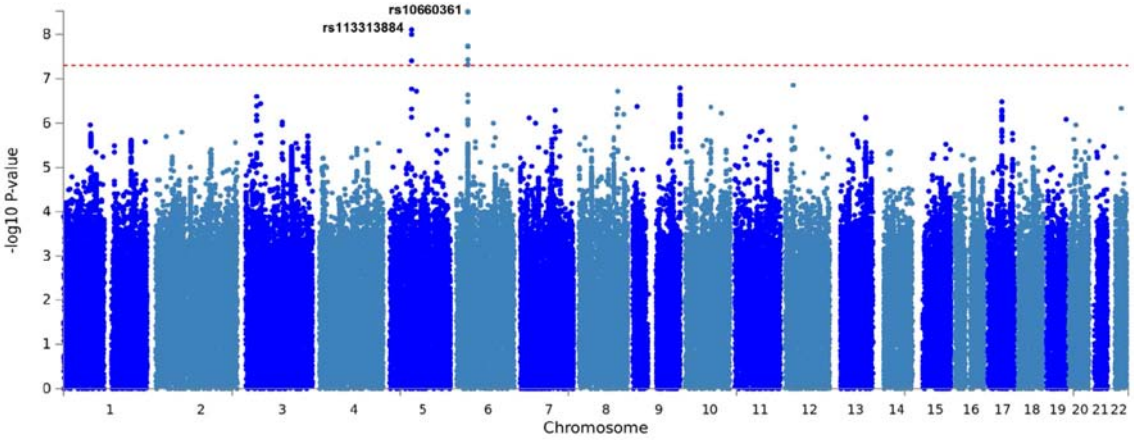

Figure 1A. Manhattan plot from genome-wide association analysis of persistent pain (PP) occurring in any body region for more than 3 months (cases N=209,426; controls N=78,691), with two novel independent genome-wide significant 'hits' or lead SNPs (single nucleotide polymorphisms) at $p<10^{-8}$ — rs113313884 and rs10660361 — mapped to genes ADAMTS6 (chromosome 5) and LEMD2 (chromosome 6), respectively.

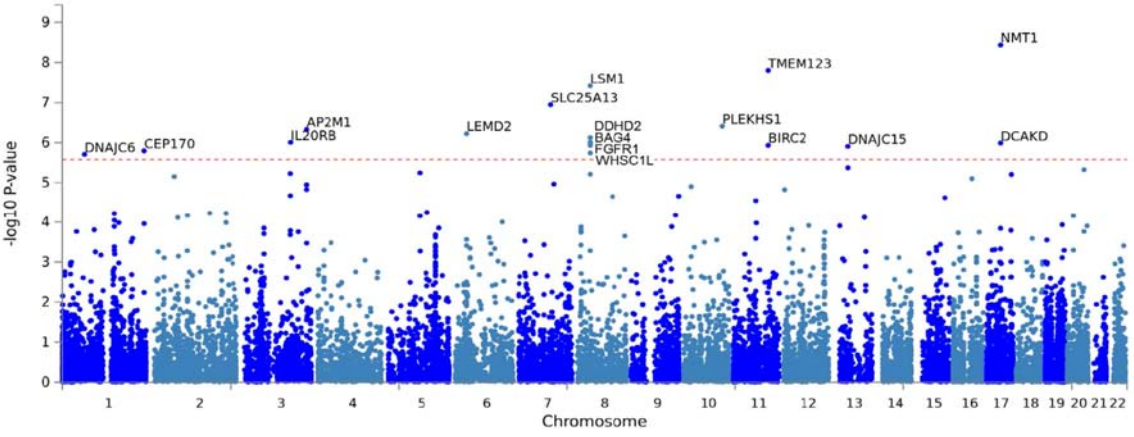

Figure 1B. A gene-based test ($p<10^{-5}$) revealed 17 novel genes associated with PP.

study has contributed to better understanding PP with the goal of achieving novel translational applications in pain medicine.

Objectives

1. Introduce statistical genetics methodologies to the neuromodulation field;

2. Stimulate establishment of large international consortia between neuromodulation researchers, geneticists/bioinformaticians, allied health clinicians & medical specialists;

3. Advance interdisciplinary translational research to improve PP diagnosis, prognosis, prediction & treatment.

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Poster Presentations - May 27 - May 30
Late-Breaking Research

217. INS19-0367

DIRECTIONAL OR OMNIDIRECTIONAL DEEP BRAIN STIMULATION FOR PARKINSON'S DISEASE: RESULTS OF A PROSPECTIVE BLINDED-COMPARISON MULTI-CENTRE CROSSOVER STUDY

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Introduction: PROGRESS is a large, prospective, multi-centre, post-market crossover study conducted to evaluate clinical performance of directional Deep Brain Stimulation (DBS). Directional leads have four ring electrodes, with the two middle rings divided into three segments. The DBS system is able to deliver omnidirectional stimulation to all three segments or directional stimulation to only one or two segments.

Materials/Methods: A DBS system with directional leads was evaluated in 66 subjects with bilateral subthalamic nucleus DBS for Parkinson's disease to satisfy European post-market study requirements. Data were collected at baseline, 3, 6 and 12 months after initial programming. Subjects were blinded to the stimulation parameters for the first 6 months. The primary endpoint was the blinded evaluation of difference of therapeutic window (the amount of current separating efficacy and side effect thresholds) in 66 subjects for directional vs. omnidirectional stimulation. Additional endpoints included UPDRS part III motor examination, quality of life, safety, subject and clinician preference and a detailed programming assessment.

Results: The primary endpoint was evaluated in 66 subjects (32% female, 63±9 years). Therapeutic window was larger with directional stimulation than omnidirectional stimulation in 59/66 subjects (89%), exceeding the 60% performance goal for superiority ($p<0.001$). Therapeutic window was 3.00±1.39 mA for directional stimulation, compared to 2.22±1.27 mA for omnidirectional stimulation ($p<0.001$). Directional stimulation required less therapeutic current strength to achieve symptom relief (1.19±1.34 mA vs. 1.70±1.51 mA). When assessed by the clinician, directional stimulation was preferred in 66% of cases (42/64), while omnidirectional stimulation was preferred in 16% (10/64).

Discussion: PROGRESS is a large prospective multi-centre experience with directional DBS. Results at the 3- and 6-month follow-up visits include larger therapeutic window and lower current required for symptom relief with directional DBS.

Conclusions: In a large clinical study, 89% of subjects experienced greater therapeutic window with directional DBS than omnidirectional stimulation. Directional stimulation also achieved symptom relief at lower therapeutic current, and was preferred by clinicians who observed both types of stimulation.

Objectives

To evaluate the efficacy of directional DBS by assessing the therapeutic window using directional versus omnidirectional stimulation.

To compare energy requirements of directional versus omnidirectional stimulation from the same DBS lead.

To evaluate subject and clinician preference after experiencing both omnidirectional and directional stimulation.

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Poster Presentations - May 27 - May 30
Late-Breaking Research

218. INS19-0182

PRELIMINARY OUTCOMES FROM A PROSPECTIVE, MULTI-CENTER, FIRST-IN-HUMAN TRIAL (NPOWER) UTILIZING A NEW BATTERY-FREE, MICROSTIMULATOR SCS SYSTEM AND NOVEL, PULSED STIMULATION PATTERN

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Introduction: A new, battery-free, micro-sized spinal cord stimulation (SCS) system has been created for the treatment of chronic pain. The system utilizes an external power source that dynamically interacts through feedback-control with a lead and small, implantable pulse generator assembly (1.5 cc volume). Preliminary testing on human factors, patient comfort and the use of a proprietary stimulation pattern has led to this first-in-human clinical study.

Materials/Methods: A prospective, multi-center, open-label clinical trial (nPower) was recently initiated to demonstrate the safety and performance of a new microstimulator in the treatment of trunk and limb pain. Specifically, subjects with leg and back pain, meeting all of the inclusion and exclusion criteria will be recruited and consented for inclusion into the study. Subjects will undergo a minimally invasive procedure to trial the new SCS system with multiple stimulation paradigms. If subjects qualify, they will continue onto the long-term implant phase and followed-up at multiple, pre-defined timepoints for up to 1 year following implantation. Clinical and usability outcomes will be obtained at baseline, out to the end of the study. Research subjects will also utilize a novel, pulsed stimulation pattern as a part of the clinical study.

Results: Four chronic back and leg pain study subjects signed informed consent and completed a 2-week trial period with the pulsed-stimulation pattern. All 4 subjects showed greater than 50% pain reduction and moved on to the long-term implant phase of the study. At the 1-month follow-up visit, the overall average pain reduction in the low back was 76%, whereas the overall pain reduction is the leg was 90%. In addition, all subjects are wearing the external power source continuously and rating its comfort below 1 on a 10-point scale.

Discussion: Conclusions: These early results demonstrate the favorable efficacy and usability of an externally powered SCS system. Study subjects are finding the external power source to be comfortable when worn 24/7, and the system, as a whole, to deliver strong clinical outcomes. These preliminary findings need confirmation in a large population of chronic pain patients.

Objectives

1. Results from a prospective, multi-center clinical study (nPower) will be reported
2. The utility and performance of a new battery-free, micro stimulator will be reported
3. Outcomes from use of a novel, pulsed SCS pattern will also be reported

References

Poster Presentations - May 27 - May 30
Late-Breaking Research

219. INS19-0407

HUMAN TRIAL OF MEDIAN NERVE ACTIVATION BY HIGH SPEED ROTATION OF A BIPOLE MAGNET CONFIGURATION

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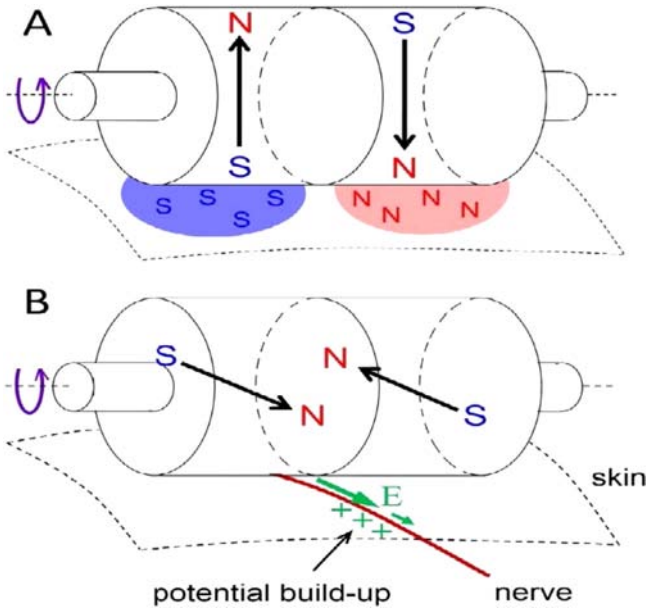
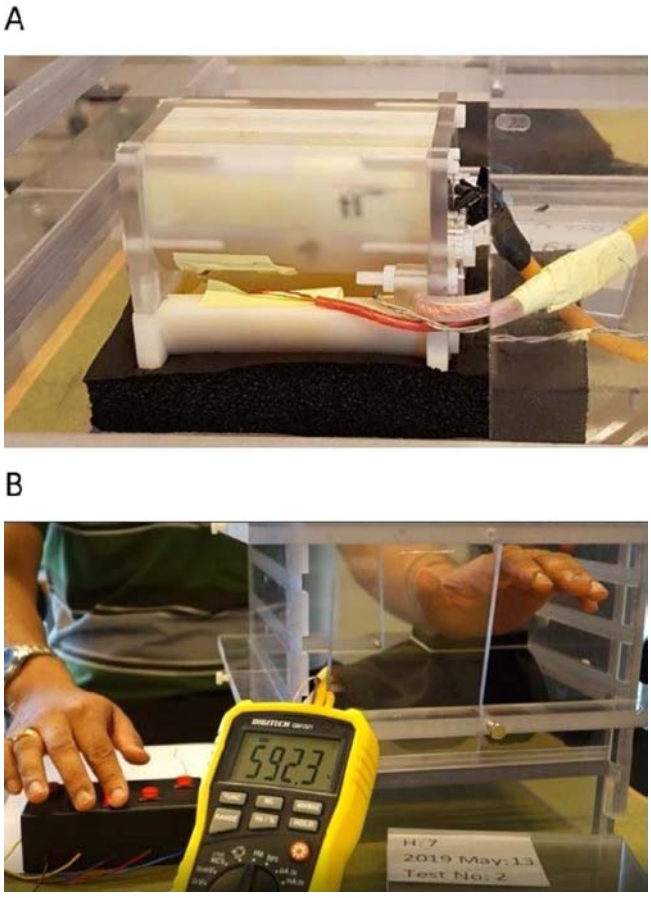
Introduction: High speed rotation of a configuration of two antiparallel cylindrical magnets has been found capable of activating an animal nerve-muscle preparation [1]. Rotating the bipole magnetic field produces electric fields within adjacent tissue (Figure 1). This paper reports a double-blind trial on activation of the median nerve at the wrist of healthy adults.

Figure 1. Figure 1. (A) Bipole magnetic field. (B) Perpendicular electric field.



Materials and Methods: The prototype device [1] was modified for control by an ESCON 50/5 with 36V supply. A spacer cap was attached to the device underside (Figure 2A) so that when inverted, the electric field was at sham level. The rotor was accelerated to 47,000rpm, held there, then decelerated, over 60s each. Institutional ethics approval was granted (UTS-HRECETH15-0084) and followed. Each participant was given a sham familiarisation run, then three tests each of active and sham orientations in random order, blind to the participant and the experimenter interacting with them. Participants continuously adjusted their wrist position and pushed buttons corresponding to fingers in which they felt sensations other than vibration (Figure 2B).

Figure 2. (A) Device. (B) Participant's non-dominant wrist perpendicular to the rotor axis of the device, under fabric.



Results: Table 1 records how often each of the n=7 participants pressed one or more buttons representing fingers 1 (thumb) to 4, enervated by the median nerve. Three of the 7 participants (43%) successfully identified all of their 6 tests. Overall, test sensitivity was 81% and test specificity 76%. The Wilcoxon sum of the signed ranks is W=15 with sample size N=5 (equal scores are not counted) [2], indicating that participants reported finger sensations for active tests more often than for sham tests at p=1/32=0.03125.

Table 1. Tests summary.

Participant	Number of active tests when button(s) pressed (max 3), *A* =	Number of sham tests when button(s) pressed (max 3), *S* =	Difference, *A* – *S* =	Signed Rank
H1	3	0	3	4
H2	1	1	0	–
H3	3	0	3	4
H4	3	0	3	4
H5	1	0	1	1
H6	3	3	0	–
H7	3	1	2	2
Sum	17	5	12	*W* = 15

Discussion: Tingling in the fingers was the most common sensation described. Over all active tests and fingers 1 to 4, the median rotation frequency when sensations were reported was 715 Hz.

Conclusions: It can be concluded, at significance level 0.05, that the median nerve sensory fibres at the wrist can be stimulated by the device. Performance will be improved by planned modifications, increasing speed and reducing vibration.

Learning Objectives

1. Inform the neuromodulation community of this new stimulation technology.

2. Report statistics on activation by the first prototype device of the median nerve at the wrist.

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Conflict of Interest Disclosures and *Acknowledgements*: PAW owns intellectual property relating to the technology (granted Chinese and US patents and pending European patent application). Device manufacture was nearly entirely funded by the University of Technology Sydney, with a very small contribution from SpinStim Pty Ltd, of which PAW is sole shareholder.

Commercial Products or Services and Off-Label Use Discussed in the Presentation: None

Poster Presentations - May 27 - May 30

Late-Breaking Research

220. INS19-0289

THE EFFECT OF HIGH FREQUENCY SPINAL CORD STIMULATION ON NEURAL FUNCTION IN CHRONIC LOW BACK PAIN: AN EXPLORATORY INVESTIGATION USING DETAILED NEUROPHYSIOLOGICAL TESTING

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Introduction: Following a prospective randomised trial reporting superiority of high frequency (HF: 10,000 Hz) over low frequency (LF, <120Hz) spinal cord stimulation (SCS) for axial low back pain (LBP)[1] the use of HF SCS has significantly increased. While the mechanisms underlying LF SCS are becoming clearer[2], our understanding of HF stimulation remains limited. Animal studies have raised concerns about the potential for long-term neural changes with HF SCS[3,4], although no definitive evidence of neural dysfunction has been found on clinical examination[1]. To further explore these concerns, a detailed quantitative assessment of neural function will be undertaken over one year, in patients implanted with HF SCS for chronic LBP.

Materials/Methods: Fourteen patients with chronic LBP (18–65 years) suitable for SCS implantation were recruited from private pain centres within NSW, Australia. Baseline assessment was performed prior to SCS trial. Patients were reassessed at 1, 6 and 12-months post implantation. Given the proximity of SCS electrodes to the spinal dorsal column[2], vibration perception was chosen as the primary outcome. Changes in vibration perception threshold (VPT) were determined using a computerised vibrameter (VSA-3000, Medoc Ltd, Israel) validated in a separate reliability study[5]. Medical history, clinical examination, quantitative sensory testing[6], nerve conduction studies (sensory conduction, h-reflex studies) and validated questionnaires[7] were also performed each time. Testing was performed after stopping SCS for 24 hours at the hand and both lower limbs. Data between time points were compared using paired t-tests.

Results: To date, eight patients (7 males, mean age 47) receiving HF SCS have data to 1-month and were included in this analysis. No statistically significant VPT changes at 1-month were observed at the hand (Δ=-0.01μm, p=0.94) and bilaterally at the first metatarsophalangeal joint (right Δ=-0.41μm, p=0.69; left Δ=0.39μm, p=0.48). *Complete **six-month data** will be available for May 2019.*

Discussion: No suggestion of dysfunction was found from nerves close to the stimulator at 1-month post implantation. Longer term data will be essential to confirm this is maintained.

Conclusions: In this exploratory study, no short-term spinal cord neurological dysfunction was detected.

Objectives

1. Outline possible mechanisms of HF SCS.

2. Discuss patient characteristics potentially increasing risk of neural injury with HF SCS.

2. Discuss the clinical application of neurological monitoring in patients receiving SCS.

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Poster Presentations - May 27 - May 30

Neuroprosthetics and Neural Engineering

221. INS19-0188

NEW APPROACH TO ABDOMINAL POCKET CREATION FOR INTRATHECAL PUMP IMPLANTATION

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Introduction: Intrathecal drug delivery systems are a popular intervention for chronic pain management.

In the conventional approach to intrathecal pump implantation, the abdominal pocket is created by making a horizontal incision in the lateral upper or middle quadrant of the abdomen and dissecting a pocket between the myofascial planes below the incision. The intrathecal catheter is inserted via a midline back incision, tunneled to the abdominal incision and connected to the pump. The pump is inserted into the pocket below the incision and secured to the abdominal wall. This approach has been well adopted worldwide. However, drawbacks include difficulty in tunneling directly to the lateral edge of the horizontal incision and sagging of the pump below its intended position.

Materials/Methods: We describe an alternative method of pocket creation that entails making a vertical incision between the subcostal margin and the iliac crest. The authors have implanted about 50 pumps in the past three years using this method. As with the well-established techniques, the patient is placed in a lateral decubitus position and intrathecal catheter placement is achieved. A vertical incision is made in the lateral abdomen. The pocket is dissected medially to the incision. The catheter is then tunneled towards the abdominal incision, connected to the pump, and implanted into the abdominal pocket.

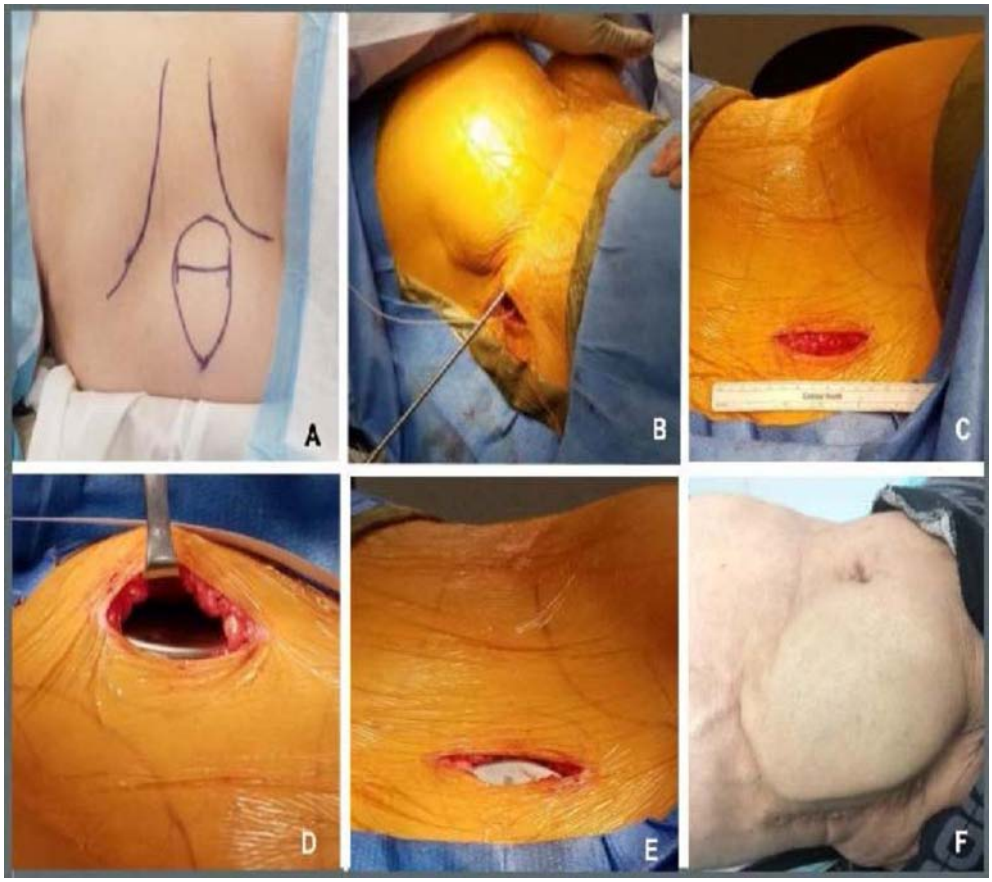
Results:
(A) Planned location of pump between subcostal margin and iliac crest
(B) Shorter catheter tunneling distance
(C) Vertical abdominal incision
(D) Pump inserted
(E) Final Pump site
(F) Example of outcome

Discussion: We believe this approach to abdominal pocket creation is advantageous for several reasons:

•This approach favors creation of a more spacious subfascial pocket with improved visualization of the surgical field.

•Tunneling towards the incision is technically less challenging as traction on the vertical incision decreases the tunneling distance. Moreover, the target of the tunneling is significantly wider, providing leeway for the proceduralist to modify trajectories.

•The vertical incision follows Langer's skin lines more so in the mid-abdomen, providing better surgical incision healing conditions.



•The direction of pocket dissection better supports pump placement, making it less likely to migrate caudally with time.

Conclusions: The approach to abdominal pocket creation we have described has yielded promising results, with improved patient and proceduralist satisfaction.

Objectives

Summarize the conventional technique for abdominal pocket creation for intrathecal pumps

Describe a new technique used for pocket creation

Discuss advantages of the new technique described above

References

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Poster Presentations - May 27 - May 30
Neuroprosthetics and Neural Engineering

222. INS19-0293

A PLATFORM FOR MACHINE LEARNING DISCOVERY OF STABLE NEURAL BIOMARKERS FOR CLOSED-LOOP NEUROMODULATION

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Introduction: BIOS has developed a neural data platform to facilitate the discovery of peripheral nervous system neural biomarkers in pre-clinical models. The platform is used to capture and synchronise months of continuous data from multiple embedded physiological sensors and bi-directional neural transducers. The data captured from these long-term, high-fidelity recordings allows us to monitor neural activity on timescales long enough to observe persistent neural biomarkers and their relation to changes in organ function in large animal models.

Materials/Methods: Herein we use sequential autoencoders to discover the underlying latent structure of acquired neural data from which we estimate neural biomarkers. The system relays biomarkers alongside physiological metadata on all subjects to a web portal to monitor the progress of the study. Using the portal it is easy to assess study endpoints, such as the response of a particular bodily variable, or neural biomarker, to a stimulation event. Neural data was collected continuously during natural mobilization of a porcine model, 15 simultaneous channels were gathered at 30 kHz across two trials: 1) A 6 week recording of the Tibial nerve, 2) a 12 week recording of the Vagus nerve.

Results: Our sequential autoencoder method was applied to 3 hours of high dimensional neural data across the recording periods to extract a lower dimensional latent space. The latent space is then put through a t-sne algorithm for display in 2D (figure), here it can be seen that each neural biomarker (cluster of points) is observed to contain neural segments (single dots) from across the recording period, indicating that the signal features pertaining to that neural biomarker can be found in a time-invariant manner.

Discussion: This work demonstrates the ability of machine learning latent space analysis to generate time invariant neural biomarkers from long term neural interfaces. The time invariant stability of these neural biomarkers over weeks to months makes them suitable candidates for triggering chronic closed loop neuromodulation treatments as they represent the activity of the neural population. This represents a significant advancement for closed loop PNS devices.

Conclusions: Stable machine learning neural biomarkers are a feasible candidate for trigger closed loop PNS treatments. This platform allows researchers to find these neural biomarkers and conduct the closed loop experiments to easily test new neuromodulation therapies on new targets.

Objectives

1) How Machine Learning can be used to understand neural data

2) Neural Biomarkers for triggering treatments

3) How researchers can implement these methods in their own work

References

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223. INS19-0388

NANO-MAGNETIC STIMULATION OF THE NERVOUS SYSTEM

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Introduction: Micromagnetic stimulation (μMS) near excitable tissue induces a localized current gradient in both time and space adequate to activate neurons, as demonstrated *in vitro* by activating retinal ganglion cells [1], and in-vivo in rodent models, using acutely implanted micro coils to activate neurons of the inferior colliculus [2]. These experiments have shown that μMS has the promise of introducing new paradigms in the stimulation of the human nervous system with several advantages over electrical stimulation. First, μMS does not require charge-balanced stimulation waveforms as in electrical stimulation. In μMS, neither sinks nor sources are present when a current is induced by the time-varying magnetic field, thus μMS does not suffer from charge buildup as can occur with electrical stimulation. Second, μMS is capable of activating neurons with specific axonal orientations. Moreover, as the probes can be completely insulated from the brain tissue, we expect to significantly reduce the problem of excessive power deposition into the tissue during magnetic resonance imaging (MRI). Our Finite Elements numerical simulations show the feasibility of nano-scale magnetic stimulation or nMS.

Materials/Methods: The Finite Element Method (FEM) is being used to study power dissipation and the induced field inside and around the nMS coils. The simulations were performed in Multiphysics 5.2 (COMSOL, Burlington MA). The geometry consisted of a solenoidal coil of 5.85 μm diameter, which is placed on top of cylinder containing physiological solution. The coil is driven with 70V voltage and have a total of 7 turns.

Results:

The preliminary results show in the left of Fig that we can generate very large B-fields strength peak of 92 Tesla using nMS coils, but mostly inside the 450nm inner diameter. The electric fields peak at over 7 V/m.

Discussion: This type of EM simulations will allow us to optimize coil design and strength for neuromodulation. Moreover, because of their ultra-small size, will allow stimulating very small unmyelinated nerve and neuronal axons.

Conclusions: nMS has the potential of a transformative impact on the applicability of non-invasive brain stimulation, as it allows for a well-controlled stimulating and mapping of the human cortex with an unprecedented resolution.

Objectives

1. optimize nano coil geometry.
2. Study peak E and B field.
3. Study electromagnetic field penetration in the tissue.

References

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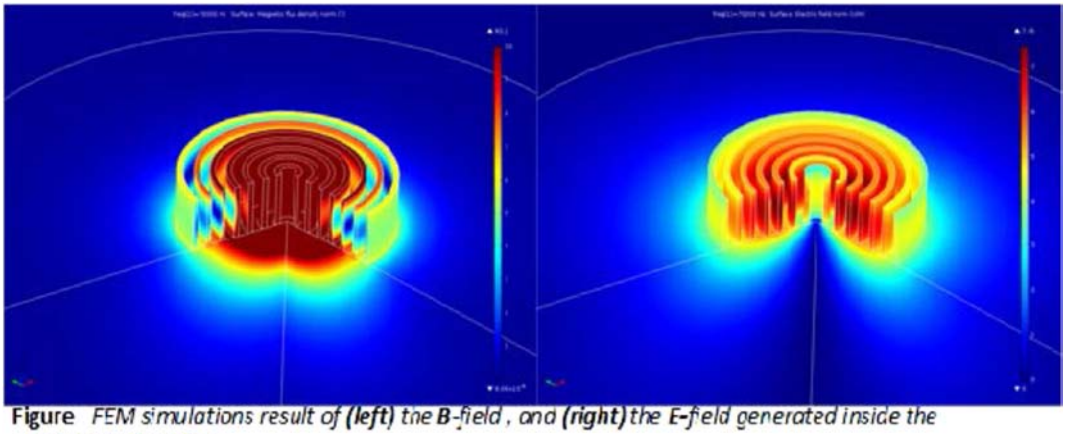

Figure *FEM simulations result of* ***(left)*** *the* ***B****-field , and* ***(right)*** *the* ***E****-field generated inside the physiological solution.*

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224. INS19-0355

TRANSCUTANEOUS NEUROMODULATION OF SPINAL CORD TO RESTORES BLADDER AND BOWEL FUNCTION AFTER SPINAL CORD INJURY

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Introduction: Following a spinal cord injury (SCI), lower urinary tract (LUT) and bowel dysfunction are universal and significantly impacts the patient's quality of life and are high priorities. Current therapies focus on managing symptoms and complications associated with LUT and bowel dysfunction without attempting to restore function. Traditionally, it is thought that bladder function resides in the cortex/brainstem (Gad et al., 2014). We have demonstrated, however, neural centers for bladder control in the lumbosacral spinal networks. This study investigates the use of non-invasive spinal cord stimulation to activate the LUT and bowel to enable recovery of function in paralyzed individuals.

Materials/Methods: Ten patients with SCI (AIS A-C) at T11 or above who relied on intermittent catheterization were recruited for a two-day period. Baseline urodynamic data were recorded, as well as urodynamic data with the stimulation to measure acute changes. Three (AIS A) returned for a 8 week study and received stimulation 3x/wk and maintained bladder diaries to track changes. Validated bladder and bowel questionnaires, urodynamic studies were collected at the beginning and end.

Results: During the initial testing period, stimulation at 1Hz delivered to T11 acutely increased voiding efficiency (42% vs 22%; $P<0.05$). Stimulation at 30 Hz at T11 increased bladder storage capacity (249ml vs 151ml; $P<0.05$). For the long-term study, there was a significant inverse correlation between average episodes of incontinence over time for all three patients (Spearman correlation = -0.641; $P<0.05$). All 3 patients reported a return of sensation of fullness of the bladder, observed as contractions of abdominal muscles or cortical sensation, thus allowing them to determine the catheterize schedule. All subjects self reported improved clinical questionnaires scores.

Discussion: 2/3 patients reported improvements in bowel movements with lower time needed to complete (75 vs 20min) or reduced reliance on digit stimulation and suppository. New sensation associated with bladder fullness allowed the patients to time catheterization cycles in a more efficient and safe manner. Moreover, the ability to void urine in on command by stimulation gave the patients an increased sense of independence and satisfaction. No adverse events were observed.

Conclusions: These data suggest the ability of non-invasive spinal stimulation to improve both bladder and bowel function in patients with SCI both acutely and long term.

Objectives

1) Induce bladder voiding
2) Improving sensation of bladder fullness
3) Non-invasive spinal neuromodulation

References

Gad, Parag N., et al. "Initiation of bladder voiding with epidural stimulation in paralyzed, step trained rats." *PloS one* 9.9 (2014): e108184.APA

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225. INS19-0395

FEASIBILITY AND EFFICACY OF ELECTRICAL STIMULATION WITH ENDOVASCULAR ELECTRODES IMPLANTED IN CEREBRAL VEINS

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Introduction: Electrical stimulation from within blood vessels provides a less invasive method to stimulate neurons in the brain. We recently developed the first chronic, endovascular, multi-electrode, stent-based brain interfacing system that elicited visible movements through direct motor cortex stimulation (Opie et al. 2018). Here, we present a systematic investigation of the feasibility and efficacy of endovascular brain stimulation.

Materials/Methods: Endovascular interfaces (Stentrodes^{TM}) were deployed in cortical veins in two sheep. After device stabilisation (> 28 days), subdural arrays were used to record brain activity during endovascular brain stimulation in anaesthetised sheep. Flash-evoked visual potentials were also acquired. Electrical stimuli were monopolar and bipolar, biphasic current pulses.

Results: Endovascular electrodes elicited repeatable responses to monopolar and bipolar stimulation. Post-mortem responses to stimulation were not significant. The mean threshold required to elicit brain responses for monopolar, biphasic stimulation with 400 μs pulse width was 2.68 ± 0.25 mA (mean ± SD; charge density ~ 243 μC/cm2). The threshold for bipolar, biphasic stimulation was 4.0 mA (charge density 362 μC/cm2). A power-law function fitted to the strength-duration curve data demonstrated a strong correlation between threshold current and stimulation pulse length ($r2=0.96$, $p << 0.01$); rheobase was 1.39 mA and chronaxie was 340.18 ms. Electrically evoked potentials provided the strongest responses on subset electrodes on the subdural grid with more focal and separate center of activation compared with visual evoked potentials.

Discussion: Neural activation was elicited by endovascular electrodes implanted chronically. Monopolar stimulation with the Stentrode activated the brain with lower currents than bipolar stimulation. However, bipolar stimulation does not require implantation of return electrodes in the brain, thus preserving a fully endovascular approach. Thresholds for neural activation exceeded safe limits. However, surface roughening may be used to increase electrode surface and increase safe charge injection limits.

Conclusions: While further research is required to optimize efficacy with varying stimulation parameters and demonstrate the safety of chronic implantation, our results indicate that endovascular stimulation may be a new approach for the design for implantable neuromodulation devices.

Objectives: Endovascular cortical stimulation evoked neural activation. Threshold for neural activation and stimulation pulse width are related by a typical power-law function. Electrically evoked activity was distinct and more focal than visually evoked activity.

References

Opie, John et al., 2018. Focal stimulation of the sheep motor cortex with a chronically implanted minimally invasive electrode array mounted on an endovascular stent. *Nature Biomedical Engineering*.

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226. INS19-0047

DEEP BRAIN STIMULATION PARAMETERS IN INTRACTABLE EPILEPSY: AN EEG BASED INNOVATIVE APPROACH

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Introduction: Since the study is a postulation, the abstract cannot be structured as per recommended format; hence, the abstract is submitted as one paragraph below.

Deep brain stimulation (DBS) of anterior thalamic nucleus (ATN) has established as an effective adjunctive therapy for patients with intractable epilepsy (IE) not suitable for epilepsy brain surgery and/or vagal nerve stimulation. The judicious selection of DBS parameters (DBSPs) plays a crucial role in the success of ATN-DBS. Conventionally, DBSPs are selected by trial and error requiring multiple sessions and hospital visits warranting a strong need for optimization of the DBSPs with objective assessment of its effects. The author presents an EEG-guided novel and superior approach to the selection of effective DBSPs targeted to induce EEG-desynchronization, which is known to exert potent antiepileptic influence with possibly possession of an additional anti-kindling effect that can suppress or even arrest the ongoing process of epileptogenesis in the patients with intractable epilepsy in addition to exercising control over the intractable seizures. It is further claimed that the innovative EEG-guided approach can successfully optimize the DBSPs resulting in (a) minimum sessions of DBSP adjustments, thereby reducing the frequency of hospital visits (b) minimum side effects and (c) minimum consumption of the device battery; thus, prolonging its life. Preliminary results of the clinical application of the novel approach in the selection of the DBSPs in a small case series have been very promising and encouraging despite which it is strongly recommended that well designed large sized studies are required for its validation and successful clinical outcome.

Materials/Methods: Not applicable.

Results: Not applicable.

Discussion: Not applicable.

Conclusions: Not applicable.

Objectives

Not applicable.

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Poster Presentations - May 27 - May 30
Neuroprosthetics and Neural Engineering

227. INS19-0349

PERSONALISED NEUROMODULATION: EARLY CHARACTERISATION OF FULLY STRETCHABLE, PATIENT-SPECIFIC ELECTRODE ARRAYS FOR CHRONIC NEURON-ELECTRODE INTERFACING

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Introduction: The intersection of engineering and medicine has the potential to provide new approaches to the treatment of human disease. This is evident in the increasing applications of deep brain stimulation, from movement disorders to psychiatric disease, and in the applications of neuromodulation to a wide variety of pathologies. Further promise has been shown by the development of neuron-electrode interfaces for the restoration of sensory and motor function following damage to the nervous system.

Despite this potential, our ability to create long-term interfaces between electronics and the nervous system remains limited by inflammatory reactions at the tissue-electrode interface and a rapid degradation in function over time. The development of stretchable electrode arrays with tailored mechanical properties represents a promising method of overcoming these limitations. By producing arrays with properties close to those of surrounding tissue, the mechanical mismatch across the interface is minimised, reducing inflammation and increasing the long-term viability of the array. However, the use of current stretchable electronic technologies remains limited by complex, inflexible production methods that limit the ability to rapidly produce custom-designed arrays for a given application.

Materials/Methods: We build on these advances by developing a novel means of producing fully stretchable, mechanically stable arrays with minimal rigid components using a rapid fabrication method that allows easy customisation of array design and small feature size.

Produced arrays are based on silicon polymer - conductive nanowire composite materials suitable for rapid fabrication and prolonged implantation.

Mechanical and electrical performance were assessed using standard characterisation methods.

Results: Using custom designed 3D printed templates, application specific arrays were produced. Arrays demonstrated mechanical stability over a range of strains, allowing stretch of up to 100% of normal length. Electrodes maintained performance over this range of strains, over high-volume stimulation and over lifetime testing in vitro.

Discussion: We demonstrate that it is possible to rapidly produce application-specific electrode arrays with mechanical and electrical performance suitable for long term implantation in challenging biological environments.

Conclusions: This supports the possibility of long-term patient and application specific implants for chronic neuromodulation. Further characterisation and in vivo assessments of functional performance will be required to fully elucidate the promise of this approach.

Objectives

Understand the limitations of current interfacing technologies
Appreciate the potential of stretchable electronics
Outline the possibility for patient-specific device development

References

Martinez V, Stauffer F, Adagunodo MO, Forro C, Vörös J, Larmagnac A: Stretchable Silver Nanowire–Elastomer Composite Microelectrodes with Tailored Electrical Properties. ACS Appl Mater Interfaces:150611145631000, 2015

Poster Presentations - May 27 - May 30
Neuroprosthetics and Neural Engineering

228. INS19-0211

HEART ACTIVITY SIGNAL ACQUISITION USING TEXTILE ELECTRODES FOR SMART HEALTHCARE

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[2]*Catholic Kwandong University, Department of Medicine, Gyeonggi Province, Republic of Korea*
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Introduction: The purpose of this study was to investigate the effect of the contact type textile electrode structure on heart activity signal acquisition for smart health care.

Materials/Methods: We devised six type textile electrodes that were different in electrode size and configuration for measuring heart activity signals using computerized embroidery, and we detected heart activity signals using modified lead II by attaching them to the chest band. We detected heart activity signals with each textile electrode for four healthy male subjects in a standing static posture and measured the signals four times repeatedly for all types of electrodes. To compare the performance of heart activity signal acquisition based on the different structures of the textile electrodes, we conducted a qualitative analysis using the signal waveform and size as parameters. In addition, we performed a quantitative analysis by calculating the signal power ratio (SPR) of the heart activity signals obtained through each electrode. We analyzed differences in the performance of heart activity signal acquisition based on the different structures of the six electrodes by performing difference and post-hoc tests with a nonparametric statistics methods on the calculated SPR.

Results: The results of the study showed that a significant difference exists in terms of both the qualitative and quantitative aspects of heart activity signals based on the specific structure of the textile electrode. Regarding the configurations of the contact type textile electrodes, the three-dimensionally inflated electrode was found to obtain better quality signals than did the flat electrode. However, regarding the electrode size, no significant difference was found in terms of the performance of heart signal acquisition for the three electrode sizes.

Discussion: These results suggest that the configuration, which is one of the two requirements of a textile electrode structure for heart activity signal acquisition, has a critical effect on the performance of heart activity signal acquisition for wearable health care.

Conclusions: Based on the results of this study, we plan to develop a smart clothing technology that can monitor high-quality heart activity without time and space constraints by implementing a clothing platform integrated with the textile electrode and by developing a performance improvement plan. Since patients suffering from posttraumatic stress (PTS) symptoms are reported to suffer from increased heart rates at rest and as a response to traumatic slides, textile electrodes combined with homecare system will provide convenient method for PTS patients to constantly monitor their heart activities and get appropriate care when needed.

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229. INS19-0381

AN IMPLANTABLE NEURAL STIMULATOR PACKAGED WITH SEMI-HERMETIC POLYMER FOR REDUCED VOLUME

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[2]*Yonsei University, Department of Neurosurgery, Seoul, Republic of Korea*

Introduction: We present an implantable neural stimulator using polymer material. Unlike conventional ones, which use metal based packaging and manually assembled electrode array, the new ones employ light weighted, polymer semi-hermetic packaging and microfabricated electrode arrays.

Materials/Methods: A liquid crystal polymer (LCP) is used as packaging material for stimulation electronics and substrate material for electrode array. It is featured with low moisture absorption rate, moderate flexibility, and compatibility with batch process. The implantable neural stimulator is an inductive link based device. An external device sends power and data through inductive link, and the stimulator receives them to generate stimulation pulses. The functionality of the fabricated stimulator is evaluated *in vitro* for wireless operation in saline solution.

Results: The size of the implantable stimulator is approximately 2.5 cm $\times$ 1 cm $\times$ 0.2 cm (width, length, thickness). In the wireless control experiment, the stimulator operated as intended, generating biphasic current pulses in accordance with incoming data. *In vivo* and long-term reliability testings are on the way, and the results will be presented at the conference.

Discussion: The electrode array is microfabricated using semiconductor process. It can be custom designed according to specific need such as spinal cord stimulation, peripheral nerve stimulation, surface(cortex) stimulation, or deep brain stimulation.

Conclusions: A miniaturized implantable neural stimulator was fabricated using a semi-hermetic polymer. Efficacy of the fabricated device was demonstrated *in vitro*.

Objectives: Material aspects of implantable neural stimulator 2. Electronics needed for wireless operation of implantable devices 3. Fabrication of microfabricated implantable devices

References

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Poster Presentations - May 27 - May 30
Neuroprosthetics and Neural Engineering

230. INS19-0382

A MULTI-FACETED NEURAL PROBE WITH SIDE AND TIP ELECTRODE CONTACTS

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Introduction: Neural probes are desired to have multi-faceted electrode contacts for full spherical sensitivity and spike sorting with triangulation. However, technological difficulty arises in fabrication of such probes because of two-dimensional nature of microfabrication process. Previously, we reported a multi-sided neural probe based on liquid crystal polymer (LCP) films laminated with heat press [1]. Here, we present advanced multi-faceted LCP neural probe having side and tip electrode contacts. Fabrication process and preliminary animal experiments are described.

Materials/Methods: The objective of the design was to record signals from most undamaged neural cells and to enhance the spike sorting. Neural probe was designed to have recording electrodes at the tip, left side, and right sides of the shank as in Fig. 1A. The electrodes were placed with tetrode-like configuration to support triangulaion in volume during spike sorting. Fabrication of the probe was facilitated with micro-electro-mechanical systems (MEMS) technology, thermal lamination process of metal-patterned LCP film, and precision laser micro-machining. Detailed fabrication steps are explained in Fig. 1B. As a preliminary study, spontaneous neural activities were recorded from retrosplenial cortex of mouse, and visually induced neural activities were also recorded. Animal experiments were approved by KAIST IACUC (KA2016-23).

Results: The fabricated probe had shank with 10 mm-length, 300 μm-width, and 300 μm-thickness. The probe could be inserted into deep brain of mouse without mechanical support. Recording electrode had dimension of 150 μm x 5 μm, and impedance of 120 ± 110 kΩ. Spikes recorded from the animal experiments were further processed as in Fig. 1C-E. Spike sorting using threshold discriminated similar waveforms from spontaneous and evoked neural activities.

Fig. 1. A) Design of the neural probe, B) fabrication process, C) spike sorting of spontaneous activities recorded with multi-facet probes, D) visually evoked activities recorded with probes having only tip electrodes, E) spike sorting of the evoked activities.

Discussion: Future works include more animal experiments with localized stimuli and enhancement of spike sorting with triangulation. The presentation poster will include the results of these works.

Conclusions: Multi-faceted neural probe could be manufactured with LCP fabrication process. Preliminary results confirmed the efficacy of the fabricated probe.

Objectives

Advantages of Multi-faceted Neural Probe with side and tip contacts,
Designed features of the device, and
Fabrication method including difficulties and limits

References

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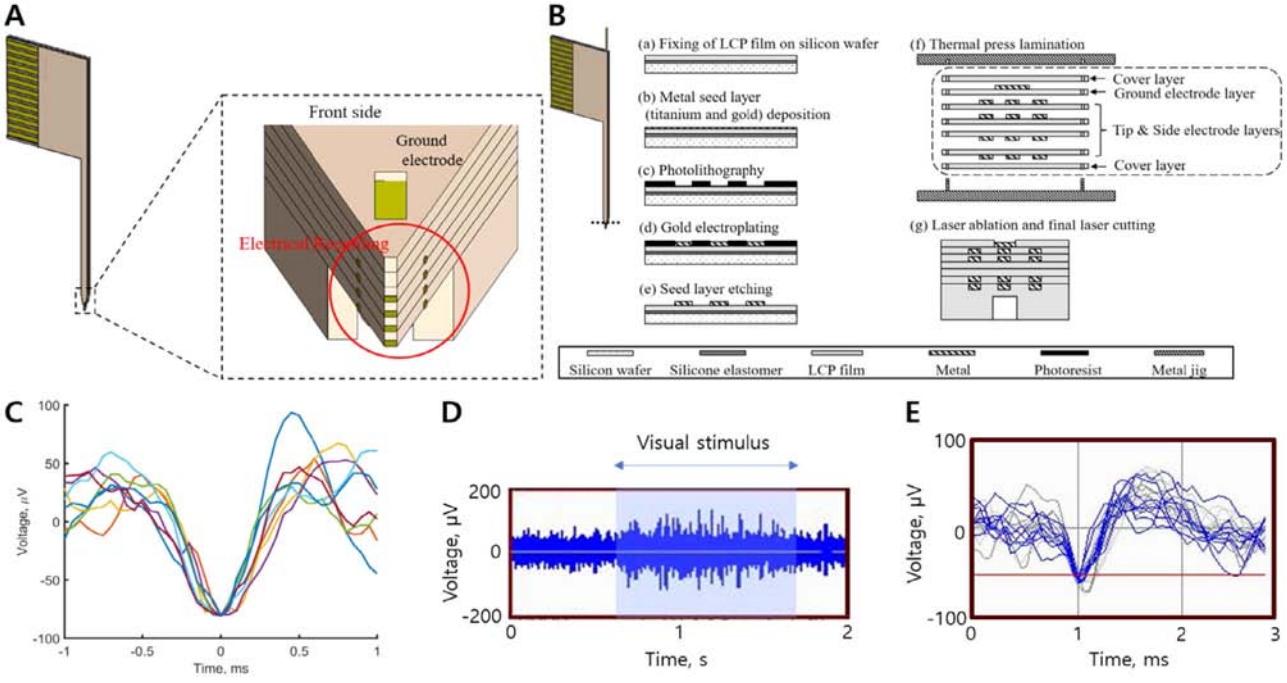

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231. INS19-0010

TRANSCRANIAL ULTRASOUND SELECTIVELY BIASES DECISION-MAKING IN PRIMATES

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Introduction: Transcranial focused ultrasound (US) has been shown to non-invasively modulate neural activity in specific regions deep in the brain [1, 2, 3]. Successful US neuromodulation has been reported by multiple groups using cell cultures and anesthetized rodents. This body of work opens the possibility that this method could be applied in awake behaving primates including humans. We used the macaque model to test whether 1) US stimulation can directly influence behavior 2) long-term stimulation is safe 3) the neuromodulatory effects are excitatory, inhibitory, or a combination thereof.

Materials/Methods: We engaged two macaque monkeys in a choice task in which the animals decided to look at either a rightward or a leftward target, whichever appeared earlier. US (270 kHz, 0.6 MPa, 300 ms) focused into either left or right frontal eye field (FEF) was applied through the intact skull and skin, 100 ms before the onset of the first target. We interleaved short blocks of trials in which US was applied and in which it was not.

Results: We found that US stimulation of left (right) FEF shifted the animals' choices to the rightward (leftward) target (see Figure 1). The effect was significant ($p < 0.01$, $n = 16$, t-test) for both left and right FEF stimulation sessions (see histograms). The contralateral nature of the effects suggests neuronal excitation within FEF.

The effect was immediate and fully reversible.

Discussion: This work shows that transcranial focused ultrasound excites neurons in macaque frontal eye fields to the extent that the effect can be observed in contralateral shifts of the animal's saccadic choice preference.

Conclusions: The finding that transcranial US can excite neurons in the primate brain to the extent that the effect is observed in behavior paves the way to noninvasive stimulation of specific brain regions in humans. Future applications of the approach will include the diagnosis and treatment of deep brain circuits involved in movement disorders, chronic pain, and depression.

Objectives

We tested whether

1) US stimulation can directly influence behavior in macaque monkeys

2) long-term stimulation is safe

3) the neuromodulatory effects are excitatory, inhibitory, or a combination thereof

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N/A.

Poster Presentations - May 27 - May 30
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232. INS19-0087

CHARACTERIZATIONS OF CLOSED-LOOP ADAPTIVE DBS IN RAT MODELS OF PARKINSON'S DISEASE

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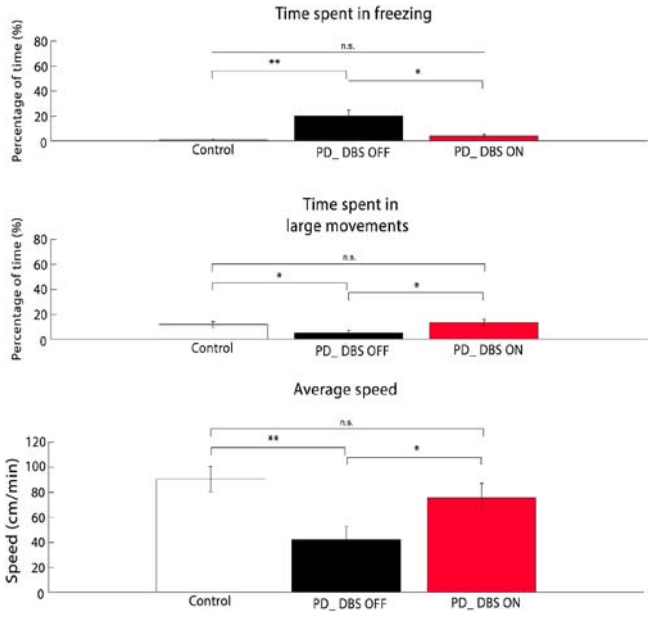
Introduction: Deep Brain Stimulation (DBS) is a known therapeutic procedure to treat Parkinson's disease. Ongoing DBS therapy needs routine calibration by clinicians to achieve the best possible therapeutic result for each individual. In contrast, adaptive DBS (aDBS) (Little et. al. 2013) triggers the stimulation on/off according to demand and tries to autonomously adjust stimulation parameters to improve efficiency. Such system would be activated and adjusted based on electrophysiological biomarkers and tremor severity and it is turned off when it's not needed, to save battery lifetime.

Materials/Methods: A closed-loop system (Castano et.al. 2017) used for recording and stimulation. Female Sprague Dawley rats, unilaterally lesioned by 6-OHDA injection into the nigro-striatal pathway are used in this study to model the known dopamine degeneration in Parkinson's disease. Micro-electrodes were implanted for recording from motor Cortex MI for recording, and subthalamic nucleus (STN) for stimulation and recording, were targeted during stereotaxic surgeries. Electrophysiological signals together with the video footage recorded during open-field test, were then used for further analysis.

Results: Behavioral analysis from open-field test shows a significant differences between control rats vs. PD rats while the DBS is off. DBS can compensate significantly, and bring the status of the PD rats more closer to the control ones. Figure 1. illustrates the behavioral results from open field test.

Discussion: Beta enhancement is a well-known marker for PD patients. We established the beta power analysis as the trigger in closed-loop DBS



(Castano et.al. 2017). It was seen that motion artifacts in freely moving rats had a large overlap with the beta frequency band, that reduced the accuracy of the trigger.

Conclusions: We conclude, a successful closed-loop system should benefit from robust biomarkers, that are independent of external interferences, like motion artifacts. The PD rat models are shown to be very useful for studying Parkinson's disease, with lower risk in comparison to human PD patients. However, it should be taken into considerations that PD rat models might not well represent the human PD. Therefore we'll continue to investigate and evaluate hemi-PD models.

Objectives

- Deepening our knowledge on how basal ganglia and motor cortex are connected.
- How DBS can influence PD rat models.
- How dopamine loss and super-sensitivity of dopamine receptors can influence brain.

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233. INS19-0141

NEURAL STIMULATION WITH AN ENDOVASCULAR ELECTRODE ARRAY

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Introduction: While direct electrical stimulation has been demonstrated to alleviate symptoms associated with many neurological conditions and disorders, access to the brain with existing electrode arrays requires risky, open-brain surgery. Removal of a portion of the skull and implantation of electrodes directly into neural tissue can cause inflammatory tissue responses, brain trauma and device failure.

We have demonstrated the feasibility of stimulating the brain with a device implanted within a blood vessel, and consequently, have mitigated the deleterious impact of open-brain surgery. The device is a **minimally invasive endovascular brain machine interface**, a stent-mounted electrode array that can be delivered via blood vessels to deep cortical regions using a minimally invasive angiographic technique.

Materials/Methods: Stent-electrode arrays were implanted over the motor cortex in eight sheep using minimally invasive angiographic techniques (1, 2). Stimulation induced responses from the stent-mounted intravascular electrodes, delivered after 4 weeks were compared to responses observed from subdural electrodes and penetrating electrodes that were inserted after open-brain surgery. Responses were evaluated, and compared to electrode location and electrode orientation.

Results: Electrical stimulation delivered with the stent-electrode array was able to elicit visually observable movements of the lip, face, jaw, neck and upper limb, consistent with responses observed from subdural and penetrating electrodes.

There was a relationship between the location of the electrodes along the superior sagittal sinus and the muscle movement for the stent-electrode array, but not for the other array types.

Electrode orientation did not appear to impact the ability of endovascular electrodes to deliver stimulation.

Discussion: We have shown that an endovascular electrode array is capable of delivering stimulation to the motor cortex and eliciting a focused response. We have also demonstrated that this can be achieved with an array suitable for delivery into cortical vessels of less than 2 mm, suitable for deep brain stimulation of regions that were previously inaccessible.

Conclusions: This work demonstrates a novel approach to deep brain stimulation that mitigates risks associated with open brain surgery. Potential applications include suppression of epileptic seizures, alleviation of Parkinson's tremor and non-invasive treatment for depression and post-traumatic stress disorder.

Objectives

1. Cortical stimulation is possible from within a blood vessel
2. Focused, deep-brain stimulation is possible with an chronically implanted stent-electrode array
3. Stimulation responses observed with a stent-electrode array are comparable to invasive electrodes.

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234. INS19-0306

THE LONG TERM EFFECT OF TEMPORARY SPINAL CORD STIMULATION FOR ZOSTER-RELATED PAIN

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Introduction: The zoster-related pain, including Acute /Subacute herpetic neuralgia(AHN/SHN), and postherpetic neuralgia(PHN), is a refractory pain that impairs the patient's quality of life (QoL), it's very difficult to achieve a good pain relief with medications for many patients because of the side effect. Therefore, it's important to find an optimal intervention treatment. We evaluated the efficacy of temporary spinal cord stimulation (tSCS) in patients with refractory zoster-related pain in this retrospective study.

Materials/Methods: A total of 102 patients who presented with AHN (n = 54), SHN (n = 31) and PHN (n = 17), and had previously failed conventional therapies, underwent tSCS treatment. Visual analog scale (VAS), Pittsburgh sleep quality index (PSQI), and analgesic consumptions were recorded before tSCS, post-tSCS 2 weeks, and 1, 3, 6, 9, and 12 months after tSCS stimulation.

Results: The VAS scores at post-tSCS, 2 weeks, and 1, 3, 6, 9, and 12 months after tSCS treatment were significantly decreased compared with the baseline score ($P < 0.001$). Sixty-six patients (64.7%, 66/102) achieved the long-term pain relief (VAS ≤ 30mm and PSQI ≤ 10), including 29 patients (28.4%, 29/102) who achieved complete pain relief (VAS = 0mm) at the time of 12 months follow-up.

24 (44.4%) patients with AHN, 5 (16.1%) with SHN and 0 patient with PHN reported complete pain relief (VAS=0 mm) at the time of 6 months follow up, the difference between the three group was significant ($P < 0.001$). After 12 months follow up, only 17.65% (3/17) patients with PHN achieved long-term pain relief, which was significantly lower compared to the AHN patients with 75.9%(41/54) and SHN patients with 70.9% (22/31) respectively ($P < 0.001$). No serious adverse effects were observed in the entire follow-up period.

Discussion: The zoster-related pain often happened in elder patients and was a challenge for pain physicians. tSCS was an alternative optimal method for the zoster related pain patients after they could not tolerated the side effect of medications.

Conclusions: tSCS is a safe, effective, and less invasive analgesic method for patients with refractory zoster-related pain. The patients with AHN and SHN could get more benefit from tSCS compared with PHN patients.

Objectives

safe

effective

no side effects

References

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Non-and less-Invasive Brain Stimulation

235. INS19-0361

MODULATORY EFFECT OF TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) ON HAND SENSIBILITY MEASURED BY OBJECTIVE QUANTITATIVE ANALYSIS DEVICE

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Introduction: tDCS facilitates or inhibits brain activity, targeting different neural networks by varying electrode placement on selected areas of the head. tDCS can modulate somatosensory processing and treat some conditions as fibromyalgia, but there are insufficient data about its effect on hand sensibility.

Materials/Methods: In a randomized, sham-controlled cross-over trial 30 healthy volunteers received 6 sessions (20 minutes each) of tDCS over 6 weeks (3 sessions over M1 and 3 sessions over S1, with 3 modes at each site: anodal, cathodal and sham). We assessed sensory thresholds (STh) using PainVision before and immediately (T0) and 30 min (T30) after each intervention. PainVision provides a steadily increasing electric current; the participant presses a stop button on first perceiving the sensation. Electrical STh is represented by CPT, defined as lowest electric current at which the subject first perceives the sensation. This research was approved by the Clinical Research Ethics Review Committee of Hiroshima University from the viewpoint of scientific, ethical and medical validity, and implemented with the permission of Hiroshima University Hospital Director.

Results: Anodal and cathodal tDCS over S1 significantly modulated hand sensibility at T0 and T30 with significantly higher STh at T30 in anodal tDCS compared to cathodal and sham. STh significantly increased after anodal and cathodal tDCS over M1. Cathodal tDCS over M1 showed significantly higher STh at T0 in comparison to anodal and sham and at T30 in comparison to sham. Sham mode did not show significant STh effects at either site.

Discussion: Our findings suggest that 1 session of anodal tDCS at S1 and cathodal tDCS at M1 significantly increased CPT, indicating a higher current needed to elicit the first sensation, suggesting increased STh and decreased sensitivity of hand to sensory stimuli. This a concept may be important for future studies in patients with hyperalgesia or allodynia.

Conclusions: Anodal and cathodal tDCS significantly modulates hand sensibility in healthy subjects.

Objectives

To assess modulatory effects of anodal tDCS on hand sensibility over S1/M1.

To assess modulatory effects of cathodal tDCS on hand sensibility over S1/M1.

To assess modulatory effects of sham tDCS on hand sensibility over S1/M1.

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236. INS19-0391

A SYSTEMATIC REVIEW OF PAIRED ASSOCIATIVE STIMULATION (PAS) TO MODULATE LOWER LIMB CORTICOMOTOR EXCITABILITY (CME): IMPLICATIONS FOR STIMULATION PARAMETER SELECTION AND EXPERIMENTAL DESIGN

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Introduction: Non-invasive neuromodulatory interventions have the potential to influence neural plasticity and augment motor rehabilitation in people with stroke. PAS typically involves the repeated pairing of pulses of electrical stimulation to a peripheral nerve, with transcranial magnetic stimulation (TMS) over the corresponding primary motor cortex (1). Efficacy of PAS in the lower limb of healthy and stroke populations has not been systematically appraised. Optimal protocols including stimulation parameter settings have yet to be determined. This systematic review examines the efficacy of PAS on lower limb CME in healthy and stroke populations whilst specifically appraising the stimulation parameters employed.

Materials/Methods: Five databases were searched for randomised, non-randomised, experimental studies evaluating lower limb PAS in healthy and stroke populations. Two independent reviewers identified eligible studies and assessed methodological quality using a modified Downs and Blacks Tool and the TMS Checklist. Intervention stimulation parameters and TMS measurement details were also extracted and compared.

Results: Twelve articles, comprising 24 experiments, met the inclusion criteria, four included people with stroke. Nine articles were considered moderate and three poor quality. Modulation of CME after a single session of PAS was reported in 21 experiments lasting up to sixty minutes. Stimulation parameter settings varied largely across experiments.

Discussion: Whilst evidence supports the efficacy of lower limb PAS in healthy and stroke populations to modulate CME within a single session, the research lacks methodological rigour. Stimulation parameters appear to influence efficacy, however the ability to draw robust conclusions about optimal parameter delivery is hindered by: 1) limited evaluation of stimulation parameter settings within and across experiments; 2) variability in the muscle contraction state during PAS; 3) inter-individual variance in the magnitude of response to PAS; and 4) the influence of the method of measuring CME on the ability to elucidate an effect.

Conclusions: Lower limb PAS research requires further investigation before considering its translation into stroke rehabilitation. Researchers should consider systematic testing of stimulations parameters, based on sound methodological research designs.

Objectives

1. To evaluate the stimulation parameters employed.
2. To appraise methodological rigor of the research.

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237. INS19-0049

DOES CEREBELLAR NON-INVASIVE BRAIN STIMULATION AFFECT CORTICOSPINAL EXCITABILITY IN HEALTHY INDIVIDUALS? A SYSTEMATIC REVIEW OF LITERATURE AND META-ANALYSIS

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Introduction: To evaluate the effects of the cerebellar NIBS on the CSE, the NIBS techniques have been divided into the facilitatory and inhibitory interventions mainly based on their effects on M1 1,2. The facilitatory interventions were expected to facilitate the purkinje cells in the cerebellar cortex, which in turn inhibits the neurons located in the deep nuclei. These neurons may decrease facilitation of thalamic neurons, which may lead to reduction of the CSE in M1. The inhibitory interventions were expected to have the reverse results.

Materials/Methods: A systematic review was carried out of studies identified through seven search engines up to June 2018. We searched for any trial evaluating the CSE before and after one session cerebellar NIBS in healthy individuals. Primary outcomes was CSE. Meta-analysis was used to pool the findings from multiple studies. Effects were expressed as mean differences (MD) and the standard deviation (SD). Risk of bias was assessed with the Cochrane tool.

Results: The meta-analysis of 26 included studies showed, paired associative stimulation (PAS) with 2 msec interval, combination of PAS and anodal transcranial direct current stimulation (a-tDCS), and repetitive transcranial magnetic stimulation (rTMS) with frequency of < 5 Hz are able to increase the CSE significantly. On the contrary, the effects of the continuous TBS and PAS with 6 msec interval decreased the CSE.

Discussion: Cerebellar NIBS is promising tool to modulate CSE and can be used as non-invasive techniques for treatment of cerebellar conditions.

Conclusions: This review indicates that the effects of different type of cerebellar NIBS on the CSE is different.

Objectives: Good understanding of how facilitatory or inhibitory cerebellar NIBS affects the CSE, will pave the way for the use of NIBS in pathological conditions. Identifying the individual effect of cerebellar NIBS techniques on the CSE is critical in picking the best technique for different needs. Since different cerebellar diseases such as cerebellar degeneration may differently affect CSE, the findings of this review might be used for restoration of the normal CSE is vital for motor control of human movements.

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238. INS19-0441

DESIGN AND IMPLEMENTATION OF A NOVEL TRANSCRANIAL ELECTROSTIMULATION SYSTEM FOR NEUROPLASTIC APPLICATIONS

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Introduction: Recently, a specific repetitive transcranial magnetic stimulation (rTMS) waveform, namely the theta burst stimulation (TBS) protocol, has been proposed for more efficiently inducing neuroplasticity for various clinic rehabilitation purposes[1]. However, few studies have explored the feasibility of using the TBS combined with direct current (DC) waveform for brain neuromodulation; this waveform is transcranially delivered using electrical current power rather than magnetic power.

Materials/Methods: This study implemented a prototype of a novel transcranial electrostimulation device that can flexibly output a waveform that combined DC and the TBS protocol and assessed the effects of the novel combinational waveform on neuroplasticity. An in vivo experiment was conducted first to validate the accuracy of the stimulator's current output at various impedance loads. Using this transcranial stimulator, a series of transcranial stimulation experiments were conducted on the brain cortex of rats, in which electrode–tissue impedance and motor evoked potentials (MEP) were measured. These experiments were designed to assess the feasibility and efficacy of the new combinational waveforms for brain neuroplasticity.

Results: Our results indicated that the transcranial electrostimulation system exhibited satisfactory performance, as evidenced by the error percentage of less than 5% for current output. In the animal experiment, the DC combined with intermittent TBS protocol exerted a stronger neuroplastic effect than the conventional DC protocol.

Discussion: These results demonstrated that the combination of electrical DC and TBS protocols in our system can produce a new feasible therapeutic waveform for transcranially inducing a promising neuromodulatory effect on various diseases of the central nervous system.

Conclusions: We have implemented the transcranial burst electrostimulator for providing electrical stimulation and detecting stimulation potential between electrodes. The current system can be miniature and extended for various applications of neuromodulation in neural prosthetic applications.

Objectives: This study provided the information of designing, implementing, and evaluating a novel transcranial electrostimulator system for neuroplastic applications.

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239. INS19-0237

QUADRILATERAL ECOG MONITORING WITH DUAL RESPONSIVE NEUROSTIMULATION DEVICES TO GUIDE RESPONSE TO ANTISEIZURE MEDICATION

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Introduction: Epilepsy afflicts 65 million people worldwide. In 1/3, seizures persist despite antiseizure medications (ASM). While resective surgery can be curative, for seizures arising from eloquent cortex, or multiple foci, resection is not an option. Responsive neurostimulation (RNS) is a treatment in this instance. Each device allows placement of 2, 4 contact electrodes, for continuous electrocorticography (ECoG) and RNS.

In patients with drug resistant epilepsy (DRE), treatment response is assessed through patient self-reporting. These data are often unreliable, leading to suboptimal management.

Materials/Methods: 30 year-old gentleman underwent placement of second RNS device, with bifrontal coverage. He initially established care 8 years after placement of RNS with bitemporal coverage, and continued to have frequent seizures. He underwent video EEG monitoring, which captured multiple seizure types with multifocal onset. The majority of seizures showed bifrontal onset, which were not captured on the bitemporal RNS contacts. After extensive review in the multidisciplinary epilepsy surgical conference, the decision was made to place a second RNS device, considered as standard clinical intervention due to the multifocal nature of his epilepsy.

Results: Two months after placement of the second device, he continued with frequent seizures. Review of ECoG revealed seizure onset in the bitemporal lobes with spread to the frontal lobes. The patient and family were interested in changing ASM, due to adverse effects and limited response. He had a history of status epilepticus; the decision was made to transition under vEEG monitoring.

Over 4 days, he was transitioned from carbamazepine to brivaracetam. vEEG revealed interictal improvement, resolution of clinical and subclinical seizures. No changes were made to RNS settings. Over several weeks, RNS data revealed a 50% reduction in seizure detection. Fewer electrographic events spread to the frontal lobes. Multiple clinical events were reported, which were not captured by RNS, suggesting they were not ictal. The RNS was able to provide objective data regarding seizure improvement with ASM changes.

Discussion: Our case represents one of two patients implanted with dual RNS devices, providing broader coverage in a patient with multifocal epilepsy. ECoG data provided objective data regarding seizure improvement after changes in ASM, and identify ictal events.

Conclusions: Longterm RNS data can determine etiology of clinical events, seizure frequency and ASM response.

Objectives

Review RNS treatment
Understand ECoG, seizure propagation
Assess ASM response

References

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240. INS19-0271

FEASIBILITY OF MINIMALLY-INVASIVE DEEP BRAIN STIMULATION USING ENDOVASCULAR FOCUSSED ULTRASOUND

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Introduction: Existing Deep Brain Stimulation (DBS) systems require a craniotomy for implantation and precise placement within a target brain region. Furthermore, electrical charge spread and diffuse stimulation may miss the target neural population [1]. To overcome the limitations of existing DBS systems, we propose an endovascular focused ultrasound (EFUS) array. Focused ultrasound has the potential to stimulate deeply and precisely into neural tissue and to mitigate issues of lead misalignment [2]. Achieving a tight focal point requires ultrasound frequencies in the MHz range and may be achieved from within a blood vessel.

Materials/Methods: Major veins in the human brain were mapped from the MNI152 brain [3,4] and compared with coordinates of known DBS targets [5] to determine the minimum distances between neural stimulation targets and veins. Different designs of EFUS arrays were simulated, with focal lengths equal to the minimum distances between veins and targets, using FOCUS and COMSOL Multiphysics, to determine their ability to produce focal stimulation.

Results: The subthalamic nucleus and internal globus pallidus were assessed to be the closest targets to any of the mapped blood vessels, just 8.5mm and 6.1mm from the basal vein of Rosenthal, respectively. Simulations demonstrated that the volumes of tissue stimulated in the target regions were potentially smaller than can be achieved by existing electrical DBS systems.

Discussion: DBS by EFUS may be feasible for treating Parkinson's disease and other neurological conditions. Experiments are now underway to validate the simulation results.

Conclusions: EFUS may be a feasible DBS technique that supersedes existing technology.

Objectives

(1) Determine anatomical limitations of endovascular DBS

(2) Understand the design parameters affecting feasibility DBS by EFUS

(3) Understand the potential advantages and limitations of EFUS compared with existing DBS techniques

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241. INS19-0348

MODULATION OF AUDITORY ATTENTION PROCESSING USING TRANSCRANIAL DIRECT CURRENT STIMULATION

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Introduction: The ability to selectively direct our attention to a given sound source is essential to normal communication and to making sense of the complex auditory world, with disorders of auditory processing resulting in a profound impairment in normal functioning.

Recent evident has implicated an area of the left temporal cortex in the processing of auditory attention (Power et al., 2012), identifying this as a promising target for attentional neuromodulation. Furthermore, recent advances in EEG processing techniques have allowed measures of the neural representation of stimuli to be derived from continuous single-trial data (O'Sullivan et al., 2015), allowing objective assessment of the modulation of auditory processing.

Materials/Methods: We manipulated activity in left temporal cortex using transcranial direct current stimulation. Attention was assessed using a dichotic listening task. Attentional performance was measured using a behavioural task with questions on speech content.

We investigated the impact of stimulation on the underlying neural processing using a tDCS-EEG paradigm through reconstruction of the attended stimulus envelope from EEG data using decoders trained on all other trials in leave-one-out cross-validation approach, with comparison of the reconstructed envelope to that of the original stimulus.

40 subjects were assessed over 30 trials under 1mA anodal and cathodal stimulation using a within-subjects crossover design, with random assignment to anodal or cathodal stimulation.

Results: We show changes in behavioural measures between stimulation conditions, as well as alterations in the ability to reconstruct stimulus representations from simultaneous EEG data, indicating changes in the underlying processing.

Discussion: This demonstrates polarity-dependent modulations of attentional performance in a dichotic listening task as well as a selective enhancement of the representation of features of the attended auditory stimulus in simultaneously recorded electrophysiological data.

Conclusions: This represents causal evidence of the proposed role of the left temporal cortex in attentional processing, and potentially identifies this area as a novel target for therapeutic neuromodulation for the rehabilitation of attentional deficits. Further assessment will be necessary in patients with existing deficits to clarify any potential therapeutic benefit.

Objectives

Appreciate the potential for noninvasive neuromodulation for attentional processing

Understand the investigation of modulation of neural processing using combined tDCS-EEG

Outline the potential for targeted tDCS-EEG approaches for functional assessment of cortical areas

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242. INS19-0207

EFFECTS OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION ON LOWER LIMB MOTOR FUNCTION AND GAIT SPEED IN STROKE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction: Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive brain stimulation utilized for modulating cortical excitability. Previous studies showed positive correlations between activation of ipsilateral sensorimotor cortices and improvement in ambulation, yet no study has systematically reviewed the effects of rTMS on lower-extremity and gait function in stroke. Thus, we investigated the effects of rTMS on lower-extremity function and gait velocity by a systemic review and meta-analysis.

Materials/Methods: We performed a systematic search in PubMed, PEDro, Medline, and Cochrane to identify the related publications from year 2012 to 2018.

Results: Among 115 screened titles and abstracts of studies, 8 were included in the review (n=190) and 6 of which were used for meta-analysis (n=124). Lower-limb motor function improved in rTMS group, including high-frequency alone, low-frequency alone, and combined with exercise as compared to sham stimulation. We also found the rTMS exerted benefits in lower-limb motor function for individuals with either short < 6 months or long > 6 months post-stroke duration. Significant improvement of walking velocity in the rTMS group, despite high-frequency or low-frequency stimulation was also demonstrated.

Discussion: According to the included studies, the high-frequency rTMS was applied bilaterally or ipsi-lesionally, yet the low-frequency rTMS was only applied contra-lesionally for lower-extremity recovery. In addition, rTMS could be applied alone or in combination of exercise for lower-extremity motor function. rTMS in both frequency seems to be safe for individuals with stroke due to no severe adverse effect during or after rTMS application.

Conclusions: The application of rTMS for improving lower-limb motor function and gait velocity in stroke survivors is supported. Well-designed studies with larger sample sizes are needed to validate the effectiveness of the rTMS regarding its parameters, combining effects, and induced brain changes.

Objectives: This study enables the delegates to (1) systematically understand the application of rTMS on lower-limb function and walking ability and (2) know further about the variations in rTMS parameters, and hopefully (3) this study could provide support for the use of rTMS in lower-limb motor recovery and gait speed.

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243. INS19-0266

THE EFFECT OF CEREBELLAR TRANSCRANIAL DIRECT CURRENT STIMULATION ON MOTOR LEARNING IN HEALTHY ADULTS: EARLY RESULTS OF AN RCT

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Introduction: Motor skill acquisition requires training and repetition to result in permanent change in performance. Anodal cerebellar transcranial direct current stimulation (ctDCS) can enhance acquisition of motor performance, however, evidence for the efficacy of this method beyond transient changes is limited (1). This study examines the effect of ctDCS on motor learning in healthy adults performing a novel split-belt walking task.

Materials/Methods: In a double-blinded RCT (Institute Ethics Committee: 16/338), thirty healthy adults were randomly allocated to sham or real anodal ctDCS (2mA) groups. The number of strides to steady-state performance on the split-belt treadmill was assessed as the participants received the intervention over three consecutive days and again one week later without intervention. Data was analysed using a linear mixed model, with height as a co-variate, and a participant-wise random effect.

Results: Group analysis revealed no significant difference in the number of strides to steady-state performance in either group (p=0.19).

Discussion: This study evaluated for the first time the effect of ctDCS following a multi-day stimulation protocol. Anodal ctDCS did not result in faster gains to steady-state performance compared to sham. A possible explanation for these results could be that repeated exposure to the same task may not provide sufficient stimulus to necessitate cerebellar contribution (2).

Conclusions: ctDCS did not enhance motor learning. However, these findings need to be validated in a protocol with increasing task difficulty.

Objectives

1. To determine if multiple ctDCS sessions result in faster achievement of steady state performance.
2. To establish permanence of ctDCS effects.
3. To have a greater understanding of ctDCS effects on the healthy brain to improve protocols for future studies.

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244. INS19-0483

EFFECTIVENESS OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION AND VISUAL FEEDBACK EXERCISE ON NEUROPLASTICITY AND LOWER LIMB FUNCTION IN PERSON WITH CHRONIC STROKE

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Introduction: Stroke is one of leading cause of long-term disability and affects cognition function, walking ability, balance, functional activity, quality of life and etc [1]. Repetitive transcranial magnetic stimulation (rTMS) and visual feedback exercise (VFE) are both important issues in the advanced rehabilitation medicine [2,3]. Therefore, the aim of this study is to investigate the effect rTMS and VFE technologies on cortical excitability and walking ability in persons with stroke.

Materials/Methods: Fifteen subjects with chronic stroke participated in the study. Participants were allocated to three groups: rTMS and VFE group, sham rTMS and VFE group, as well as sham rTMS and traditional rehabilitation group. All participant underwent three week, 3 sessions per week, and 30 minutes per session intervention. Motor evoked potential (MEP), Fugl-Meyer Assessment (FMA), and Timed Up & Go Test (TUG) were assessed before and after intervention.

Results: Baseline characteristics were similar among three groups. rTMS and VFE training shorten the latency of MEP and completing time of TUG. Sham rTMS and VFE intervention shorten the latency of MEP and had a trend of improvement in TUG and FMA scores. Sham rTMS and traditional rehabilitation showed a trend of improvement in MEP, TUG, and FMA scores.

Conclusions: These results imply that rTMS and VFE training may have a potential to enhance the cortical excitability and walking ability in individuals with chronic stroke. However, large population and longer time of intervention are necessary in future studies. Key words: stroke, repetitive transcranial magnetic stimulation (rTMS), visual feedback exercise (VFE)

Objectives: This study provided 1. the information of designing and implementing novel visual feedback system 2. assessment of the effects of repetitive transcranial magnetic stimulation and visual feedback exercise 3. the measurement of motor evoked potential.

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245. INS19-0204

CURRENT PRACTICES OF ELECTROCONVULSIVE THERAPY IN MENTAL DISORDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF COGNITIVE EFFECTS

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Introduction: Electroconvulsive therapy (ECT) remains one of the most effective treatments for major depressive disorder, but stigmatisation and fear of cognitive side effects limit its use. Uncertainties persist regarding the best cognitive tests to be included in ECT clinical routine. The current meta-analysis aimed to review the most frequent immediate, subacute, and long-term cognitive effects post-ECT.

Materials/Methods: We searched for English or French-language studies published between 2000-2017 with the terms: "Electroconvulsive Therapy", "Electroconvulsivotherapy", or "electroshock[s]" and "innocuity", "adverse effect [s]", "side effect[s]", "cognitive", "neuropsychology", or "neuropsychological".

Quantitative studies measuring cognition before ECT and at least one time after ECT using standardized tests were included. There was no exclusion based on diagnosis, age, psychical/psychiatric comorbidities or ethnicity. We excluded research on animals and studies using sine wave.

The review protocol was registered on PROSPERO (CRD42018085654).

Results: Ninety-one studies, with a total of 3762 individuals were included in the meta-analysis. Twenty-nine standardized cognitive tests were separated into 10 different cognitive domains for analysis. Comparisons between cognitive measures included pre-ECT baseline with post-ECT cognitive measures at 3 times: a) Immediate effects (within 24h post-ECT=P01), b) Subacute (within 1-month post-ECT=P02), and c) Long-term (more than a month post-ECT=P03).

Discussion: Although studies showed high heterogeneity, subacute effects indicated that post-ECT, individuals present cognitive decline as indicated by a decrease in autobiographical memory, verbal fluency, and verbal memory. Conversely, executive functions improved significantly post-ECT. The impact on verbal fluency showed an inverse correlation with age, being significantly greater in people under 60 years-old.

Long-term effects showed an improvement on almost all cognitive domains.

Conclusions: This is the first meta-analysis focusing on modern ECT practices. The results are consistent with the previous literature. The relationship between verbal fluency and age had not been previously described. It seems important to assess verbal fluency, especially in younger patients, and the autobiographical memory. The most common test, MMSE, failed to show any cognitive effects of ECT.

Objectives

Review the most frequent cognitive effects of current practices of ECT in individuals with mental disorders

Explore the different population at higher risk of cognitive deficits

Explore the best cognitive tests for clinical practice in ECT

References

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246. INS19-0424

EFFECT OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION ON A PATIENT WITH MAJOR DEPRESSIVE DISORDER: CHANGES OF SERUM NEUROTOPHINS LEVELS

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Introduction: While the antidepressant potential of repetitive transcranial magnetic stimulation (rTMS) is widely recognized [1], the impact on neurotrophins related to major depressive disorder (MDD) has not been fully investigated in humans. [2]. We probed rTMS on refractory depression and serum levels of some neurotrophic factors.

Materials/Methods: A 41-years old MDD patient underwent TMS-Motor Evoked Potentials (MEPs) from the right first dorsal interosseous muscle with a figure-of-eight coil, at baseline and after 2 weeks of high-frequency (10 Hz) rTMS at 120% of resting motor threshold over the left dorsolateral prefrontal cortex. Serum brain-derived growth factor (BDNF), vascular endothelial growth factor (VEGF), and Endothelin-1 were measured by Enzyme-Linked Immunosorbent Assay. Mouse monoclonal specific antibodies were used for detection, followed by horseradish peroxidase-conjugated goat anti-mouse IgG secondary antibody and using enhanced Western Lighting Chemiluminescence Reagent Plus. Changes in protein levels were then evaluated by imaging and densitometric analyses. The Ethics Committee of the "Azienda Ospedaliero-Universitaria Policlinico-Vittorio Emanuele", Catania (Italy), approved the study (N. 9/2018/PO).

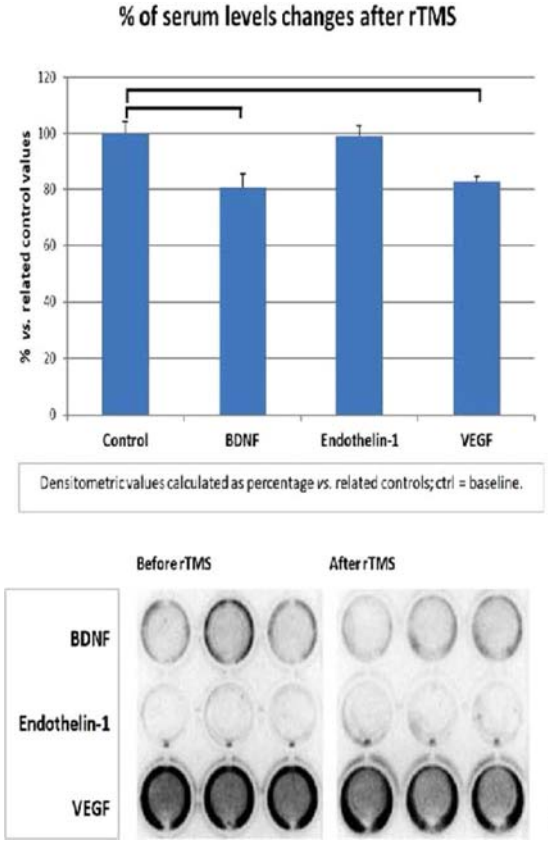
Results: Clinical improvement of depression was observed. Compared to baseline, MEPs amplitude increased by 54%, central motor conduction time decreased by 32%, and cortical silent period shortened by 12%. BDNF and VEGF significantly reduced by 20% and 18%, respectively (Figures), while Endothelin-1 was unchanged.

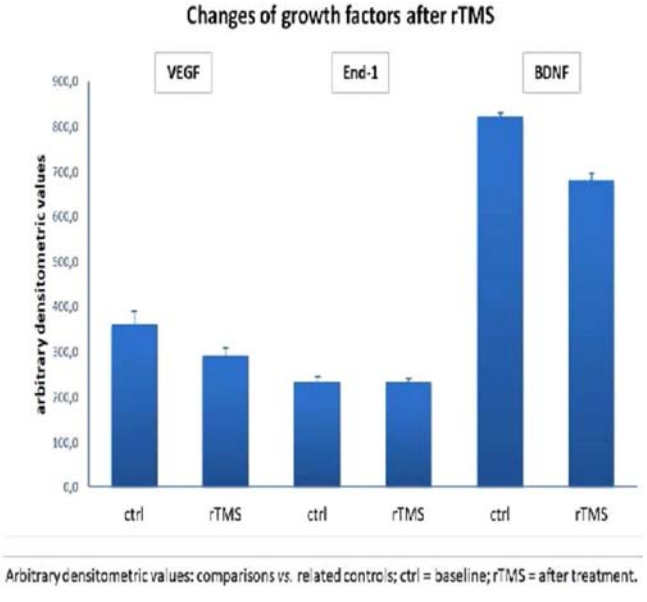
Discussion: A more excitable motor cortex and cortico-spinal tract was found, supporting the hypothesis of left-sided frontal hypoexcitability in MDD and the role of rTMS in balancing this asymmetry [1]. Several studies demonstrated an increase of VEGF in depressed patients [3], therefore its decrease after rTMS can predict treatment response, possibly due to changes in tissue secretion or blood-brain barrier permeability. Although drugs and electroconvulsive therapy can increase BDNF in depression, a recent meta-analysis showed that rTMS does not increase peripheral level [4]. Therefore, its suitability as an index of antidepressant response and neuroprotective factor requires further understanding [5,6].

Conclusions: Though obtained from a single patient, neurotrophins are involved in the pathophysiology of depression and antidepressant effect of rTMS. Future trials with homogenous populations, wider neurotrophins dosages, randomized controlled protocols, and follow-up assessments are needed.

Objectives

rTMS feasibly explores cortical circuit neuroplasticity and neurochemical pathways in mood disorders. This intervention led to modulation of VEGF and BDNF, although the involvement of Endothelin-1 cannot be excluded.





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247. INS19-0318

PROPAGATION OF TMS-INDUCED EEG PHASE-LOCKED INFORMATION FOR ASSESSMENTS OF MAJOR DEPRESSION

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Introduction: Neuromodulatory techniques such as electroconvulsive therapy (ECT) have been used for the treatment of major depressive disorder (MDD). However, it remains unclear about the detailed neural mechanisms of both ECT and MDD. To evaluate the therapeutic effects of neuromodulation, we focused on neuromodulation-induced functional changes with the combination of transcranial magnetic stimulation and electroencephalography (TMS-EEG). Recent TMS-EEG study demonstrated the propagation of the effect of single-pulse TMS-induced phase resetting from visual to motor areas by calculating the phase locking factor (PLF) [1]. This study attempted to explore the relationship between the TMS-induced PLF changes and clinical changes of depression induced by ECT in patients with MDD.

Materials/Methods: Ten patients with MDD completed all experiments. Disease severity was evaluated using Montgomery–Åsberg Depression Rating Scale (MADRS) before and after ECT. Single-pulse TMS was applied to the visual areas to induce phase propagation in the visuo-motor network at eye-closed resting state. We used the visual (TMS-targeted area) and motor (TMS-distant area) PLFs to measure local synchronisation ability and network-mediated local synchronisation ability, respectively.

Results: All patients showed transient enhancements of PLFs of visual areas in alpha bands (9-12Hz) at both pre- and post-ECT. In contrast, the PLFs of motor areas showed small alpha transient enhancements in patients with high pre-ECT MADRS scores. The alpha PLF of motor areas were negatively correlated with MADRS scores at pre-ECT, but not at post-ECT. The differences in alpha motor PLFs between the pre- and post-ECT were negatively correlated with differences in MADRS scores between pre- and post-ECT. Moreover, the time differences of alpha PLF peak latencies on the post-ECT were significantly and positively correlated with MADRS scores.

Discussion: The negative correlation between pre-ECT TMS-induced PLF at the motor area (i.e. transmission intensity) and the severity of depression suggests that ECT-induced network alterations are more prominent in patients with moderate or severe symptoms of depression. Moreover, the differences in PLF peak latencies between the two areas, which represent the time of propagation in the network, suggest that the speed of information transmission decreases in MDD and that ECT increases this transmission speed.

Conclusions: The transmission intensities and speeds of TMS-induced PLF within visuo-motor networks is useful to assess moderate or higher depressive states.

Objectives: Evaluation of the therapeutic effects of neuromodulation.

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248. INS19-0301

ENHANCED FUNCTIONAL CONNECTIVITY WITHIN PRIMARY MOTOR CORTEX CORRELATES WITH PAIN RELIEF INDUCED BY REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (RTMS)

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Introduction: We have previously suggested that rTMS of an alternative M1 site provides comparable pain relief to that from rTMS of the conventional "hotspot"(1). The analgesic effect of rTMS is thought to be related to its interference with pain-related cortico-cortical and cortico-subcortical processes. We hypothesised that the greater the coupling between each M1 stimulation site and the connecting structures the better the resultant pain relief.

Materials/Methods: The subjects were 14 patients with chronic unilateral neuropathic pain who, as part of a randomised, sham-controlled two-way cross-over rTMS trial on neuropathic pain (1), underwent resting-state fMRI at baseline. Five sessions of rTMS (10Hz at 90% resting motor threshold; 2000 pulses) were delivered over two M1 stimulation sites: (i) the conventional "hot spot" and (ii) an alternative site within M1 (representing an area of cortical reorganization); for the sham the interhemispheric fissure on the vertex was targeted. Total pain reduction at 1 week after each 5-session cycle was calculated from patients' daily pain scores. Based on the pain outcome, either M1 site was categorized as 'optimal' (OS) or 'non-optimal' (N-OS).

For the fMRI analysis, OS and N-OS were used as connectivity seeds, alongside with the sham stimulation site and two corresponding contralateral M1 sites (cl OS and cl N-OS). The CONN Toolbox was used to generate Individual connectivity maps which were implemented in a correlation analysis with pain reduction scores.

Results: Median pain relief after rTMS of OS was 16% (range 44% to 5%), N-OS 1.3% (10% to -13%) and sham 1.4% (34% to -11%). Pain relief strongly correlated with functional connectivity of the OS site with a cluster located deep in anterior bank of precentral gyrus (maxima -28, -22, 50 at MNI space), r=0.91, p<0.001. Correlation maps regarding other sites (sham, cl OS, cl N-Os) failed to show any significances.

Discussion: The present results suggest that functional connectivity within M1, itself dependent on the exact stimulation site, is a key factor determining the analgesic effect of rTMS. Future studies will be conducted to see if resting state fMRI combined with trial rTMS sessions can be used to identify an optimized stimulation site for an individual patient with neuropathic pain.

Conclusions: The analgesic effect of rTMS is related to functional connectivity within M1

Objectives: The attendees will learn how the mechanisms of non-invasive brain stimulation can be investigated using resting state fMRI and that for rTMS induced pain relief, "target site matters".

References

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249. INS19-0291

IMPROVEMENTS ACROSS FUNCTIONAL OUTCOMES IN PATIENTS TREATED FOR CHRONIC BALANCE DEFICIT AFTER MILD-TO-MODERATE TRAUMATIC BRAIN INJURY WITH TRANSLINGUAL NEUROSTIMULATION

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Introduction: Noninvasive translingual neurostimulation (TLNS) primarily stimulates cranial nerves V and VII and is a novel therapy for brain injury. Improvements in chronic balance deficits have been observed in patients with mild-to-moderate traumatic brain injury (mmTBI) after treatment with TLNS plus targeted physical therapy (PT).[1] This subanalysis evaluated whether-improvements in posturography correlated to improvements in gait and other functional assessments.

Materials/Methods: Patients with mmTBI-related balance and gait deficits who had mmTBI ≥1 year, balance impairment (NeuroCom® Sensory Organization Test [SOT] composite equilibrium score ≥16 points below normal, after adjustment for age), and who failed conventional PT were enrolled in a double-blind, randomized controlled trial.[1] Patients received TLNS with the investigational Portable Neuromodulation Stimulator (PoNS®) plus a 5-week targeted protocol, including in-clinic and home-based vestibular PT and breathing and awareness training. The primary analysis compared outcomes of both high- and low-frequency stimulation. Least squares mean differences were calculated for SOT responders (increase of ≥15 points after 5 weeks of treatment) and nonresponders for patient demographics, symptom scores, functional balance assessments, and cognitive performance. Participating institutional review boards approved the study.

Results: 82 of 122 enrolled patients were SOT responders (67.2%). Significantly better functional outcomes were observed for responders than for nonresponders for the 6-minute walk test (P=0.0010), Dynamic Gait Index (P=0.006), Quality of Life Measure Index (P=0.0433), reaction time (P=0.0039), and Scaled Delis–Kaplan Executive Function System Trails letter sequencing (P=0.0426). Post-concussion score (P=0.0893) and California Verbal Learning Test free recall (trial 5, P=0.0583; list B, P=0.0699) and long-delay (cued, P=0.0556; yes/no, P=0.0513) scores approached, but did not reach statistical significance.

Discussion: Persistent symptoms and functional deficits are often linked to impairment after injury, such as balance impairment after mmTBI, but current treatment may not give broader improvement. This subanalysis demonstrates that gains in posturography during a clinical trial were accompanied by improvements in gait and other functional areas.

Conclusions: TLNS plus targeted therapy can significantly improve symptoms of mmTBI-related chronic balance deficit. This subanalysis indicates that patients who respond to TLNS plus targeted therapy with improved SOT scores are also likely to demonstrate significant improvements in gait and other functions, in addition to improved quality of life.

Objectives

Correlate recovery of balance and gait deficit

Determine how balance improvements are linked to other functional outcomes

Understand how improved balance correlates with quality of life

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250. INS19-0108

PREDICTING THERAPEUTIC RESPONSES TO CRANIAL NERVE NONINVASIVE TRANSLINGUAL NEUROSTIMULATION IN PERSONS WITH MILD-TO-MODERATE TRAUMATIC BRAIN INJURY USING POOLED DATA FROM TWO RANDOMIZED CLINICAL TRIALS

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Introduction: Two randomized clinical studies[1,2] have investigated the treatment of chronic balance deficits after mild-to-moderate traumatic brain injury (mmTBI) using noninvasive translingual neurostimulation (TLNS), to primarily stimulate cranial nerves V and VII, combined with targeted therapy. Pooled study data were used to investigate predictive factors for treatment response.

Materials/Methods: Enrolled subjects had: 1) an mmTBI ≥1 year; 2) plateaued in conventional physiotherapy (PT); 3) shown a significant balance impairment (NeuroCom® Sensory Organization Test [SOT] composite score ≥16 points below normal, after adjustment for age). High- and low-frequency stimulation conditions in both studies were pooled for this subanalysis. Subjects received TLNS plus targeted PT (investigational Portable Neuromodulation Stimulator [PoNS®] treatment) for 5 weeks. Logistic regression analysis (LRA) of the 5-week data was performed for those subjects showing a significant improvement in SOT score (≥15-point increase from baseline to 5 weeks; n=82). Variables assessed included: age; sex; days since injury; baseline SOT, dynamic gait index (DGI), and Pittsburgh Sleep Quality Index (PSQI); and Headache Disability Index (HDI). Odds ratios (ORs) were also calculated.

Results: LRA indicates a direct relationship between SOT responders and greater time since injury, along with higher baseline values for DGI, HDI, SOT, and PSQI. ORs for these variables were near 1, suggesting low-level strength for predicting SOT response. Negative LRA estimates and ORs for sex and 2-week DGI indicate better responses for females versus males and subjects with lower versus higher 2-week DGI.

Discussion: Outcomes from LRA indicate that subjects with higher baseline values for several variables may be more likely to be SOT responders after TLNS plus targeted therapy. Although a higher baseline DGI score may predict positive response, a lower DGI result at 2 weeks indicates a better chance for an improved SOT response, suggesting that subjects with minimal improvement after 2 weeks of treatment may yet respond at 5 weeks.

Conclusions: This subanalysis of treated persons with mmTBI suggests a direct relationship between high baseline functional assessment and SOT response at 5 weeks and that female subjects are more likely than male subjects to respond to treatment.

Objectives

- To determine subject characteristics that predict significant improvement in balance deficits with TLNS plus targeted PT
- To identify subject characteristics that may indicate a reduced chance for successful treatment
- To investigate the ability of functional outcomes to predict significant SOT response

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251. INS19-0203

THE EFFECTS OF NON-INVASIVE TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) ON POSTURE OVER STABLE AND UNSTABLE SURFACES IN HEALTHY OLDER PEOPLE: A RANDOMISED DOUBLE-BLIND SHAM-CONTROLLED STUDY

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Introduction: The number of older people is growing rapidly in most countries. The risk of falling is higher in older people compared to younger adults due to several reasons including poor posture and balance. Older adults have greater difficulties in performing simultaneous cognitive and motor operations (e.g. talking on the phone while walking) than younger adults [1]. It is suggested a single session of tDCS over the left dorsolateral prefrontal cortex (Left-DLPFC) could improve postural control in the context of secondary cognitive tasks in healthy older people [2].

Materials/Methods: tDCS (1 mA; 20 minutes) was applied with the anode electrode (5x7 cm^2) over the Left-DLPFC, and the cathodal electrode (10x10 cm^2) over the right supraorbital area [1,2]. 16 healthy older participants (63.13 $\pm$ 0.97 years) completed four single tDCS sessions in a randomised order: real or sham stimulation, or whilst standing on stable or unstable surface. There were four testing blocks (1 pre-stimulation, 2 mid-stimulation and 1 post-stimulation). Path length COP was recorded and analyzed.

Results: Path length COP was greater on the unstable surface than the stable surface ($P < 0.001$), and was greater during the dual task compared to the single task ($P < 0.001$). There was a significant Stimulation X Surface interaction effect ($P < 0.001$). Real stimulation significantly increased path length on the stable surface ($P < 0.001$) relative to sham stimulation. In contrast, there was a trend of decreased path length on the unstable surface ($P = 0.055$) relative to sham stimulation.

Discussion: Contrary to the previous study [2], tDCS resulted in significantly worse balance on the firm surface. However, tDCS showed a tendency to improve balance performance on the unstable foam surface.

Conclusions: A single session of tDCS targeting F3 may result in adverse effects on path length depending on the surface conditions. tDCS applied to F3 may improve postural control on the unstable surface. Thus tDCS may induce either negative and positive effects on postural stability depending on both environmental and task constraints. These results highlight the involvement of cortical brain networks in postural control and implicate the modulation of prefrontal cortical excitability as a potential therapeutic intervention.

Objectives: This study aimed to investigate whether tDCS would have a beneficial effect on balance control during single and dual task conditions while standing on stable and unstable surfaces in older individuals.

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252. INS19-0302

PREDICTION OF TREATMENT RESPONSE TO ELECTROCONVULSIVE THERAPY WITH DIFFUSION TENSOR IMAGING IN PATIENTS WITH TREATMENT-RESISTANT SCHIZOPHRENIA

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Introduction: Electroconvulsive therapy (ECT) under general anesthesia with adequate muscle relaxation is an effective treatment for schizophrenia[1]. However, there are no reliable markers available that can help predict the patients' response to ECT. Previous reports show that altered WM microstructure in some pathways are modulated by ECT and relate to therapeutic response which occur in MDD[2]. This study examined whether the radiological features based on diffusion tensor imaging (DTI) can predict treatment response to ECT for individual patients.

Materials/Methods: Research procedures were approved by the local Institutional Ethics Committee. Fifty-seven patients with treatment-resistant schizophrenia were enrolled and written informed consent was obtained from them. Their T1-weighted scans and DTI scans before the course of ECT were collected. 23 regions were defined as effective stimulation regions (regions-of-interest (ROIs)) which included the orbital prefrontal lobe (OFC), medial temporal lobe and some subcortical regions. Then 37 fibers connecting ROIs and other regions of the Automated Anatomical Labeling were reconstructed by deterministic tractography. 15 radiological features were extracted from the histogram of each fiber. A total of 555 radiological features were used for feature selection and prediction. The prediction process was performed using a linear regression model based on a Leave-one-out cross-validation (LOOCV) framework.

Results: We found that the radiomics model including seven features (Table1) from fibers could predict treatment response to ECT with a low root mean square error of 0.1485 and a high R-squared of 0.4691. The Pearson's correlation coefficient between the predicted and actual values was 0.6926 (Figure1, $p<0.0001$). The most important feature which had the biggest weight was the seventh feature in Table1.

Discussion: These important features could complement other biomarkers in the development of precision medicine approaches for this severe mental disorder.[3]

Conclusions: These results demonstrated that the radiological features from DTI might predict treatment response to ECT, which could provide a critical step toward individualized treatment response prediction in schizophrenia.

Objectives

1. To examine whether radiological features from DTI can predict treatment response to ECT.
2. Provide theoretical basis to support that radiomics can be used for diagnosis and prediction of mental illness.
3. Provide evidence that machine learning can be used for diagnosis and prediction of mental illness.

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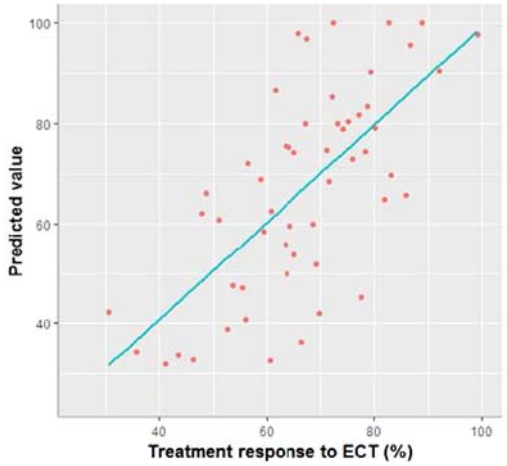
Table 1

No.	ROI1	ROI2	Feature	Weight
1	Frontal_Med_Orb_L	Temporal_Pole_Sup_L	Minimum	29.382
2	Temporal_Mid_R	Temporal_Inf_R	Median	20.258
3	Frontal_Sup_Orb_L	Rectus_L	Minimum	17.885
4	Temporal_Mid_L	Temporal_Inf_L	Minimum	-24.384
5	Lingual_L	Temporal_Mid_L	Kurtosis	-26.136
6	Occipital_Mid_R	Temporal_Sup_R	Median	20.387
7	Frontal_Inf_Orb_L	Occipital_Mid_L	Range	39.812

Abbreviation: Frontal_Med_Orb_L: Left medial orbitofrontal cortex; Temporal_Pole_Sup_L: Left superior temporal pole; Temporal_Mid_R: Right middle temporal gyrus; Temporal_Inf_R: Right inferior temporal gyrus; Frontal_Sup_Orb_L: Left superior frontal gyrus, orbital part; Rectus_L: Left gyrus rectus; Temporal_Mid_L: Left middle temporal gyrus; Temporal_Inf_L: Left inferior temporal gyrus; Lingual_L: Left lingual gyrus; Occipital_Mid_R: Right middle occipital gyrus; Temporal_Sup_R: Right superior temporal gyrus; Frontal_Inf_Orb_L: Left inferior frontal gyrus, pars orbitalis; Occipital_Mid_L: Left middle occipital gyrus.

Figure 1



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253. INS19-0320

THETA-BURST STIMULATION EVOKE MORE SIGNIFICANT BRAINSTEM AND CEREBRAL CORTEX RESPONSES THAN TONIC STIMULATION: A CONCURRENT TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION (TAVNS) AND FMRI STUDY

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Introduction: Transcutaneous auricular vagus nerve stimulation (taVNS) has been used to treat a variety of brain-related diseases, such as depression, epilepsy, etc. However, the mechanism is still unclear. Using functional magnetic resonance imaging (fMRI), several recent studies explored the brain response pathway evoked by taVNS. They found that the brain activation patterns of taVNS is significantly dependent on the targets and parameters of the stimulus. Previous studies explored the optimal stimulation patterns by comparing various parameters, however, all of them used the tonic stimulation mode. Considering the invasive vagus nerve stimulation using in clinic mainly employed the burst stimulation mode, we compared the brain activation patterns evoked by theta-burst and beta-tonic stimulation of taVNS.

Materials/Methods: 24 healthy subjects were recruited, and fMRI data during their taVNS were collected. Three parameters were considered: targets (left cymba conchae and shoulder, left earlobe and shoulder), polarity (positive or negative pole on shoulder), stimulation mode (theta-burst vs beta-tonic). Therefore, eight sessions were employed for each subject, and the orders were counterbalanced across subjects. For each stimulus mode, the pulse width is 500 μs. The theta-burst mode consists 5 times of 500Hz stimulus. Each stimulus mode was achieved in a seven minutes fMRI run with one minute of rest and stimulation alternate. The interval time between each stimulus mode was at least fourty minutes.

Results: In general, the theta-burst stimulation mode evoked more significant brainstem deactivation (mainly at locus coeruleus) and cerebral cortex responses (activations at insula and deactivation at anterior cingulate cortex and medial prefrontal cortex) than tonic stimulation. Positive pole on left cymba conchae has stronger brain responses than the opposite situation.

Discussion: The theta-burst stimulation mode may be more in line with the neural coding pattern of the vagus nerve ascending pathway and may have a better potential for disease treatment.

Conclusions: The present study provides evidence that theta-burst stimulation evoke more significant brainstem and cerebral cortex responses than tonic stimulation of taVNS, thus extending the research direction for finding optimal stimulation parameters.

Objectives

1) Compared the brain responses of theta-burst and beta-tonic stimulation during taVNS.

2) exploring the polarity effects of taVNS on the brain responses.

3) exploring the interaction effect of targets and stimulus modes on the brain responses evoked by taVNS.

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254. INS19-0176

EFFICACY OF REPETITIVE TDCS ON AD LIBITUM SMOKING BEHAVIOUR: AN ECOLOGICAL MOMENTARY ASSESSMENT STUDY

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Introduction: The efficacy of repetitive transcranial Direct Current Stimulation (tDCS) over the dorsolateral prefrontal cortex (DLPFC) as treatment for tobacco smokers has been studied with mixed results. The aim of the present study was to investigate the efficacy of repetitive tDCS as a tool to reduce *ad libitum* smoking behaviour. We also aimed to determine the course of treatment effects by studying smoking behaviour for three months on a daily basis. Since smoking behaviour can fluctuate over time, we choose to use mobile ecological momentary assessments (EMA) instead of retrospective self-reports to measure changes in *ad libitum* smoking behaviour.

Materials/Methods: The current study had a between subject, double-blind, randomized, sham-controlled design (https://clinicaltrials.gov/ct2/show/NCT03027687). Smokers were randomly allocated to six sessions of either active tDCS (n = 35) or sham tDCS (n = 36). They were asked to keep track of their cigarette consumption and craving in an application on their mobile phones for three months.

Results: Multilevel analysis showed that the mean number of smoked cigarettes slightly decreased from the first tDCS session up to one week after the last session (b=-.07, t(471)= -2.086, p =.038) for both active tDCS and sham tDCS (see Figure). However, active tDCS had no additional effect on reducing cigarette consumption and craving compared to sham tDCS.

Discussion: The findings of the current study are in contrast with observations from previous studies that have shown that tDCS is effective in reducing cigarette smoking and cigarette craving. Methodological differences that may explain the contradicting findings are the number of tDCS sessions, the motivation of smokers to quit, and the use of EMA instead of retrospective self-reports.

Conclusions: Repetitive bilateral tDCS over the DLPFC had no effect on daily smoking behavior in *ad libitum* smokers.

Objectives: Future studies need to investigate to what extent motivation to quit smoking and the number of tDCS sessions influence the efficacy of repetitive tDCS. The use of EMA is recommended for its ecological validity.

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255. INS19-0308

EFFECT OF THE DURATION OF ELECTROCONVULSIVE THERAPY TREATMENT ON RESTING STATE BRAIN FUNCTION IN PATIENTS WITH SCHIZOPHRENIA

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Introduction: Electroconvulsive therapy (ECT) is recommended to treat refractory schizophrenia and has shown good efficacy. A large number of previous studies have found that ECT could cause plastic changes of the brain. However, it is still unclear whether the duration of the ECT treatment will produce different impact on the brain. The present study investigated the effects of different duration of ECT intervention on the whole brain functional connectivity (FC).

Materials/Methods: 35 schizophrenia patients were divided into high_ECT group (more than 10 of ECT, n=21) and low_ECT group (less than or equal to 10 of ECT, n=14). All patients had a brain imaging session at baseline and after ECT treatment finished. Positive and Negative Syndrome Scale (PANSS) score was used to evaluate the clinical symptom.

Results: The numbers of ECT in High_ECT and low_ECT groups were 11.86±0.36 and 8.5±1.87 respectively. ECT treatment caused significant PANSS score reduction in both groups ($P < 0.001$), but no difference between two groups. Significant group × ECT interactions were found in four FC ($P < 0.05$, FDR corrected, Figure. 1), including the right precuneus and left paracentral lobule, right Rolandic and left amygdala, left precuneus and left paracentral lobule, and left cuneus and right lingual gyrus. In addition, the connectivities of the precuneus and the cuneus with other regions showed significant changes only in the low_ECT group after ECT treatment, while the connectivity between amygdala and rolandic showed significant change only in the high_ECT group (Figure 1).

Discussion: Although there was no difference in behavioral performance in our present study, different ECT durations caused different effects on resting state brain function. This phenomenon was similar to several previous studies [1]. But which ECT duration is beneficial to patients, it still needs further study in which healthy controls need to be included.

Conclusions: Our results suggest that the effect of ECT on brain function in schizophrenia patients is modulated by ECT treatment duration. The function of precuneus and cuneus is probably more sensitive to shorter-term ECT treatment.

Objectives

1. Understanding the effect of ECT duration on clinical outcome;
2. Understanding the effect of ECT duration on resting brain functional connections;
3. Providing a new idea for future research on the effect of ECT on the brain structure and functional.

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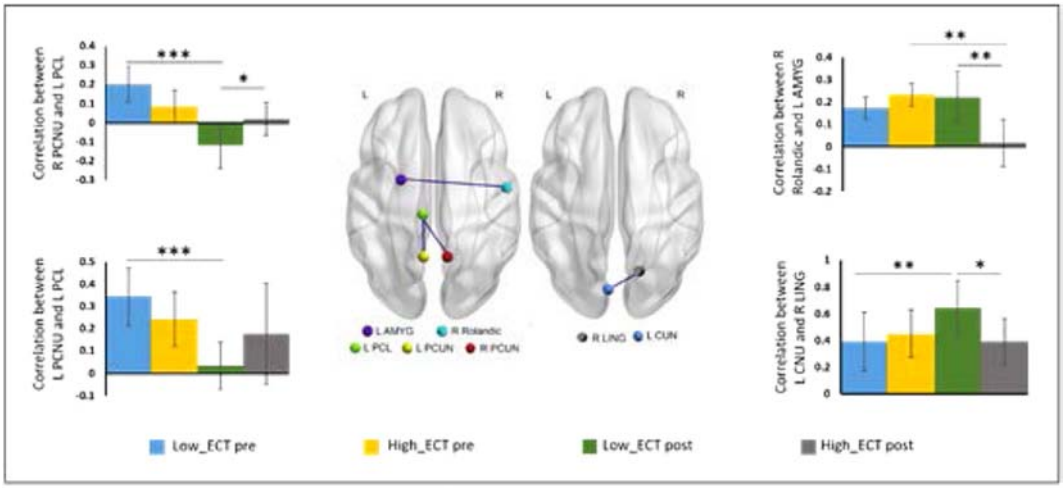

Figure 1. Effect of electroconvulsive therapy (ECT) duration on resting state brain functional connectivity (FC). Brain map shows the FC with group × ECT interactions. Column charts show the results of post hoc test. L AMYG, left amygdala gyrus; L CUN, left cuneus; L PCL, left paracentral lobe; R LING, right lingual gyrus; L PCUN, left precuneus; R PCUN, right precuneus; R Rolandic, right rolandic.

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256. INS19-0268

EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION FOLLOWED BY UPPER BODY EXERCISE ON NEUROPATHIC PAIN IN INDIVIDUALS WITH CHRONIC SPINAL CORD INJURY

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Introduction: Neuropathic pain (NP) is the most common type of pain after spinal cord injury (SCI). Anodal transcranial direct current stimulation (tDCS) over motor cortex can provide moderate effects on SCI-related NP. The use of multimodal treatment strategy is suggested to maintain its effects. Exercises were proved to have the potential to improve NP after SCI by modulating neural/neuronal activity in spinal cord and brain. The purpose of this study is to determine the effects of tDCS followed by exercise on NP in individuals with chronic SCI.

Materials/Methods: This study was a double-blinded, randomized controlled trial with pre-, post-test, and 4-week follow-up measurements. The experimental (control) group received 20-minute anodal real (sham) tDCS followed by 50-minute upper body exercises 3 sessions a week for 4 weeks. The outcomes included pain intensity (numerical rating scale, NRS), characters of NP (Neuropathic Pain Symptom Inventory, NPSI), self-rating change of pain (Patient Global Impression of Change, PGIC), and quality of life (International Spinal Cord Injury Quality of Life Basic Data Set 1.0 Chinese version).

Results: Nine patients with moderate neuropathic pain were enrolled and randomly assigned to experimental (n=5) or control group (n=4). After real tDCS and exercise, the pain intensity (from 5.4±1.8 to 4.0±1.8) and characters of NP (from 26.4±11.6 to 17±4.1) were both improved, and such improvements maintained at 4-week follow-up(4.8±2.7, 15±5.5 for pain intensity and characters of NP respectively). Participants receiving real tDCS indicated better impression of improvement in pain. However, quality of life did not seem to change significantly in the experimental group.

Discussion: Multiple sessions of anodal tDCS followed by exercise may provide analgesic effects to NP possibly by modulating brain activity in individuals with chronic SCI. However, the NP did not decrease by exercise only. People with chronic SCI and NP also indicated the pain is somewhat better to moderate better after the tDCS and exercise.

Conclusions: Anodal tDCS followed by exercises may have potential to relieve SCI-related NP and such improvement may not be achieved by exercise alone in patients with chronic spinal cord injury.

Objectives: This study reported (1) the effects of anodal tDCS combined with exercises on SCI-related NP, (2) a possible treatment protocol for SCI-related NP, and (3) the safety of applications of multiple sessions of tDCS and exercises.

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Peripheral Nerve

257. INS19-0072

COMPARISON OF CLINICAL EFFECTIVENESS OF LASER ACUPUNCTURE AND AMITRYTYLINE IN DIABETIC PERIPHERAL NEUROPATHY (DPN) A SHAM CONTROLED RANDOMIZED CLINICAL TRIAL

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Introduction: Painful neuropathy is a very common complication in diabetic patients. Various treatment strategies like manual therapies, conservative management, drugs and exercise have been opted for this problem. Studies have shown clinical effectiveness of laser acupuncture as well. On the other hand, Amitriptyline is also a commonly used treatment for this disease. We aim to compare the efficacy of both treatments.

Materials/Methods: This study was conducted in Diabetic and Endocrine Management Center (DEMC) Lahore General Hospital, Lahore, Pakistan. A randomized control trial (RCT) was opted and a total of 164 patients were chosen using Non-probability purposive sampling technique. Pain was graded by using a patient friendly Visual Analogue Score (VAS), scoring from 0 to 10. Treatment was done involving organized fortnightly follow ups. Data of all patients was recorded on Performa and was entered and analyzed for descriptive statistics in PASW 18 (IBM®. SPSS).

Results: A total of 164 subjects were included in the study who were subdivided into three groups labeled as A, B and C for laser acupuncture treatment, amitriptyline treatment and controls respectively. The mean age of subjects was 51.54±10.46 in Group A, 49.38±10.56 in Group B and 51.70±11.43 in Group C. The mean pain score in Group A was 5.95±0.91 before treatment, whereas after treatment it was 4.31±0.98. The mean pain score in Group B before starting the treatment was 6.87±0.71 and after treatment, it was 6.23±0.98. The mean score for daily life activities in Group A was 9.56±2.37 before treatment, while after treatment it was 7.56±1.54. The average score for daily life activities in Group B before starting the treatment was 9.05±1.93 and after treatment, it was 8.11±1.71. Average depression and anxiety score in Group A was 9.29±2.28 before treatment, whereas after treatment it was found to be 7.42±1.91. Similarly, the mean depression and anxiety score in Group B before starting the treatment was 9.38±2.21 and after treatment, it was 8.38±2.14.

Discussion: Early diagnosis and system identification has also been stressed on by many researchers for successful and better management of this problem.

Conclusions: The mean score in our study reveals that laser acupuncture shows better outcomes in improvement of pain relief, depression, anxiety and daily life activities compared to amitriptyline in patients of diabetic neuropathy.

Objectives: To assess the safety and effects of laser acupuncture in patients suffering from painful diabetic neuropathy, and its comparison amitryptalline.

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Peripheral Nerve

258. INS19-0066

HIGH FREQUENCY SPINAL CORD STIMULATION AT 10 KHZ FOR THE TREATMENT OF FOCAL, CHRONIC, POST-SURGICAL NEUROPATHIC PAIN

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Introduction: Chronic post-surgical pain (CPSP) is one of the most common and serious complications after surgery. A recent multicenter observational study reported a 12-month incidence of 11.8% moderate CPSP and 2.2% severe CPSP. In this study, we tested the hypothesis that a standard midline lead placement using high frequency spinal cord stimulation (HF-SCS) at 10 kHz (may provide effective pain relief in CPSP conditions without the need for a focal stimulation target.

Materials/Methods: Subjects with focal chronic neuropathic pain of ≥5 cm visual analog scale (VAS) score of the trunk or limb from CPSP were enrolled in this single center prospective study, after approval from ethics committee and completion of written informed consent. Two epidural leads were implanted spanning the appropriate vertebrae based on location of pain. Subjects with successful trial (≥50% pain reduction) received permanent implant and were followed-up for 12 months to collect safety and effectiveness data. Interim 3-month results are presented as mean ± SD.

Results: Out of 12 enrolled subjects (8 with lower extremity pain, 1 with upper extremity pain and 3 with trunk pain), 10 had a successful trial (83.3%) and received a permanent implant. Baseline pain scores of 7.5±0.9 cm (n=10) improved to 1.0±0.6 cm (n=10), 1.2±0.9 (n=10), 1.0±0.8 cm (n=6) at the end of trial, 1- month and 3-month follow-ups respectively. The responder rate was 100% at both 1- and 3-month follow-ups. Pain Disability Index improved from 43.9±9.7 to 27.6±12.7 and 20.2±14.3 at 1-month and 3-month follow-ups, respectively. One adverse event, infection of the percutaneous trial leads, was reported.

Discussion: Early results from this study suggest that a midline epidural, anatomically guided lead placement may offer an effective treatment to focal pain in subjects with chronic post-surgical pain.

Conclusions: Early results from this study suggest that a midline epidural, anatomically guided lead placement may offer an effective treatment to focal pain in subjects with chronic post-surgical pain.

Objectives

- HF SCS at 10 kHz treatment for peripheral neuropathic pain
- importance of treatment for post-surgical neuropathic pain
- safety and effectiveness of treatment

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Poster Presentations - May 27 - May 30
Peripheral Nerve

259. INS19-0419

NEUROPATHIC PAIN AFTER THORACIC SURGERY: AN EXTERNAL PERIPHERAL NERVE STIMULATION CASE REPORT

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Introduction: In 2014, Mrs. S, a 34-year-old woman was undergoing thoracic surgery to perform the removal of a left lateral thoracic vascular tumor. In the direct postoperative time, she presented pain aggravated by respiratory movement without sensory deficit and a functional limitation of her left shoulder. In 2017, we met Mrs. S for these two issues and decided to carry out a block test performed under echo guidance with a little volume of local anesthetic solution to confirm long thoracic nerve injury diagnosis. After this block test, the pain disappeared and shoulder mobility returned to normal. An implantable peripheral nerve stimulation system was proposed to Mrs. S.

Materials/Methods: The aim of this case report is to evaluate medical benefits of the Stimrouter®. After confirming the diagnosis of long thoracic nerve injury and proposing the use of an external peripheral nerve stimulator, we assessed in the preoperative time and 6-month follow-up pain intensity, functional disability, anxiety and depression and quality of life of Mrs. S to evaluate the outcome.

Results: Mrs. S use the device 8 hours per day. Pain intensity assessed by the VAS decreased from 65/100 to 7/100. Functional disability assessed by ODI decreased from 44/100 to 28/100. Quality of life assessed by EQ5D increased from 0,119 to 0,357. Anxiety assessed by HAD-A remained the same (11), but depression assessed by HAD-D decreased from 11 to 4.

Discussion: Prevalence of post-operative pain after thoracic surgery is estimate between 30 and 40 %1 of which 5-10% are considered as severe1. Most of these pains have neuropathic connotations and are often considered as refractory to traditional medical and interventional management2. After failure of medication, and in case of refusal of an internal stimulation, external peripheral nerve stimulation could be suggested.

Conclusions: External peripheral nerve stimulation should be investigated as an alternative solution for patients with long thoracic nerve injury. In our case, it allowed Mrs. S to reduce pain intensity, functional disability, depression and to improve quality of life.

Objectives: NA

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Peripheral Nerve

260. INS19-0075

SALVAGE THERAPY OF PATIENTS WITH CHRONIC COMPLEX REGIONAL PAIN SYNDROME BY CATHETER ASSOCIATED LOCAL TREATMENT OF PERIPHERAL NERVES

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Introduction: In spite of pharmacotherapy, physiotherapy, psychotherapy and peripheral neurostimulation there are patients who are pain treatment refractory. In cases with a severe life threatening allodynia where every single touch is avoided, extremities are kept in a forced posture and a development of incurable contractures are observed, which reinforces this syndrome with often no alternatives.

Materials/Methods: we treated 14 patients with refractory neuropathic pain. All of them had a minor trauma at their extremities and common treatments as mentioned above were gone out of use. Some were suicidal! Our method is a perineural local pain therapy. With general anaesthesia proximal to the side of the lesion the correlated peripheral nerve is surgical explored and a silicone catheter is placed parallel to the peripheral nerve after neurological-topical diagnosis. Then this catheter is subcutaneously tunneld to an accessible part of the body and connected to a subcutaneous implanted port. From the first postoperative day patients get their first injection with a local anaesthetic agent like Xylocaine to wash around this nerve. This flow leads to a sudden pain reduction, an anaesthic block. The first injections are performed by medical control. The patients are educated to do it by their own by aseptic conditions at home for about 10-14 days. Patients with sustained relief will receive an implantation of a pump for continuous irrigation and will be seen for 4-6 weeks refill.

Results: Therefore we had patients who treated their own on demand, 9 patients with an implanted high –volume medical pump. We had no (!) failures among these hopeless cases by a follow-up period up to 9 years. There were no real dose increase. 2 patients stopped their treatment after 2 respectively 3 years. We observed 2 infections with necessitated explantation of the system, 1 with reimplantation after 6 months, 2 catheter dislocations with reinsertion. 6 patients returned to work.

Discussion: Due to this treatment patients got physiotherapy, stopped analgetic treatment by opioids. Allodynia disappeared and often observed trophic alterations vanished. As there are nearly always concomitant psychic disorders with depression and anxiety the recovery in these circumstances is remarkable.

Conclusions: This method is an additional tool of Neuromodulation in chronic progressive neuropathic pain of peripheral origin with no addiction.

Objectives

1. anesthetic flow around peripheral nerves
2. for hopeless patients with refractory neuropathic pain (CRPS) if other standard regimen fail
3. in future it might be performed minimal invasive by ultrasound guided percutaneous implantation

Poster Presentations - May 27 - May 30
Peripheral Nerve

261. INS19-0224

IMPROVING TACTILE SENSITIVITY OF PATIENTS WITH HIV-RELATED PERIPHERAL SENSORY NEUROPATHY

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Introduction: Subsensory Electrical Nerve Stimulation (SENS) has been shown to improve the 50 Hz vibrotactile sensitivity of elderly participants (>65 years) with sensory neuropathy [1]. HIV-related peripheral sensory neuropathy (HIV-PN) is both prominent [2] and has a detrimental effect on quality of life [3]. We investigated the effect of SENS on vibration perception thresholds (VPTs) at three different vibration frequencies for 20 patients on antiretroviral therapy, diagnosed with HIV-PN (age 42±7 years). We also present the first investigation into the effects of this type of intervention on pain, common among those with HIV-PN [2].

Materials/Methods: An extensive double-blind protocol was used to measure VPT for 50 Hz vibration under the Hallux in a sham condition and four different SENS amplitudes (30 mA, 45 mA, 60 mA and 90% of electrical perception threshold). The best performing SENS amplitude for each participant was then retested against sham conditions for 25 Hz and 128 Hz VPT. After each VPT test, symptoms of "pain", "numbness" and "pins-and-needles" were assessed on a visual numeric scale.

Results: Tests for the effect of SENS on VPT indicate that similar to previous results with elderly participants[1], VPT improved 7.5% at 50 Hz for a SENS amplitude of 45 mA RMS ($p = 0.02$), but not at other SENS amplitudes. An analysis of the best performing SENS amplitude for each participant indicates that an optimal, per-participant, SENS amplitude does exist for 50 Hz VPT ($p < 0.01$). When the optimal amplitude of SENS was applied when testing VPT at 25 Hz and 128 Hz, no statistically significant effect of SENS was observed for either vibration frequency. The recorded pain data did not provide evidence that SENS had either a beneficial or detrimental effect on "pain", "numbness" or "pins-and-needles".

Discussion: NA

Conclusions: Our results indicate that SENS shows promise to be developed into a therapy for HIV-PN, but that further research is needed. Results also indicate that SENS is unlikely to have an adverse effect on neuropathic pain, which could have been a big stumbling block in its use as therapy.

Objectives: NA

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Poster Presentations - May 27 - May 30
Peripheral Nerve

262. INS19-0264

TRANSCUTANEOUS PULSED RADIOFREQUENCY STIMULATION ON CARPAL TUNNEL SYNDROME : A PRELIMINARY REPORT ON A CLINICAL TRIAL

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Introduction: Pulsed radiofrequency stimulation has been used in treating various painful conditions including peripheral painful neuropathy. However, transcutaneously application of pulsed radiofrequency stimulation on carpal tunnel syndrome has not been discussed in literature. The aim of this study was to investigate the safety and efficacy of low-voltage transcutaneous pulsed radiofrequency (TPRF) stimulation on carpal tunnel syndrome.

Materials/Methods: We conducted a clinical trial of 14 patients with the diagnosis of carpal tunnel syndrome receiving transcutaneous pulsed radiofrequency stimulation. This device was designed based on our previous animal studies on rats median nerve compression model treated by transcutaneous pulsed radiofrequency stimulation. The pulsed radiofrequency generator powered by a lithium battery was assembled inside a 3cm x 3.5 cm small device body with an electrode pad for transcutaneously delivery of pulsed radiofrequency to the affected wrist. The treatment parameters were as follows: Pulsed Frequency:2Hz, Pulsed Duration:25ms, Frequency:500KHz, Amplitude:10 volt. TPRF was delivered over the patient's affected wrist for 15 minutes (Fig1). The Visual Analogue Scale was documented after TPRF treatment on day 1, day 3, day 7, and day 14 respectively.

Results: There were no complications or adverse reactions such as motor nerve injury, numbness or paresthesia noted after TPRF treatment. 13 patients got symptoms improvement and 1 patient had no significant change on pain intensity after treatment. The results showed that a significant reduction of VAS (6.7 to 3.2) happened in the first 3 days and the effects of TPRF could be sustained for 14 days despite gradually increased pain intensity at 14-day follow up.

Discussion: Traditional transcutaneous nerve stimulation was frequently used in carpal tunnel syndrome, and there are no reports focusing on transcutaneous pulsed radiofrequency for median nerve neuropathy. The effectiveness and applications of pulsed radiofrequency for pain management was proved for decades but the actual mechanism of action is still not clear now.

Conclusions: This preliminary report demonstrated TPRF is favorable in ameliorating pain in carpal tunnel syndrome for 14 days. Although limited patients enrolled in this trial, this preliminary feasibility study provided that a new portable, non-invasive treatment modality could be developed for carpal tunnel syndrome and applied for other peripheral painful neuropathy.

Objectives

1. application of TPRF in clinical practice
2. design of non-invasive stimulation device
3. extend the indications for transcutaneous stimulation

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Peripheral Nerve

263. INS19-0267

CUNEAL NERVE STIMULATION AT 10 KHZ FOR THE TREATMENT OF CHRONIC NEUROPATHIC PAIN

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Introduction: Traditionally, neuroablative efforts at relieving chronic low back pain within the distribution of the superior and middle cluneal nerves and their medially and laterally displaced branches has provided short-term benefits (1). Neurostimulation along the anatomic pathways of the cluneal nerves is thus a highly rational approach to treating peripheral neuralgia involving these nerves. Paraesthesia-independent high frequency spinal cord stimulation (HF-SCS) at 10 kHz has demonstrated long-term safety and efficacy in back and leg pain patients when placed within the epidural space. Here, we report on the outcomes of a series of low back pain patients receiving 10 kHz stimulation to treat low back pain, with the electrodes alternatively placed subcutaneously over the cluneal nerves.

Materials/Methods: Ten patients from four separate clinics (6 females) presented with intractable chronic low back pain localised within the innervation of the cluneal nerves. Following a history of failed conventional therapies, patients underwent a 10 kHz stimulation using HF-SCS system, with leads up to two leads placed subcutaneously and laterally across the cluneal nerves. Stimulation parameters used included: 0-1.4 mA with 0.2 mA step size, 10 kHz and 30 ms. Two bipole multi area programming was used spanning over the cluneal nerve on each lead which was determined by paraesthesia testing of 60 Hz at 250 ms. Data was collected at an average of (9.3±13.2 months).

Results: Patients reported a reduction in baseline pain following implant (8.3±1.0 vs. 1.4±1.2, pain points on the numerical rating scale [NRS])

Improvements in daily function and sleeping were reported, along with all patients reporting a reduction in their medication use. One patient passed away due to an unrelated condition, whilst no further complications were noted.

Discussion: Stimulating the superior cluneal nerve more proximally, and therefore potentially stimulating branches to the fascia as well as the skin, is proving to be a more efficacious approach to cluneal nerve stimulation.

Conclusions: Subcutaneous stimulation of the cluneal nerve at 10 kHz may prove to be a viable long-term treatment option for pain localised over the cluneal nerve distribution in the lower back.

Objectives: To investigate a novel use of HF-SCS at 10kHz

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Poster Presentations - May 27 - May 30
Peripheral Nerve

264. INS19-0156

A UNIQUE CASE OF INTRAPLEURAL NEUROLYSIS FOR BRACHIAL PLEXUS CANCER PAIN

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Introduction: To our knowledge this is the first reported case of intrapleural neurolysis performed by the senior author (DJP) for pain caused by brachial plexus metastatic tumor.

Materials/Methods: A 65-year-old male with lung cancer presented with constant cervicalgia 6/10 radiating to the left arm. MRI revealed left apical lung mass tightly juxtaposed to the brachial plexus, which was contributing to his pain and tumor extension through the left intervertebral foramina at C7-T1 and T1-T2. He failed C6-C7 epidural steroid injection and cervical medial branch nerve block. Due to MRI findings, he was not a candidate for a spinal cord stimulator or intrathecal drug delivery system implantation.

Results: Focused neurological exam of left arm revealed decreased motor strength MRC (Medical Research Council) grade 4/5 and decreased sensation to light touch in C6-T1 segments. Patient underwent intrapleural placement of a standard Arrow Flex Tip epidural catheter at the T6 rib level using fluoroscopy in a sitting position and injection with 20 ml 1% lidocaine. Then patient was positioned in the steep Trendelenburg right-sided down position, monitored and re-assessed after 30 minutes. He endorsed 100% pain relief in his arm, 50% pain relief in his neck and motor strength improved to MRC grade 5/5 except wrist extensors and finger flexors (4/5), sensation remained the same. Successful diagnostic block was followed by neurolysis with injecting 20 ml 98% alcohol. The patient reported100% pain relief with no complications.

Discussion: Intrapleural block with local anesthetic was considered effective for chest pain, thoracic, breast surgery over a decade ago, then dismissed due to challenging technique and reported 2% risk of pneumothorax [1]. Later over 7000 cases were described with a total of three pneumothoraces none of which required treatment beyond supplemental oxygen [2]. Intrapleural phenol therapy has been described as an alternative for the treatment of visceral pain associated with esophageal cancer [3]. Phrenic nerve palsy resulting in respiratory failure may occur; therefore, bilateral blocks should be avoided. Intrapleural neurolysis for brachial plexus cancer pain hasn't been described previously.

Conclusions: Intrapleural neurolysis is an option for patients with brachial plexus cancer pain who fail other modalities.

Objectives: Increase knowledge about:

1. Lung cancer
2. Cancer pain
3. Options for neurolysis

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Peripheral Nerve

265. INS19-0073

A UNIQUE CASE OF NONUNION FRACTURE HEALING FOLLOWING DORSAL ROOT GANGLION STIMULATION

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Introduction: Complex regional pain syndrome (CRPS) frequently presents with severe pain, and may also demonstrate progressive osteopenia, delayed bone healing, and fracture nonunion. Current data supports dorsal root ganglion (DRG) stimulation as a highly effective therapy in patients with lower extremity CRPS. The mechanism of influence on local healing and bone metabolism are poorly understood, with no previous literature reporting on their concurrent interaction.

Materials/Methods: A 44 yo female presented with 6 months of neuropathic pain and allodynia located at the dorsomedial right foot. Symptoms began 8 weeks following bunionectomy, where surgical osteotomy and pinning of the first metatarsal was performed. Patient pain scores ranged from 6 to 8 on an 11-point scale. Physical exam showed allodynia, temperature asymmetry, edema, and skin discoloration. X-rays 6 months following bunionectomy demonstrated nonunion of the first metatarsal fracture site with minimal remineralization. After failing conservative management, the patient underwent DRG stimulation trial at L4, L5, and S1 levels with permanent implantation 1 month later.

Results: DRG stimulation at L4, L5, and S1 levels provided 90% pain relief, with improvement in allodynia, edema, and hypothermic sensation. One month post implantation showed complete union and remineralization of first metatarsal fracture site.

Discussion: This report presents a patient with CRPS of the lower extremity secondary to a protracted course of fracture nonunion following first metatarsal bunionectomy. DRG stimulation is a known effective therapy in treating lower extremity CRPS, yet to our knowledge, no previous literature has documented such acute and significant changes in bone remineralization following implantation. Mechanisms are not entirely understood, but may be attributable to vasodilation and increased mechanical loading following pain relief.

Conclusions: DRG neuromodulation is an effective therapy for patients with neuropathic pain from CRPS, and may promote bone remineralization and fracture union.

Objectives

DRG neuromodulation is an effective treatment for pain in CRPS

DRG neuromodulation may promote nonunion fracture healing in CRPS

DRG neuromodulation may promote vasodilation and mechanical loading in CRPS

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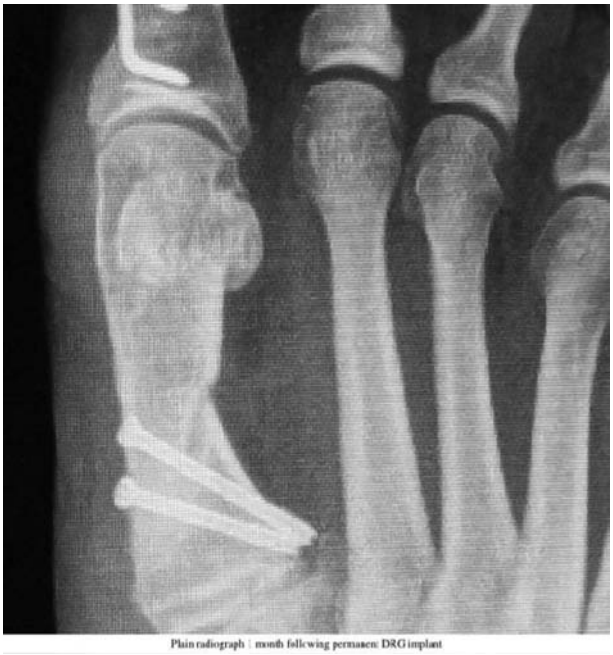

Plain radiograph : month follcwing permanen: DRG implant

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Peripheral Nerve

266. INS19-0041

ULTRASOUND –GUIDED PULSED RADIOFREQUENCY TREATMENT: NEUROPATHIC PAIN AFTER MEDIAN NERVE NEURECTOMY

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Introduction: Post-traumatic neuropathy patient usually suffers for a long time from intense pain in the innervation area of the affected peripheral nerves. Various modalities of treatment have been advocated for post-traumatic neuropathy.

Materials/Methods: A 47-year-old male, a case of post-traumatic neuropathy, presented with hyperalgesia and skin color change in the right forearm. He had lost his motor function after trauma and it was confirmed by electromyography assessments. He had undergone a surgical median nerve neurectomy prior to visiting our clinic for the control of persisting pain. In our clinic he was given NSAID, morphine, pregabalin and nortriptyline, which provided only minor relief of pain. Initially he was treated with paravertebral block and median nerve block under ultrasound. After the median nerve block showed alleviation of symptoms.

Results: After the procedure the patient showed improvement in symptoms within four to five hours and relief of symptoms by 80%. We performed radiofrequency ablation of median nerve for controlled pain. It was done for 120 seconds; two cycles each in the proximal and distal cut tip of median nerve under the ultrasound guide. However, it failed to provide complete relief and he still felt discomfort on the areas innervated by radial nerve.

Discussion: Ultrasound-guided radiofrequency ablation can be used for the alternative treatment of post-traumatic neuropathy in median nerve

Conclusions: short bursts of radiofrequency energy to the nervous tissue may result in intermediate to long-term pain relief

Objectives

1. short bursts of radiofrequency energy to the nervous tissue may result in intermediate to long-term pain relief
2. PRF procedure should be considered as an alternative treatment for all posttraumatic nerve injuries
3. PRF can be an effective therapeutic option for managing intractable neuropathic pain after neurectomy

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Poster Presentations - May 27 - May 30
Peripheral Nerve

267. INS19-0436

16-YEAR EXPERIENCE WITH OCCIPITAL NERVE STIMULATION: LONGEVITY OF THERAPY

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Introduction: Chronic headaches are one of the most common neurological disorders, affecting as many as 45 million Americans, based on recent estimates. As one of the leading causes of suffering and disability, chronic headaches, particularly the ones refractory to medical treatment, present a major public health problem in the USA and globally. The occipital nerve stimulation (ONS) has been successfully used in patients with occipital neuralgia and chronic migraines for the last 20 years or so, but the long term results remain largely unknown.

Materials/Methods: We analyzed our institutional experience with ONS use between April 2002 and November 2018 by performing a retrospective chart review in order to assess longevity and complications related to the device and therapy. In order to make the series uniform, we included all patients who were had primary ONS trial and implantation in our practice. The patients implanted with ONS in other institutions and those with combination of ONS and other neuromodulation targets (supraorbital, infraorbital, auriculotemporal nerves and/or cervical spinal cord stimulation) were excluded from analysis.

Results: The analyzed cohort included a total of 46 patients (17 men and 29 women). The age in our group ranged from 20 to 97 years old, with 82,6% in working age group (20-65 years). The average duration of headaches prior to ONS procedure was 6 years (range – 5 months-30 years). Unilateral ONS was used in 13 patients, and bilateral in 33. Thirty-five patients (76%) obtained satisfactory pain relief during the trial and proceeded with permanent implantation (28.6% unilateral and 71.4% bilateral). During the long-term follow up, 6 patients (17%) had their system explanted, 3 of them because of the worsening in condition and/or loss of benefits from ONS, and 3 due to improvement in condition and elimination of need in ONS. There was no direct correlation between results of occipital nerve block that was performed prior to ONS trial in all patients with occipital neuralgia as there were some patients who improved with trial despite lack of improvement with nerve block and vice versa.

Discussion: -

Conclusions: This study presents longitudinal single-institution experience with ONS indicating high level of long-term success and, indirectly, high predictive value of ONS trial.

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268. INS19-0437

16-YEAR EXPERIENCE WITH OCCIPITAL NERVE STIMULATION: ANALYSIS OF COMPLICATIONS

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Introduction: Occipital nerve stimulation (ONS) has been successfully used for the most common headache conditions, including migraines and occipital neuralgia. Introduction of percutaneous ONS implantation technique in 1999 resulted in widespread acceptance of this procedure, and several attempts have been made to analyze the complications associated with this modality. Most analyses have not been done over the long time period.

Materials/Methods: We performed retrospective chart review and identified all patients treated with ONS in our practice between April 2002 and November 2018. Subsequently, we analyzed all complications encountered during the long-term follow-up. To make series uniform, we included all patients with primary ONS trial and implantation in our practice. The patients implanted with ONS elsewhere and those with combination of ONS and other targets (supraorbital, infraorbital, auriculotemporal PNS and/or cervical SCS) were excluded from analysis.

Results: Of 46 patients trialed exclusively with ONS in our institution, 35 were implanted with permanent device and 11 were considered trial failures. Complications occurred in 15/35 patients (42.4%) over the entire 16-year period, and we observed that the patients with longer system presence had more chance developing a complication (average: 7y8m), whereas those with no complications had the device for shorter time (5y3m). We found migration occurring in 7 cases (20%), malfunction in 4 (11.4%), infection, pain around the generator and migration of generator in 2 each (5.6%); all migration cases occurred before 2008 when we used larger generators. Electrode fracture and stimulation-related muscle spasms were observed in 2.8% each (n=1). None of 13 patients with unilateral stimulation developed "side-shift" of pain, but this phenomenon was observed during trial in one patient who did not pursue permanent implantation.

Discussion: The introduction of 8-contact electrode appeared to be the most significant influence on trial success, with trial failure rate decreasing from 38.4% to 16.1%, likely indicating the importance of the ability to stimulate the greater, lesser and third occipital nerve with a single electrode. Interestingly enough, the complication incidence decreased from 62.5% to 38.5% after the change from 4- to 8-contact electrodes, and introduction of smaller generators reduced it further to 33.3%.

Conclusions: Our results indicate overall safety of ONS procedures in a long-term application of the modality. The material was too small to reach any statistical significance in correlation between device type and complication occurrence, but our data may eventually be pulled with similar reports from other centers for better understanding of expected effects of long-term ONS.

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269. INS19-0439

BIORESORBABLE ELECTRONICS FOR PERIPHERAL NERVE INTERFACING AND NEUROMODULATION

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Introduction: Functional electrical stimulation of peripheral nerve tissue has been demonstrated to restore sensorimotor function and accelerate axonal regeneration in vivo. Yet, existing methods of applying electrical stimulation to peripheral nerve tissue have presented significant barriers to clinical translation. The present study describes the implementation of a bioresorbable wireless nerve stimulator capable of delivering functional, therapeutic, and diagnostic electrical stimulation of injured and un-injured peripheral nerve tissue.

Materials/Methods: Fully bioresorbable electronic implants were fabricated and subcutaneously implanted into Lewis rats. Implanted devices were utilized to deliver functional and brief electrical stimulation (0-20Hz) to sciatic nerves following nerve crush, nerve transection/repair, and sham surgery. Following initial electrical stimulation, implanted wireless devices were utilized to serially assess functional recovery over 3 months postoperatively.

Results: Bioresorbable wireless nerve stimulators were shown to successfully stimulate peripheral nerve tissue in vivo for over 2 weeks prior to dissolution. Brief electrical stimulation delivered by the implants was observed to increase both the rate of functional recovery and maximal capacity for functional recovery following nerve transection and repair. Bioresorbable stimulators successfully facilitated both therapeutic stimulation of peripheral nerve tissue as well as serial assessment of nerve and muscle function following nerve crush and nerve transection injury.

Discussion: The present study highlights the ability of a new class of bioresorbable implantable electronics to successfully interface and therapeutically stimulate peripheral nerve tissue. Completely bioresorbable wireless nerve stimulators may therefore serve as a novel means of facilitating therapeutic electrical stimulation and neuromodulation in a variety of clinical settings.

Conclusions: Completely bioresorbable wireless nerve stimulators serve as a novel and effective means of facilitating therapeutic electrical stimulation and neuromodulation in a variety of clinical settings.

Objectives

1.) Introduce participants to the newly emerging field of transient and bioresorbable electronics

2.) Educate participants on the advantages of bioresorbable electronic platforms in peripheral neuromodulatory applications

3.) Highlight the regenerative potential of brief electrical stimulation on peripheral nerve regeneration delivered via implantable peripheral nerve stimulators.

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Poster Presentations - May 27 - May 30
Peripheral Nerve

270. INS19-0309

PULSED RADIOFREQUENCY TREATMENT SELECTIVELY ATTENUATES THE NOCICEPTIVE REFLEX WHILE PRESERVING MOTOR FUNCTION IN AN ACUTE PAIN MODEL

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Introduction: Pulsed Radiofrequency (PRF) is used to treat chronic pain, but its effects on acute pain (e.g. post-surgical), are not understood. Equally important, PRF is thought to selectively impact small-diameter fibers in mixed nerves, but this has not been functionally demonstrated [1]. Herein, we show that PRF selectively attenuates the Nociceptive Flexion Reflex (NFR) corresponding with acute pain, while preserving motor function in the rat sciatic nerve.

Materials/Methods: Fifteen Sprague-Dawley rats were anesthetized with isoflurane (0-1%), ketamine (15.5-32.7 mg/hr), and xylazine (0.5-1.1 mg/hr). Animals were randomly assigned to PRF (20 ms, 2 Hz, 120 s, 42 °C, 55-75 V) or sham (120 s, no PRF) treatment groups after placement of a radiofrequency probe (22-gauge, 1-mm exposed tip) tip-down on the sciatic nerve between the sciatic notch and sural-nerve branch point (≤0.5 V motor threshold). Electromyogram (EMG) recordings corresponding with the NFR (150-650 ms latency; small-diameter unmyelinated fiber reflex) and motor function (1-10 ms latency; large-diameter myelinated fibers) were collected prior to, and 60 minutes after treatment (Figs 1, 2). These EMG bursts were elicited by stimulation in the sural nerve receptive field for the NFR (8 ms, 20-80 V), and at the sciatic notch for assessment of motor function (50 µs, 5-30 V). Four Welch's t-tests were performed (with Bonferroni correction).

Results: PRF treatment reduced the rectified EMG area representing the NFR and motor responses by a group average of 70.0% (± 9.9% S.E.M.) and 12.4% (± 7.3% S.E.M.), respectively (Fig 3). For sham animals, EMG areas decreased an average of 10.4% (± 7.5% S.E.M) and 2.0% (± 2.4% S.E.M), respectively. Compared with sham, PRF-treated animals demonstrated significant reduction in EMG area for the NFR ($p < 0.0001$). The NFR exhibited more reduction than the motor response in PRF-treated animals ($p < 0.0001$).

Discussion: This research indicates that PRF selectively attenuates a small-diameter-fiber, acute-pain reflex pathway while sparing motor function (via large-diameter myelinated fibers). Ongoing research is being performed to determine the origin of these effects along the reflex pathway (e.g. axon, cell body, synapse).

Conclusions: PRF treatment selectively attenuates the NFR corresponding with acute pain, while sparing motor conduction.

Objectives

1) Determine if PRF attenuates the nociceptive flexion reflex (corresponding with acute pain). 2) Determine whether PRF effects are selective toward the nociceptive flexion reflex, while sparing motor function in a mixed nerve. 3) Confirm that PRF effects are distinct from sham probe placement.

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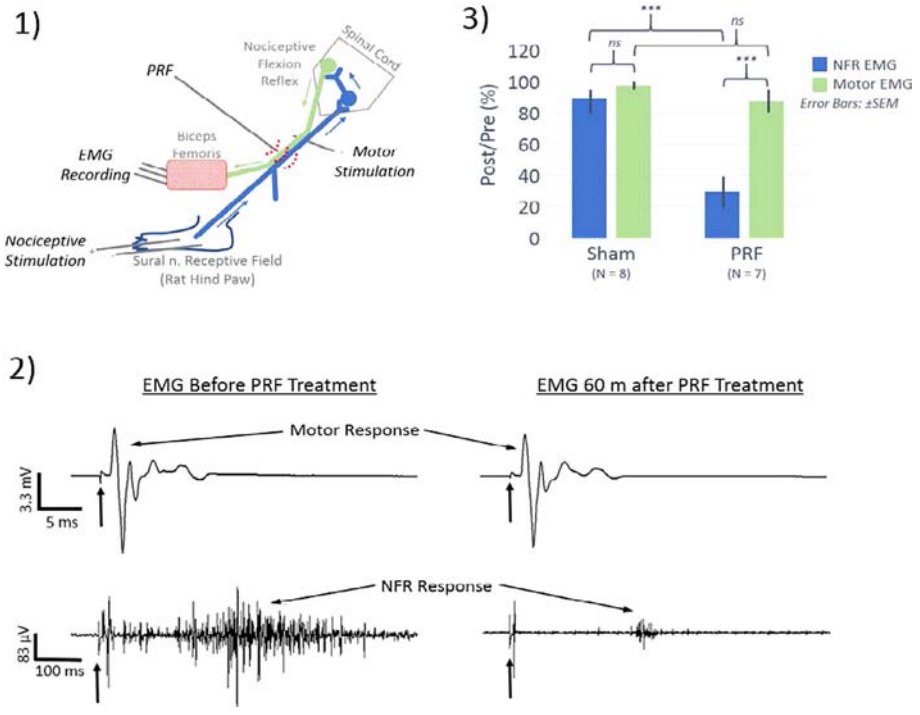

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271. INS19-0161

NEUROSTIMULATION THERAPY AND MEDICAL CANNABIS: AN INTEGRATED THERAPY FOR THE MANAGEMENT OF CHRONIC NEUROPATHIC PAIN

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Introduction: Chronic Neuropathic Pain represent a clinical condition difficult to manage because of the variability in the response and unstable ***Results: Materials/Methods***: A group of subjects with chronic neuropathic pain treated with Neurostimulation therapy (N. 35; age 55±13) was compared with a group of subjects (n.40; age 66± 13) affected by various kind of chronic neuropathic pain treated with Neurostimulation therapy integrated with Medical Cannabis assumption.

Our investigations have concerned Pain intensity, measured with Visual Analogue Scale, and psychological dimension measured with Hospital Anxiety and Depression Scale (HADS) at Baseline and at 3 months follow up.

Results: Statistical analyzes revealed that in Medical Cannabis and Neurostimulation group Pain Intensity Difference (ΔVAS) in the period between Baseline and 3 months follow up is greater and statistically significant than the Pain Intensity Difference measured in Neurostimulation group (t (74)= 2,21; p< 0,05). Pearson correlations highlights a significant statistically link between variable Age and variable Pain intensity Difference only in Neurostimulation group (r= -0,81;n.75 p= 0,002) HADS-D and HADS TOT registered a greater significant reduction in the Medical Cannabis and Neurostimulation group than in Neurostimulation group (t (74)= 2,71 p< 0,05; t(74)=3,95 p<0,05)

Discussion: Integrated therapy highlights better results than the only use of Neurostimulation approach: our study suggests that Medical Cannabis influences in a positive way the Neurostimulation effect, amplifying it

Conclusions: Our results suggest a better response on chronic neuropahic pain from integrated therapy, Neurostimulation and Medical Cannabis, than from Neurostimulation therapy alone.

Objectives

The aim of this observational study is to asses if the integrated use of Medical Cannabis and Neurostimulation therapy can be leads to greater improvements on chronic neuropathic pain than Neurostimulation therapy alone

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Peripheral Nerve

272. INS19-0048

TIBIAL NERVE STIMOLATION ON CHRONIC PELVIC PAIN, IS THIS NON INVASIVE TECHNIQUE THE WRITE WAY?

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Introduction: Percutaneus Tibial Nerve stimolation (PTNS) is a minimally invasive treatment option, in patient with chronic pelvic pain.

The device can be implanted under local anaesthesia and consist of an implant lead with an lead capteres stimulation energy delivered wirelessly transdermally from an external pulse trasmitter and electrode patch.

The external pulse trasmetter is rechargeable and is only worn on the skin surface during periods of tibial nerve stimolation. A patient program is ured to track usage and to change program in the device. The program controls the external pulse trasmitter with wireless radiofrequency

Materials/Methods: PTNS was evalutated in one young patient with chronic pelvic pain.

For the percutaneus technique, the device is inserted using a designated delivery system and positionated under ultrasound guidance.

(Figure 1-2).

The device is wirelessly powered by an external control unit that controls the electro-stimolation parameters and is worn by the patient in the lower third of the leg. (Figure 3).

Program A for pain: Program B for Overactive Bladder
2,5 mA 3,0mA
400 µsec 70 µsec
70 Hz 20 Hz

Results: VAS 10<2
(HRQL) health-related quality of life low>higt
Drug therapies <50 %

Discussion: PTNS may have place in the treatments with chronic pelvic pain who have already tried many other therapies

Conclusions: The surgical technique consists of implanting the device through a small incision and then fixating it with a single suture in close vicinity to the tibial neurovascular bundle. The procedure can be performed under local anaesthesia

Objectives

ULTRASONU SKILL
ANATOMICAL SKILL
WIRELESS DEVICE

References

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Figure 1


Figure 2

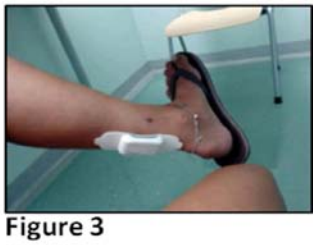
Figure 3

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273. INS19-0050

EVALUATION OF OCCIPITAL NERVE STIMULATION IN INTRACTABLE OCCIPITAL NEURALGIAS: A MULTICENTRIC, RANDOMIZED, CONTROLLED STUDY

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Introduction: Medically intractable pain caused by occipital neuralgia can be very difficult to control with traditional pain management. Peripheral nerve stimulation which is used in migraines and cluster headache can be an alternative for these patients with occipital neuralgias when medical treatment and traditional pain management have failed. Occipital nerve stimulation consists to put a lead subcutaneously in front of the occipital nerve and to connect the lead to a pulse generator. The aim of our study is to present the national controlled randomized multicenter study where occipital nerve stimulation will be compare to best medical treatment.

Materials/Methods: The primary objective is to assess the efficacy of occipital nerve stimulation in intractable occipital neuralgias after 6 months of treatment.

1) Compare between 2 groups:
- Maximal pain and average pain
- Health quality of life
- Patients global impression of change
- Efficacy after 6 months
- Relative decrease of VAS at 3 and 6 months

2) Decrease of medical treatment after 6 months in the experimental group

Results: The study presents the following characteristics: On a medical deviceMulti-center (national)
Controlled (2 groups)
Randomized
Open
Prospective
Parallel groups
8 patients included

Discussion: not applicable

Conclusions: this prospective study on occipital neuralgias is necessary to assess the efficacy of occipital nerve stimulation in refractory occipital neuralgias

Objectives
prospective study on occipital neuralgias
No CE mark on this indication for the moment
Safe treatment for refractory occipital neuralgias

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274. INS19-0235

ETHICAL CHALLENGES IN NON-SURGICAL NEUROSTIMULATION

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Introduction: Non-surgical neuro-stimulation (NSNS) has been the focus of considerable financial support and research interest over the past few years. While surgical interventions, for instance in the development of neuro-prostheses, have often been preferred primarily due to considerations of precision in output and input, non-surgical interventions afford the putative benefit of a lower risk profile. But that benefit may be only illusory.

Materials/Methods: I have undertaken a comprehensive literature review, conceptual and ethical analysis of issues arising in transcranial electrical stimulation, transcranial magnetic stimulation, and trigeminal nerve stimulation, as well as other peripheral nerve stimulation modalities.

Results: NSNS interventions remain invasive even if not surgically invasive, and the potential reduction in precision of NSNS may yield more unintended consequences than are evident in surgically based neuro-stimulation. Moreover, NSNS interventions will be considerably more widely deployed, especially in consumer and civilian contexts.

Discussion: The trade offs between surgical and non-surgical neuro-stimulation efforts must be critically explored in order to advance the overall promise of neuro-stimulation.

Conclusions: I propose a framework for assessing these tradeoffs in advancing translational research and development in neuroscience and neurotechnology.

Objectives

- Review risk profiles of non-surgical neuro-stimulation modalities
- Explore trade-offs between surgical and non-surgical neuro-stimulation modalities.
- Propose a framework for ethical evaluation of trade-offs.

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275. INS19-0335

SPINAL CORD STIMULATION IN PHANTOM UPPER LIMB SYNDROME. CASE REPORT

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Introduction: Phantom limb pain (PLP) is usually challenging to treat, requiring several kinds of treatments. First it is common to treat with pharmacological therapies, but, when these fail, neuromodulation appears as a good alternative.

Materials/Methods: We present a case of a 66 years old male that had a traumatic accident that led to an amputation of his right arm in 1977. Seven years ago he started feeling pain in his right shoulder, and with some kind of phantom limb pain. He felt continuous pain, with neuropathic characteristics and visual analogue score ranging from 6 to 9. He was referred to our unit one year ago and he was treated with antiepileptics, tricyclic antidepressants and low dose fentanyl as a first line and topical capsaicin with bad response.

As a last step of the treatment we decided to implant a cervical epidural lead to stimulate the dorsal horn to manage his pain. The trial was made using tonic stimulation.

Results: After the trial period the patient referred an improvement of 100%; so an internal battery (Prodigy MRI, Cardiva, Abbot) was placed in the gluteal region.

Discussion: PLP is a pathology with some difficulties to treat, even pharmacological treatment can be a good choice in some patients we cannot forget about Spinal cord stimulation (SCS). A great number of these patients are young at the moment of the amputation and they can complaint about the secondary effects of the medication. SCS offers a great tolerance and few side effect and it appears as a good option for treating this pathology.

Not only tonic stimulation is a good choice but the newer "paresthesia free" modes, and the dorsal ganglion root stimulation can be alternatives in this illness.

Conclusions: SCS is one of the best options to treat PLP in patients refractory to pharmacological treatment or patients that don't tolerate medication's side effects.

Objectives

Sometimes PLP is refractory to pharmacological therapy.

PLP is a good indication for SCS.

New kinds of SCS should be tested to treat PLP refractory to tonic stimulation.

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276. INS19-0177

SPINAL CORD STIMULATION IN TERMINAL CANCER. A CASE REPORT

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Introduction: Neuropathic pain is sometimes difficult to treat. It is associated with a wide variety of symptoms and it affects life quality. The treatment with spinal cord stimulation can be a good option for this kind of pain, but it is usually contraindicated in patients with cancer pain.

Materials/Methods: We present a case report of a patient that complained of progressive dyspnoea and arm neuropathic pain. A CT scan was performed showing lung tumor with extension to the laterocervical lymph nodes that compressed the braquial plexus. After he was diagnosed with an intractable cancer he was referred to our unit to treat his pain.

He presented continuous neuropathic pain in his right arm, with an analogue visual score of 8 points and with irruptive pain crisis. He was treated with amitriptyline and anti epileptics until reaching maximum doses with little improvement.

In this situation we think of a more invasive treatment despite of his clinical situation as he was supposed to die in a year-time.

Results: A 4-pole epidural electrode was implanted with the leas in the level of C3 vertebrae. Tonic stimulation was performed.

The patient tolerated the procedure and he was discharged home the same day the leads were implanted.

He showed an improvement of an 80% percent of his pain, expressing and VAS score of 1 most of the time without irruptive crisis.

Discussion: Cancer pain can have several etiologies. It can appear as mechanical, neuropathic, related to the treatment. . In our patient the principal component of his pain was neuropathic. As life expectancy in some of these patients is very limited pharmacological treatment is the first and sometimes the only choice.

Even though we can not forget invasive treatments in these situations. Intradural pumps, SCS appear as last chances for refractive cancer pain when pharmacological treatment is at their highest dose.

Conclusions: Spinal cord stimulation could be a good choice in refractory neuropathic cancer pain.

Objectives

Cancer Pain can be treated with spinal cord stimulation

Cancer Pain can cause refractive neuropathic pain

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277. INS19-0366

WIRELESS PERIPHERAL NERVE STIMULATION FOR COMPRESSIVE NEUROPATHY OF THE LOWER EXTREMITY

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Introduction: An 86-year-old male presented with chronic right leg pain due to compressive sural and superficial peroneal neuropathy. Lumbar sympathetic and peripheral nerve blocks provided only transient relief. Due to complex post-surgical spinal anatomy, he was a poor candidate for spinal cord (SCS) or dorsal root ganglion (DRG) stimulation. Ultimately, durable pain relief was achieved using a dual-lead, wireless peripheral nerve stimulation (WPNS) system.

Materials/Methods: With the patient in a left lateral decubitus position, the right leg was prepped and draped. Ultrasound was used to identify the target nerves. Parallel lead paths running 0.5 to 1 cm adjacent to the target nerves, clear of the anterior compartment and peroneal tendons, and extending to a point overlying the lateral malleolus were marked. A 3 cm horizontal incision was made two fingerbreadths below the fibular head. Two wireless PNS electrodes were then implanted under ultrasound guidance. The final lead positions were confirmed with fluoroscopy. Wireless stimulation provided pleasant paresthesia and analgesia over the painful area. Visual analog scale (VAS) fell to 2 from a baseline at 9. After a successful trial, a permanent WPNS was implanted. Routine care was then performed at monthly clinic visits over the following year.

Results: At 1-year follow-up, the WPNS still provided excellent pain relief with VAS 1-2, allowing the patient to discontinue opioids. No complications occurred.

Discussion: PNS placement in the distal lower extremities can seem daunting due to concerns about lead-migration, lead-fracture, and the absence of a suitable implantable pulse generator placement site. However, in some cases, WPNS placed with careful surgical planning and using appropriate imaging modalities can provide much-needed pain relief, improved function, and a path to opioid reduction for difficult-to-treat cases of peripheral neuropathy. Here, the use of ultrasound guidance was essential to precise lead placement, ensuring safe and optimal orientation to the nerves.

Conclusions: In this case, WPNS provided sustained pain relief of refractory chronic neuropathic pain, thereby facilitating opioid discontinuation. WPNS systems are a promising option for patients with chronic neuropathic pain of the extremities who have failed other therapies and who may not qualify for DRG or SCS.

Objectives

1. WPNS can effectively treat compressive neuropathy of the distal lower extremity.

2. Careful surgical planning and a detailed anatomical knowledge are crucial to good clinical outcomes.

3. Complementary use of ultrasound and fluoroscopy is a simple and effective imaging strategy.

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278. INS19-0343

COOLED RADIOFREQUENCY ABLATION PRODUCES GREATER REDUCTION IN NERVE FUNCTION

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Introduction: Radiofrequency ablation (RFA) is a minimally invasive procedure used to denervate the pain-transmitting peripheral nerves in chronic pain patients. Standard RFA (SRF) utilizes an 80°C probe tip to create a thermal lesion in which the temperature drops as the radius from the tip increases. Cooled RFA (CRF) overcomes the lesion size limitations inherent to SRF by circulating fluid around a 60°C probe tip to remove heat from tissue adjacent to the electrode, thereby delivering energy within a larger radius. While RFA lesion size has been evaluated previously in ex vivo tissue models, a thorough characterization of the physiological changes elicited in response to RFA is lacking. As previously reported(1), sciatic nerve RFA can be performed in rats to mimic clinical applications for rapid assessment of changes that occur over extended durations in humans. (Note: Two weeks of a rat lifespan corresponds to one human year.) Here, we present the first *in vivo* analysis of changes that occur to an ablated nerve in response to RFA. We hypothesized that enhanced delivery of thermal energy provided by CRF correlates with reduced nerve function when compared to SRF.

Materials/Methods: Lewis rats were exposed to optimized levels of SRF (50s, 80°C, 22 gauge/5mm active tip) or CRF (80s, 60°C, 17 gauge/2mm active tip) on the sciatic nerve to allow for the evaluation of nerve ablation over time with minimal collateral damage to surrounding tissues and severe adverse events. To understand the impact of ablation on nerve function, a positive control group of animals received a complete transection and surgical repair of the sciatic nerve. Animals were repeatedly evaluated for nerve function (electromyography-EMG) for 12 weeks post-ablation. All studies received IACUC approval.

Results: Significantly greater attenuation in compound motor action potential (CMAP) amplitude was found immediately after ablation in and for up to 6 weeks post-ablation in CRF treated nerves, similar to the nerve-transection control group. A return of function was found as early as 4 weeks in SRF treated nerves. By week 8, both CRF and SRF treated groups show signs of return-to-function.

Discussion: Recent clinical results report CRF provides pain relief that lasts more than twelve months(2). Greater impact on nerve function, may elucidate the mechanisms underlying pain relief provided by CRF to chronic pain patients. Further work is warranted to the understand mechanistic differences between SRF and CRF procedures and their impact on pain related outcomes.

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279. INS19-0249

PERCUTANEOUS ELECTRICAL NERVE BLOCK OF ACUTE PAIN IN ABLE-BODIED SUBJECTS

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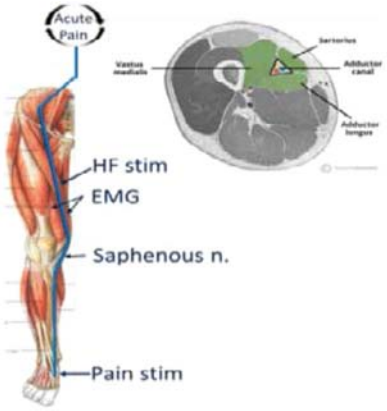

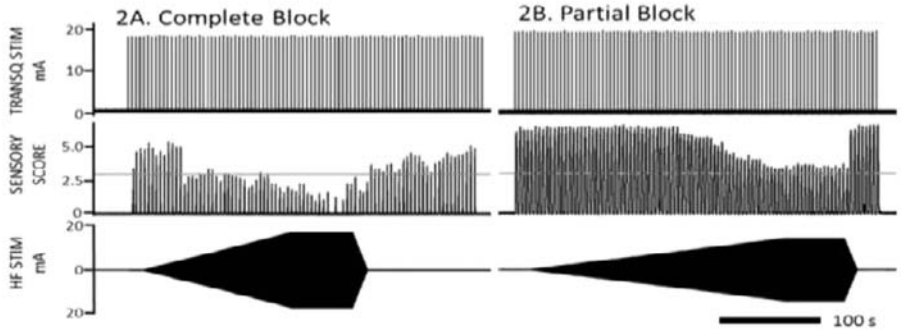

Introduction: Introduction: High-frequency (HF) electrical stimulation delivered to a peripheral nerve through a cuff electrode can reduce post-amputation pain [1]. The need for surgical implantation of a nerve cuff, however, considerably burdens the use of HF stimulation for acute applications. This study investigates the effects of HF electrical stimulation delivered percutaneously to the saphenous nerve in the adductor canal on acute pain in able-bodied subjects.

Materials/Methods: Able-bodied subjects (N=5) and underwent multiple trials of electrical stimulation. Acute pain sensations were elicited by transcutaneous electrical stimulation of the saphenous nerve at the ankle. High-frequency electrical stimulation (10 kHz; sinewave) was then simultaneously delivered to the saphenous nerve at the adductor canal (Fig. 1) via a percutaneous lead. Various HF stimulation amplitudes (≤ 25 mA) and durations (seconds-to-minutes) were used. Outcome measures included acute pain score and muscle activity. Subjects described their pain intensity on a 0-to-10 scale via a handheld potentiometer, where 3 was defined as the pain-threshold. Muscle activity was monitored both visually and by EMG recordings.

Results: All subjects reported reduced pain scores when HF electrical stimulation was applied. Painful sensations were completely abolished in 4 subjects (Fig. 2A), and were still present, but reduced in 1 subject (Fig. 2B). In all subjects, pain scores returned to baseline values within seconds after the stimulation was terminated (Fig. 2). High-frequency electrical stimulation was well tolerated by all subjects and did not elicit EMG activity or visible contractions of the thigh muscles. No serious adverse effects were reported.

Discussion: This study demonstrates that HF electrical stimulation of the saphenous nerve can block acute pain sensations that were elicited distally without eliciting unwanted contractions of the nearby muscles. This is reasonable since multiple layers of fascia and connective tissues separate the stimulation site from the muscular borders of the adductor canal. Lastly, blocking effects were reversible and did not demonstrate signs of carry-over, like described previously [1]: this finding may be due to differences in stimulation durations and/or pain type tested.

Conclusions: Percutaneous high-frequency electrical stimulation of a sensory nerve in the adductor canal can reversibly block acute pain sensations in humans, without causing co-excitation of nearby muscles.

Objectives

Learning Objectives: Determine if HF electrical stimulation can block acute pain sensation in able-bodied subjects Determine if HF electrical stimulation delivered through a percutaneously-placed electrode would activate the muscles forming the adductor canal Investigate timeline of block reversibility

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280. INS19-0250

PERCUTANEOUS HIGH-FREQUENCY ELECTRICAL STIMULATION COMFORTABLY BLOCKS ACUTE PAIN SENSATIONS IN HUMANS

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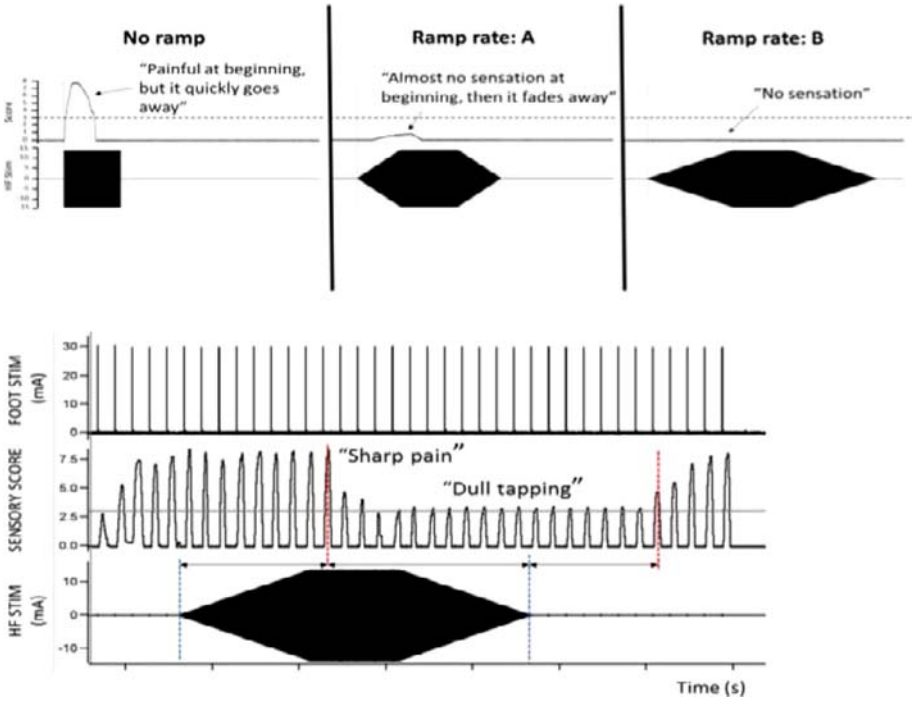
Introduction: High-frequency (HF) electrical stimulation can block the transmission of signals through a peripheral nerve [1]. Animal studies demonstrate that the blocking effects are reversible and always preceded by "onset activity". Onset activity refers to a short-burst of neural discharges that are elicited when the stimulation is first delivered and may lead to painful sensations and/or motor contractions. Herein, we investigate sensory onset and acute pain block efficacy during percutaneous HF stimulation in able-bodied subjects.

Materials/Methods: Able-bodied participants (N=5) underwent multiple trials of HF electrical stimulation to determine the quality, intensity,



and time-course of any elicited sensations. Afterwards, the effects of HF stimulation on acute pain signals were assessed. High-frequency electrical stimulation (10 kHz; sinewave; ≤ 25 mA) was delivered to the saphenous nerve at a site 5-to-10 cm proximal to the ankle, via a percutaneously-placed electrode. Traditional electrical stimulation was used to elicit acute pain sensations and was delivered via surface electrodes placed over-top the saphenous nerve at the ankle. Participants verbally described the quality of the evoked sensations and marked its intensity on a 0-to-10 scale via a handheld potentiometer, where 3 was defined as the pain-threshold.

Results:

High-frequency electrical stimulation elicited sensations in each participant. The sensations were described as a vibration or tingling at lower stimulation intensities and as pain at higher intensities. The sensations began at the onset of the stimulation and quickly faded over a few seconds (≤ 15 s) while the stimulation was being delivered (Fig. 1). The intensity of the elicited sensation was reduced to comfortable levels (< 3) and completely abolished (N=3) when the amplitude of the HF stimulation was gradually ramped to blocking intensities (Fig. 2). Lastly, HF stimulation reduced (< 50%; N=1) or completely abolished (N=4) acute pain sensations (Fig. 3).

Discussion: The sensations elicited at the onset of HF stimulation are consistent with expectations of the onset response reported in animals and were mitigated by slowly ramping the amplitude of the waveform to blocking plateaus. High-frequency electrical stimulation reversibly blocked acute pain sensations in all subjects.

Conclusions: High-Frequency electrical stimulation delivered through a percutaneously-placed electrode can comfortably block acute pain sensations in humans.

Objectives

Assess the sensations elicited by percutaneously delivered, HF electrical stimulation in humans Determine a strategy to mitigate uncomfortable sensations elicited by HF stimulation Determine if HF electrical stimulation can block acute pain

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281. INS19-0438

EFFECTS OF PULSED RADIOFREQUENCY ON THE SENSE-OF-TOUCH AND ACUTE PAIN: A LONGITUDINAL STUDY IN ABLE-BODIED SUBJECTS

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Introduction: Pulsed Radiofrequency (PRF) is a non-destructive method that is used to treat chronic pain without impairing motor or low-threshold sensory function. Animal studies suggest that the voltage-field produced during a PRF treatment may elicit a short-term, block-like cellular response primarily affecting nociceptive nerve fibers.[1,2] The effects of PRF on *acute* sensations in human subjects have not been investigated. Herein, we investigate the time-course and effects of PRF on the sense-of-touch and acute pain perception in able-bodied subjects.

Materials/Methods: A single treatment of PRF (42°C; 240 s treatment duration; 20-ms pulse duration; 2 Hz) was delivered to the left-side saphenous nerve below the knee in 5 able-bodied subjects. Pain and touch sensitivity were assessed on both legs within hours before and after the PRF treatment; tests were repeated multiple times up to 21 days post-PRF. Acute pain sensations were elicited by transcutaneous electrical stimulation (9-pulse train; 500 Hz) of the saphenous nerve at the ankle. The method-of-limits was used to determine pain-threshold. Mechanical stimulation (250 Hz sinusoid; cylindrical contactor 3.0 cm^2) and two-alternative forced choice testing (300-ms interval duration; step size ref 1 dB) was used to evaluate touch sensitivity on the lower shank, and within the saphenous nerve receptive field. A clinical examination was performed at each visit.

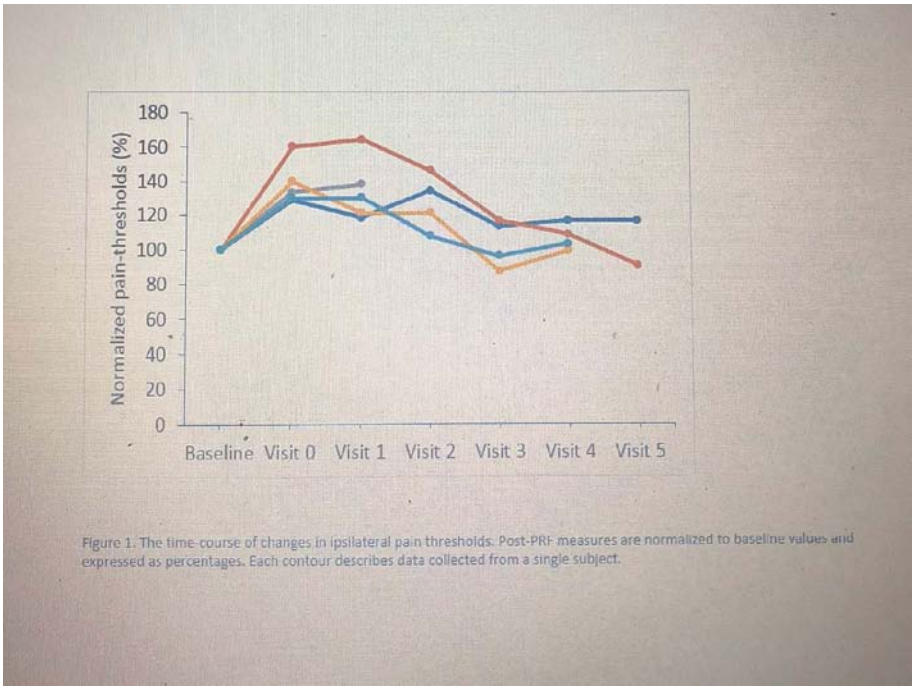

Figure 1. The time-course of changes in ipsilateral pain thresholds. Post-PRF measures are normalized to baseline values and expressed as percentages. Each contour describes data collected from a single subject.

Results: Baseline pain thresholds were 14.7±3.8 mA and 13.9±3.7 mA in ipsi- and contralateral legs, respectively. In all subjects, ipsilateral pain thresholds increased immediately after PRF, averaging 20.1±4.5 mA (138.3±12.9 % of baseline); contralateral thresholds measured 13.2±3.8 mA (95.2±6.5 % of baseline). Ipsilateral thresholds remained elevated 6-8 days post-PRF (Fig. 1). Post-treatment pain was reported as "dull" in the ipsilateral leg. No changes in touch sensitivity or clinical signs were observed.

Discussion: The present study has demonstrated that single PRF treatment can reduce acute pain sensations while preserving the sense of touch. Moreover, the quality of the pain sensations changed from "sharp" at baseline, to "dull" post-treatment. Lastly, PRF effects occurred within hours of treatment and lasted for days.

Conclusions: PRF can produce long-lasting decrease in acute pain sensations and does not alter touch sensitivity in able-bodied subjects.

Objectives

Determine how PRF affects touch sensitivity and acute pain in able-bodied subjects. Determine the time-course of PRF effects on touch sensitivity and acute pain perception. Evaluate the quality acute pain sensations following PRF

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Poster Presentations - May 27 - May 30

Peripheral Nerve

282. INS19-0067

PAIN RELIEF BY UPPER CERVICAL SPINAL CORD STIMULATION THERAPY FOR REFRACTORY PAINFUL TRIGEMINAL NEURALGIA

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Introduction: Spinal cord stimulation (SCS) is effective and safe therapy for neuropathic pain of limbs and trunk such as lumbar spine surgery syndrome and complex regional pain syndrome. However, there are few reports showing effectiveness against for facial pain and trigeminal neuralgia. We experienced very successful case of SCS against for intractable facial pain.

Materials/Methods: The case was 61-year-old female. She had suffered from symptomatic trigeminal neuralgia due to acoustic schwannoma. She had been treated with medication therapy and gamma knife, but pain control was insufficient and she was consulted to our clinic. She had shooting pain and also persistent pain in her left V1-3 region. We suspected her pain as the mixed pain of symptomatic trigeminal neuralgia and neuropathy due to gamma knife. We diagnosed it as painful trigeminal neuralgia. The main pain was the second branch of the trigeminal nerve region, so we conducted several neurolytic orbital nerve blocks with thermo-coagulation and finally with alcohol, but the effect of these neurolytic orbital nerve blocks was transient. We did not try Gasserian ganglion block, because we worried about risk of deafferentation pain. Medication therapy was also difficult due to side effects. At last, we suggested her SCS therapy, and she agreed. We performed percutaneous temporal SCS trial, we punctured at Th10 /11 and located the tip of SCS lead at C2 level.

Results: The tonic stimulation was ineffective for her pain and she felt uncomfortable, but with both burst stimulation and high-rate stimulation of 1000 Hz, her shooting pain disappeared and the persistent pain was also alleviated. (Numerical Rating Scare: NRS10→4). Thus we implanted her SCS device. After the implantation, her symptom has been alleviated.

Discussion: Conventional SCS was said to be unresponsive indication for face pain. But recently the devices of SCS is rapidly evolving, so we can use several stimulation patterns. A part of the spinal tract of trigeminal nerve is projected to the superior cervical vertebrae, so spinal cord stimulation at the superior cervical vertebrae can be a means of treatment in refractory facial pain not with tonic stimulation but with high-frequency or burst one.

Conclusions: We experienced a case in which refractory painful trigeminal neuralgia was relieved by spinal cord stimulation at the upper cervical vertebrae.

Objectives

Extension of spinal cord stimulation therapy

Treatment of intractable pain

Alternative treatment of trigeminal neuralgia

References

Upper Cervical Spinal Cord Stimulation as an Alternative Treatment in Trigeminal Neuropathy

Poster Presentations - May 27 - May 30
Peripheral Nerve

283. INS19-0055

SUCCESSFUL USE OF SPINAL CORD STIMULATION IN TREATMENT OF NEUROPATHIC PAIN IN CIDP

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Introduction: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare neurological disorder in which there is inflammation of the peripheral nerves alongside destruction of their myelin sheath. It may affect both motor and sensor nerves. Though neuropathic pain is not a universal symptom; when it occurs it can be refractory to treatment with many medications.

We describe a case of such peripheral neuropathic pain successfully treated with Spinal Cord Stimulation.

Materials/Methods: Our patient is a retired 70-year-old Caucasian gentleman who was diagnosed with sensory CIDP nearly twenty years ago. This was confirmed on biopsy and nerve conduction studies. He had been treated with steroids before starting treatment with Intravenous Immunoglobulin ten years ago. He is now on weekly courses of IVIG every five weeks. This treatment does reduce his other sensory symptoms but not his pain. Before SCS he was on Pregabalin 300mg twice daily to reduce the neuropathic pain despite experiencing side effects from it. He had previously tried many other alternatives. His past medical history included steroid-related Glucose intolerance. The pain occurred in all his four limbs and was rated at a range of 8-10/10 on NRS.

After multidisciplinary assessment and informed consent, patient underwent full implantation of SCS. Four eight-contact leads (with narrower spacing for the cervical leads) were placed at lower thoracic and cervical levels bilaterally; achieving full paraesthesia coverage with on-table testing. All the leads were connected to a Boston Scientific rechargeable 32-channel battery (Percision Spectra), which was then implanted in the left lower buttock.

Results: Recovery was uneventful and after one reprogramming patient reported more than 65% reduction in NRS which is maintained at 1, 3 and 12 months. With significant reduction in his anti-neuropathic medication, he reports no more side effects. He also reports significant improvement in his quality of life. The rest of his treatment remains unchanged.

Discussion: The nerve conduction studies obtained 12 months after the full implantation indicate progression of the underlying disease but this has not led to any reduction in his responsiveness to treatment with SCS. This highlights the role of SCS in symptomatic reduction of pain associated with CIDP.

Conclusions: SCS is a treatment option for neuropathic pain in CIDP.

Objectives

New indication for SCS

Role of SCS in rare neurological diseases

CIDP treatment options

References

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Poster Presentations - May 27 - May 30
Peripheral Nerve

284. INS19-0261

CHARACTERIZATION OF ELECTRODES FOR MINIMALLY INVASIVE DIRECT CURRENT NERVE BLOCK

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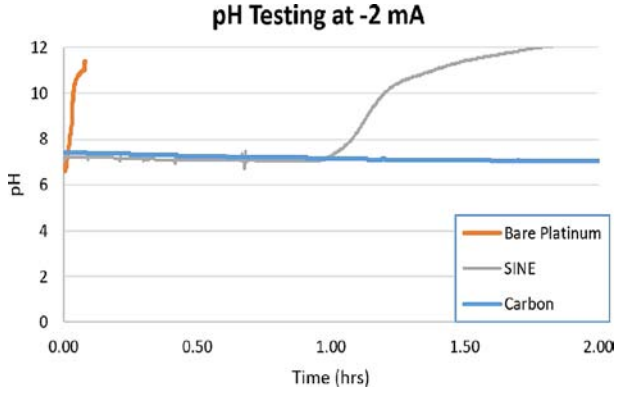
Introduction: Direct current (DC) can be used to generate electrical nerve block, providing a reversible alternative to chemical nerve blocks. Using platinum electrodes, reactions occur at the nerve interface causing damage to the nerve. The electrode can be separated from the nerve using a conducting medium, isolating the reactions in a vessel away from the nerve. This electrode is referred to as the Separated Interface Nerve Electrode (SINE) [1]. The ability of the SINE to buffer reactions is dependent on the size of the buffer vessel. In order to enhance the run time of the device, high surface area carbon was added to the buffer to increase the capacitance of the device. The buffering capability was tested in vitro by recording pH at the nerve interface of the device.

Materials/Methods: Three different electrode configurations were evaluated; bare platinum foil (0.025 mm thick) electrode (1.0 cm x 1.0 cm area), 5 mL saline SINE, and 5 mL carbon SINE. DC was applied at -2 mA for two hours or until a pH level of 10. A high impedance return path was used so that reactants could be measured. The setup includes a membrane holder with composite membrane connected to two tubes filled with conductive gel.

Results: Bare platinum electrodes produce significant pH changes at the nerve interface in less than 5 minutes. Using the SINE electrode increases the amount of time to 72 minutes. The addition of carbon to the buffer vessel increases the total time well above 2 hours.

Discussion: Without a buffer, bare platinum electrodes produce pH changes rapidly at the nerve interface. For the conventional SINE, reactants are contained in the vessel for a period of 72 minutes before migration to the nerve interface occurs. High surface area carbon increases the duration of time that the electrode behaves like a capacitor. This extends the run time before any reactants build up.

Conclusions: High surface area carbon produces significant capacity improvements over the SINE electrode, producing a smaller form factor device.



Objectives

DC nerve block requires electrodes that prevent reactants

The SINE electrode contains reactants in a buffer vessel distant from the nerve.

High surface area carbon increases the capacitance of the SINE electrode

References

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Poster Presentations - May 27 - May 30

Socioeconomics

285. INS19-0054

DESPITE AVERSION TO REGULATION: WHAT DO SCIENTISTS IN THE BIOMEDICAL FIELD THINK OF STRICTER PROFESSIONAL REGULATION?

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Introduction: Meta-research of scientific structures and methods has gained considerable significance in the last decade.[1] Centers like METRICS[2] at Stanford Medical School research issues such as replication crisis, publication bias, impact factors, Hirsch indexes and other questionable research practices.[3]

Oxford researchers Chalmers and Glasziou study the efficiency of biomedical knowledge production and estimate that a total of about 85% of the US $ 100 billion invested in biomedical research worldwide every year is wasted.[4]

Materials/Methods: Yet, despite these systemic issues, very few regulatory measures have been attempted to address and remedy them. One reason for this reluctance of the regulator could be that the academic system is and traditionally has been highly self-regulatory and averse to formal state regulation. In this survey experiment, I use questionnaires to investigate how scientists in the biomedical field perceive the impact of different hypothetical professional code of conduct regulations (on a scale from lenient to strict) on research practices.

Results: I hypothesize that stricter regulation of scientific methods is perceived as more intrusive and not beneficial to improve adherence to rules of good scientific conduct.

Discussion: This displays an evident disparity to the fact that the current deregulated system is faced with serious methodological challenges that have led to considerable scientific waste production.

Conclusions: Despite the fact that the current academic system has produced large ("above-chance") amounts of methodologically sloppy and/or fraudulent research, science regulation to reduce these systemic flaws continues to be non-existent. There seems to be a correlation between regulation-aversion of academics and continued low science regulation. As a matter of fact, scientists occupy a singular position in that they do not have to adhere to rules of professional conduct (lawyers, medical doctors or engineers for instance all do).

Objectives

In future research, it would be interesting to look at the more complex question of how different regulation of academic systems (either in

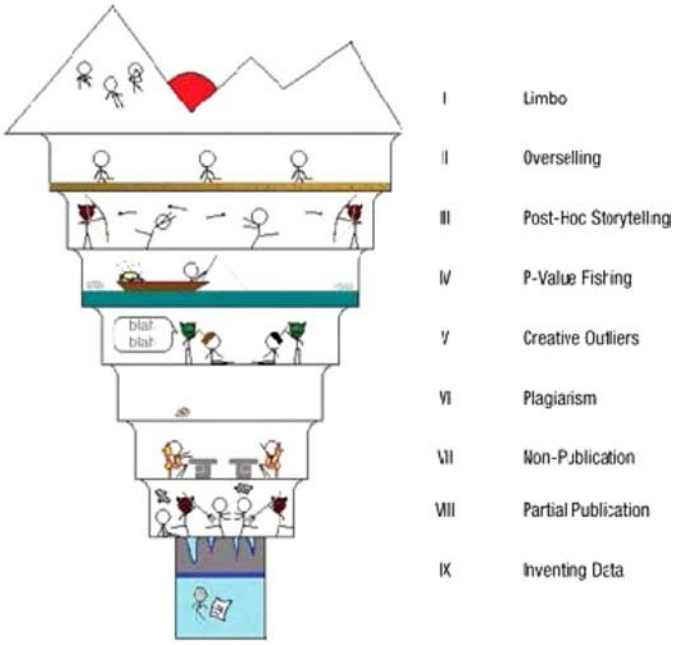

Fig. 2. The nine circles of scientific hell (with apologies to Dante and xkcd)

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different times or in different countries) has actually affected research integrity. This would provide valuable data to compare to the data on perceived regulatory impact and draw conclusions for an enlightened discussion on the topic and effective avenues to pursue for science regulation.

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1 For a recent and publicly debated case see: https://www.nytimes.com/2018/10/29/health/dr-piero-anversa-harvard-retraction.html

2 https://metrics.stanford.edu

3 Picture reproduced from: Neuroskeptic (2012) Nine Circles of Scientific Hell, Perspectives on Psychological Science, 7(6): 643-644.

4 Chalmers I, Glasziou P (2009) Avoidable waste in the production and reporting of research evidence, The Lancet, Vol. 374, p. 86-89 (86, 89).

Poster Presentations - May 27 - May 30
Socioeconomics

286. INS19-0060

IMPROVING OUTCOME OF SPINAL CORD STIMULATOR IMPLANTATION: A PROPOSAL FOR THE ANALYTICS OF SCIENCE AND PRACTICAL (SOCIAL) ANALYTICS IN SELECTING CANDIDATES FOR SPINAL CORD STIMULATION

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Introduction: Implantation of spinal cord stimulators for the control of chronic pain has burgeoned over the last decade. Parallelling the increase in scientific knowledge and applied technology, the placement of such devices has grown worldwide from about 30,000 in 2007 to 50,000 in 2019. In the USA the spinal cord stimulator industry has grown to a $2.2 billion dollar (USD) effort. Medicare (a form of national insurance for the USA elderly and disabled) reimburses providers $5071 per implantation. Our experience is that care and evaluation surrounding implantation can cost up to $160,000 (USD) per patient.

Materials/Methods: Stimulator implantation entails risk (equipment failure, electrode migration, hemorrhage, infection, neurological injury). Procedures are generally safe and serious complications are uncommon, but therapy failure rates are appreciable. Ineffective relief for one reason or another after stimulator implantation is as high as 50% in some studies.

Results: It is our contention that the failure rate in some instances is related to patient selection for this instrumental technology, and in others to a failure of treating specialists to appreciate the cultural backgrounds, reliant sources, levels of understanding and expectations of persons who are candidates for such treatments.

Discussion: We propose a series of preparatory encounters in which the science and medicine surrounding spinal cord stimulator implantation is addressed (Scientific Analytics) along with the issues of each candidate's expectations, traditional sources of information, levels of trust and cultural determinants (Particular or Social Analytics) are explored, and control comparisons are made. It is our hypothesis that the exercise of Analytics will improve outcome in spinal cord stimulator treatment which is costly and too often unsuccessful.

Conclusions: Issues such as trust, belief, sources of reliance, social and ethnic influences and religious belief can be addressed to the improvement of treatment outcome. The content and mathematical construction of this form of inquiry, first described in 1927, will be described along with research methodology testing its utility.

Objectives

1. To introduce the application of Analytics to evaluation of patients
2. To pose the use of Analytics to improve the success rates of spinal cord stimulation for pain
3. To pose the use of multi-participant studies utilizing Analytics

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Socioeconomics

287. INS19-0185

COST EFFECTIVENESS ANALYSIS OF SPINAL CORD STIMULATION IN OUR DEPARTMENT

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Introduction: Chronic Pain is one of the main problems that general practitioners face in their daily work and low back pain is the second cause of laboral absent. In our department we have been placing leads to perform spinal cord stimulation for the last 3 decades in patients with failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS) (as the principal indications).

We performed a cost effectiveness analysis in 20 patients to assess if this treatment apart from being a good outcome for our patients, it could be economically sustainable.

Materials/Methods: We included 20 patients suffering from FBSS or CRPS that were treated between 2011 and 2015 with SCS. They were randomly selected by a professional anesthesiologist that was not part of our Pain Department.

We estimate the price of the treatment before and after the SCS, and the price of the surgical intervention. We also analyzed the visual analogue score before and after the SCS system was placed.

Results: We selected 20 patients, 55% women and 45% men. Thirteen patients suffer from FBSS and seven from CRPS. VAS score was 3.8 points less after the implant of the system.

The cost of the treatment of the patients before the SCS was 94,25 € per patient per month. It diminishes to 37,86€ after the implant. Taking into account the estimated price of the SCS system and the cost of the surgical team and the procedure the total cost of the SCS would be 12813 € after 6 months.

We would need 12,2 years to amortize the price of the implant.

Discussion: SCS as a treatment of FBSS and CRPS is cost effective according to the literature and we can confirm it with our research. The results compared with the ones presented by other authors differ in time being necessary just 5 years to amortize the implant of the SCS system.

This can be justified because our patients still need more pharmacological treatment than the ones in the other studies, because we selected the treatment the patients were receiving 6 months after the implant.

Conclusions: SCS is effective as a treatment for FBSS an CRPS, and also cost effective, even though the great costs of their implant.

Objectives

Quantify the cost of our pharmacological and SCS therapy

Assess the cost effectiveness of SCS

Calculate the time it would be necessary to amortize the therapy

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Socioeconomics

288. INS19-0216

NEUROMODULATIVE PAIN THERAPY AND REINTEGRATION INTO EMPLOYMENT - AN OBSERVATIONAL STUDY

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Introduction: There is only few data available on how neuromodulative 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. Unemployment negatively affects illness, i.e. unemployed people are not healthier than those in work.

Materials/Methods: From 2008 to 2017, 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] using SPSS22®.

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. 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 into employment should always be considered as 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 and patients in supporting a return to employment, if possible.

Objectives

return to the workplace as part of chronic pain management

assessment of quality of life in the treatment appraisal

pay consideration to the workplace when planning the therapy in chronic pain patients

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Poster Presentations - May 27 - May 30
Socioeconomics

289. INS19-0221

NEUROMODULATION THROUGH EARS: PAST OR FUTURE?

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Introduction: Auriculotherapy, a method developed in the twentieth century by the French doctor, Dr Paul Nogier, comes from a reflexotherapy based on the stimulation of the auricules. In the past years, transcutaneous auricular Vagus Nerve Stimulation, has been scientifically validated as a non-invasive bottom-up brain modulation technique. More recently, the emerging concept of Auricular Neuromodulation, takes advantage of the three main nerve supplies of the ear, including the little studied, yet promising Superficial Cervical Plexus.

Materials/Methods: Bibliographic analysis of ear stimulation was undertaken in order to validate its clinical efficacy and to unravel its mechanism of action.

Results: Ear stimulation is definitely a technique of auricular Neuromodulation, even if its mechanism of action is not fully elucidated, partly because of the lack of granted means.

Discussion: It is urgent to develop clinical and basic research in this non-invasive Neuromodulation. Indeed, it could potentiate other neurotherapeutics like drugs or even invasive Neuromodulation.

Conclusions: Ears are designed by nature to reach the brain. They could turn out to be the most affordable targets for non-invasive manipulation of central nervous system functions.

Objectives

1) Define what is Auricular Neuromodulation
2) Investigate its clinical efficiency
3) Unravel its mechanisms of action

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Spine - Pain

290. INS19-0362

LONGITUDINAL DATA FROM THE TARGETED DRUG DELIVERY PRODUCT SURVEILLANCE REGISTRY: POCKET FILL RISK, IDENTIFICATION AND MITIGATION

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Introduction: Inadvertent subcutaneous drug injection during refill of implanted intrathecal infusion systems is a known risk, with immediate and delayed patient consequences. Understanding the risks of pocket fill (PF) and the signs and symptoms associated with a complete or partial PF are important for those treating patients with implanted pumps.

Materials/Methods: Medtronic established this prospective, long-term, multi-center (US, Western Europe and Latin America) registry in 2003 to monitor infusion system performance. Data are collected on product-performance following IRB/EC approval at respective sites; patients providing informed consent are enrolled at initial system implant or pump replacement. A 2010 revision to adverse event reporting added collection of details, such as PF. Patients are followed prospectively for events related to the device, procedure, and therapy. Investigators provide event descriptions, patient symptoms, and patient outcomes.

Results: An estimated 73,785 pump refills occurred in 5,746 implanted pumps in PSR between April 2010 and July 2018. Reported adverse events within the registry database indicate few confirmed PF, but only clinically significant events may have been reported. In addition to registry refill data, relevant reported adverse events reported will presented.

Discussion: PF during pump refills is a serious concern for many providers who deal with intrathecal pumps. It might cause some providers choose not to use intrathecal pumps all together. There is no published data on the incidence of pocket fill during pump refills.

Conclusions: Understanding the relative risk of PF and associated adverse events aid in the identification of events and mitigation of immediate and delayed consequences.

Objectives

Data and information presented will educate clinicians on the risk of PF, assist in identification of signs and symptoms associated with PF, and methods of mitigation and treatment.

References

None

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Spine - Pain

291. INS19-0074

THE IMPORTANCE OF SOMATOTOPY TO ACHIEVE CLINICAL BENEFIT IN MOTOR CORTEX STIMULATION FOR PAIN RELIEF

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Introduction: The aim of this study was to search the relationship between the anatomical location and the eventual analgesic effect of each contact.

Materials/Methods: 22 patients (14 men and 8 women) suffering from central and/or peripheral neuropathic pain were implanted with stimulation of the precentral cortex.

The implantation of the electrodes was performed using intraoperative: **1)** Anatomical identification by Neuronavigation with 3D MRI, **2)** Somesthetic evoqued potentials monitoring to check the potential reverse over the central sulcus, **3)** Electrical stimulations through the dura to identify the motor responses and its somatotopy.

In order to locate postoperatively the electrodes, a 3D-CT was performed in each case and fused with the preoperative MRI. The clinical analgesic effects of cortical stimulation were collected on a regular basis (VAS reduction > 50%, drugs consumption). Data were analyzed to search a correlation between the anatomical position of contacts and analgesic effects.

Results: Post implantation analgesic effects were obtained in 18 (81.81 %) patients out of 22. The analgesic effect was companied with reduction of the drugs consumption in 15 patients (68.18 %). The post-operative 3D CT analysis shows a correspondence between the effective contacts localization and the motor cerebral cortex somatotopy in the patients with post-operative good analgesic effects. No correspondence was found between the contacts localization and the motor cerebral cortex somatotopy in the 4 patients with no analgesic effects. In three out of these four patients, analgesic effects were obtained after a new surgery allowing a replacement of the electrode position over the motor cortex somatotopy corresponding to the painful area.

Discussion: Our present study also appears to demonstrate the good analgesic effects of chronic stimulation of the motor cortex, as 95.45% of our patients with refractory neuropathic pain experienced a VAS reduction of more than 40% on average.

Conclusions: This study shows the correlation between position of the contact over the precentral cortex and the analgesia obtained when the somatotopy of the stimulated cortex correspond to the painful area.

Objectives

To search the relationship between the location and the analgesic effect of each contact.

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292. INS19-0316

IS THERE A RELATIONSHIP BETWEEN LOCATION OF SCS AND OUTCOMES FOR CHRONIC PAIN? IMAGE-BASED ANALYSIS

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Introduction: Spinal cord stimulation (SCS) has been employed in the treatment of neuropathic pain for over 40 years. However, there remains a gap in understanding how specific parameters contribute to therapy-effectiveness. In this analysis, we aimed to investigate the relationship between location of SCS and clinical outcomes for chronic pain.

Materials/Methods: We analyzed X-rays during the trial period from chronic pain patients (n=41), who were implanted with two SCS leads (paresthesia-mapping (PM) approach; anatomical-midline (AM) based approach). BurstDR stimulation was applied at a paresthesia-free amplitude. We defined threshold amplitude as the intensity of sensory perception; Stimulation was decreased to 60% of threshold and reduced in 0.05mA steps until no sensations were experienced to determine target amplitude. Patients evaluated their pain at baseline and at the end of each trial period using the visual analog scale (VAS). We implemented an intensity-threshold based algorithm to localize the centroids for the active anode and cathode on each lead. We identified the intended target for AM as T9/T10 and for PM as T7/T8, T8/T9, or T9/T10 based on individual paresthesia feedback. Lastly, we computed a linear model to determine the effect of stimulation location (Figure 1).

Results: Initially, we found no relationship between stimulation location, defined as distance from intended target, and pain-relief. However, additional analysis focused on distance from individual vertebral levels showed that distance of the active contact from T8/T9 was negatively correlated with pain-relief for all patients ($p = 0.02$). Also, specifically with the AM lead, stimulation amplitude was higher when the active contact was further away from the target ($p<0.01$). We sought to redefine "location" in terms of surrounding tissue (Figure 2). With a computational model and an ANOVA analysis, we confirmed our hypothesis that if the active contact was positioned immediately ventral to the vertebrae (low conductivity), there would be low current leakage, resulting in high stimulation efficiency ($p=0.04$).

Discussion: Currently, T9/T10 is considered the golden disc for lower-back and leg pain in terms of anatomical targeting. However, our analysis implores the investigation of T8/T9 as an effective anatomical target in future studies. Further, we demonstrate that stimulation location is important when determining programming parameters and should account for surrounding tissue properties. Lower stimulation amplitudes corresponding to these "targets" allude to energy savings that could translate into longer battery life.

Conclusions: Though further analysis is necessary, these results are promising as a stepping stone for integrating objective parameters into efficient programming decisions.

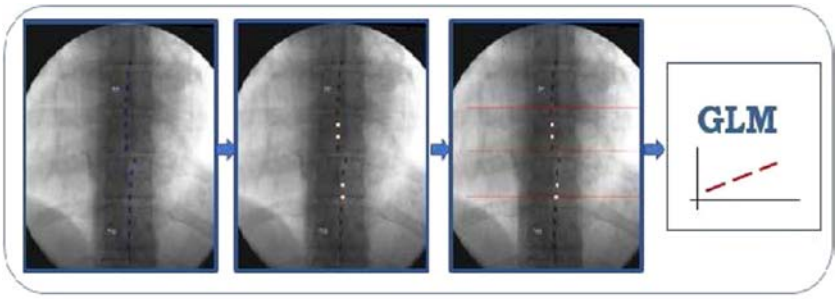

Figure 1: Image-analysis approach to determine the role of stimulation location in SCS therapy for chronic pain.

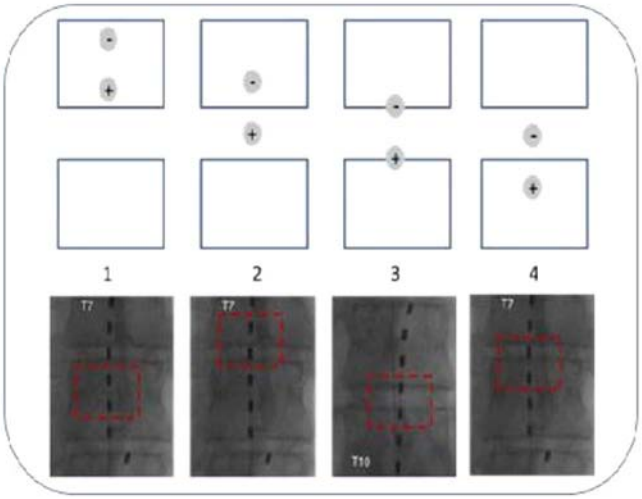

Figure 2: Location categories based on position of the bipolar pairs relative to vertebrae (low conductivity) and connective tissue (high conductivity)

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293. INS19-0317

INTRAOPERATIVE PARESTHESIA-MAPPING IS NOT REQUIRED FOR LEAD PLACEMENTS INVOLVING BURSTDR STIMULATION: RESULTS OF THE PROSPECTIVE, MULTICENTER, RANDOMIZED, DOUBLE-BLINDED CRISP STUDY

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Introduction: In this prospective, multicenter, double-blinded, randomized, crossover study, we compared the therapeutic efficacy of Burst SCS delivered using a lead implanted with the conventional paresthesia mapping approach to a lead implanted with an anatomic midline-based approach.

Materials/Methods: Patients with chronic back pain were implanted with two leads, one using paresthesia-mapping approach (PM) and the second using anatomical midline-based procedure (AM). Stimulation contacts were chosen using the standard mapping procedure for the paresthesia lead or such that the activated bipole was overlapping the T9-T10 junction for the anatomical lead. For either lead stimulation amplitude was selected such that no sensory percepts were generated. Patients were assessed at baseline and after a trial period during which they tested each lead for two weeks in random order. Proceeding trial, eligible patients had the option to receive permanent implants using their preferred AM or PM approach at end-of-trial. These patients were followed for 1 year with follow-up visits at 3, 6 and 12 months.

Results: Forty-two out of fifty-two patients (80.8%), who completed both trial periods, achieved at least 50% pain relief (65% and 67% pain relief for AM and PM leads, respectively) and proceeded to permanent implant. Moreover, twenty patients (47.6%) at end of trial were profound responders (≥80% pain relief) on at least one lead. No order effect was observed based on the sequence in which the leads were trialed. For the forty-two patients, the baseline average back pain was 78.9±12 mm on the VAS scale. Twenty-one patients preferred the PM approach while twenty patients preferred the PM approach. For AM patients, average back VAS scores were 27.3±27.3 mm (n=18), 32.8±31.3 mm (n=16), and 21±19.6 mm (n=9) for 3-,6- and 12-month follow-ups, respectively. For PM patients, average back VAS scores were 25.1±22.6 mm (n=19), 34.8±24.5.0 mm (n=15), and 23.1±17.4 mm (n=13) for 3-,6- and 12-month follow-ups, respectively. While pain scores of both approaches were significantly different from baseline at all follow-ups (p's <0.001) they were not different between themselves (p's>0.05). Similarly, both quality of life and disability measures were significantly improved from baseline, for both AM and PM approaches, but were not statistically different between the two approaches at all follow-ups. Ninety-one percent of patients were satisfied with Burst therapy at 3 months.

Conclusions: The results of this study suggest that similar clinical outcomes can be obtained without performing paresthesia mapping and implanting the leads using only anatomical imaging references.

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294. INS19-0135

SPINAL CORD STIMULATION AT 10 KHZ FOR THE TREATMENT OF CHRONIC PAIN OF THE UPPER EXTREMITIES: RESULTS OF A PROSPECTIVE, MULTICENTER, POST-MARKET, OBSERVATIONAL STUDY

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Introduction: Chronic upper extremity pain (UEP) has complex etiologies and is often disabling. Low-frequency spinal cord stimulation (SCS) offers only limited symptom relief and the variability in sensory paresthesia with movement of upper extremities compromises the performance. In contrast, high frequency SCS (HF-SCS) at 10 kHz provides pain relief without any paresthesia and has demonstrated superiority of traditional SCS for the treatment of back and leg pain[1,2]. The objective of this prospective, multi-center, post-market, observational study is to gain additional effectiveness data of HF-SCS at 10 kHz for the treatment of chronic, intractable pain of the upper extremities.

Materials/Methods: After Institutional Review Board/Ethics Committee approval, a total of 41 subjects, with significant upper extremity pain (Visual analog scale [VAS] ≥ 5 cm at baseline) underwent a trial of SCS at 10 kHz at six centers (US-5; UK-1). Subject outcomes were assessed for 12 months, and the primary outcome was the responder rate (percentage of subjects experiencing ≥50% pain relief from baseline). Other assessments included Pain Disability Index, upper limb functioning (Disability of

Predominant Pain	Baseline	12 Month
Shoulder	8.3 [7.2-9.1] (n=28)	1.0 [0.4-2.8] (n=25)
Upper Limb	8.1 [7.2-8.6] (n=33)	1.0 [0.3-2.6] (n=30)
Neck	8.8 [8.0-9.2] (n=25)	1.1 [0.7-4.1] (n=22)

Table 1. Baseline and 12-month VAS scores based on predominant pain

Assessment	Baseline	12 Month
Pain Disability Index	49 [37-56] (n=33)	15.5 [9-27.7] (n=30)
QuickDASH	70.4 [54.5-77.2] (n=33)	31.8 [18.1-47.7] (n=29)
GAF	55 [45-65] (n=33)	75 [65-84.7] (n=30)
PSQ3	25 [20-27.3] (n=33)	5.5 [1.8-13.6] (n=29)

Table 2. Baseline and 12-month scores for disability, functioning, and sleep assessment

Arm, Shoulder and Hand; QuickDASH), Global Assessment of Functioning (GAF), sleep (PSQ3), and subject satisfaction.

Results: Thirty-seven subjects successfully completed the trial (90% trial success) and 33 were permanently implanted with the Senza SCS system® (Nevro Corp., Redwood City, CA). Twelve months after permanent device activation, the responder rates for shoulder, upper limb, and neck pain subjects were 88%, 80%, and 73%, respectively. Median [Q1-Q3] VAS scores at 12 months showed a meaningful decrease from baseline values (Table 1).

Observed reduction in disability and improvement in functioning and sleep were also substantial (Table 2). Moreover, 86% of the subjects were satisfied or very satisfied with 10 kHz SCS at 12 months.

Discussion: This study provides evidence that HF-SCS at 10 kHz produces sustained and substantial pain relief in subjects with chronic UEP. Moreover, clinically meaningful improvement in functioning and sleep and decrease in disability were observed.

Conclusions: These results thus validate that SCS at 10 kHz is an effective and paresthesia-free treatment for chronic intractable pain of the upper extremities.

Objectives

Present long-term pain relief results of SCS in chronic upper extremities pain

Analyze effectiveness and quality of life outcomes in comparison to baseline

References

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295. INS19-0137

EVALUATION OF A NEW, MINIATURIZED BATTERY-FREE SPINAL CORD STIMULATOR SYSTEM CONSTRUCT: PATIENT COMFORT AND EASE OF USE DATA

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Introduction: The miniaturization of implantable neuromodulation therapies has ushered in new potentials for therapy applications. By utilizing an external power source, the implantable portion of the system is minimized in size. Past systems that have utilized this approach suffered from multiple shortcomings, including limited functionality, patient inconvenience and discomfort. We tested patient comfort and other ergonomic elements of a new neuromodulation system that encompasses a micro implant with an external power/control unit.

Materials/Methods: Chronic pain patients wore an inactive Therapy Disc, for 4 weeks. Two independent groups (n=25 each) wore the prototype device and gave feedback on comfort and other ergonomic factors. Patients were instructed on the use of an adhesive clip that held the prototype Therapy Disc. Volunteers would change the clip as needed and were encouraged to participate in normal daily activities to emulate the clinical setting as closely as possible. Patients rated comfort and usability levels on a 10-point Likert scale, where 1 was intolerable, and 10 was comfortable.

Results: Overall, chronic pain patients found the external power source very comfortable to wear. Many noted the external power source "not noticeable" when wearing it. Volunteers in group 1 rated the comfort as 8.7 (out of a possible 10) on the first day and then 9.1 after 4 weeks. Group 2 demonstrated similar ratings for up to 4 weeks. The adhesive clip was also easy to use by the patient volunteers. Removal of the adhesive clip was rated an 7.6 at the beginning, increasing to 8.5 out of a possible 10, similar to the comfort rating scale, after 4 weeks. The majority of patients (88%) also indicated that they would rather use this device configuration rather than a battery-containing, fully implantable IPG.

Discussion: These results demonstrate exceptional patient comfort and convenience ratings. While using an identical model of a device currently under development, chronic pain patients found the external power source easy to use, very comfortable to wear, and preferable to a fully-implanted system. Given these results, this new, contemporary system appears poised to provide a solution to objections and system limitations faced with prior, larger spinal cord stimulation systems.

Conclusions: With proper form factor and wearability engineering, external SCS transmitters can be comfortably worn by patients for prolonged periods of time.

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296. INS19-0297

REAL WORLD EXPERIENCE WITH A NEW RESTORATIVE NEUROSTIMULATION THERAPY FOR CHRONIC LOW BACK PAIN

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Introduction: Only 15% of Chronic Low Back Pain (CLBP) patients are suitable candidates for spine surgery with clear association between identifiable pathology on imaging and symptoms. The remaining 85% have "non-specific CLBP" which in 70% of cases is of predominantly nociceptive origin caused by mechanical stress or damage to non-neural structures. Available treatment options, including physical therapy, surgery, spinal cord stimulation, injections, denervation and drugs have limited effectiveness or serious side effects in this patient population. If symptom treatment is ineffective, should we treat the possible cause?

We present our real-world evidence with a new implantable restorative neurostimulation system for patients with CLBP and no prior spine surgery.

The therapeutic target for this therapy is the multifidus muscle which normally provides functional stability of the lumbar spine. In 80% of patients, CLBP is associated with atrophy of the multifidus. Fundamental to the therapeutic effect is the arthrogenic inhibition of the multifidus, and the associated functional instability and possible atrophy.

Twice daily, 30-minute bilateral electrical stimulation of the L2 medial branch of the dorsal ramus elicits episodic contractions of the deep multifidus muscles, thus overriding underlying arthrogenic inhibition. Reactivation of lumbar multifidus motor control and restoration of functional stability is the hypothesized mechanism of action.

Materials/Methods: Key eligibility criteria included CLBP despite medical management with at least pain medications and physical therapy in patients who were not candidates for spinal surgery. To date 11 of our patients were implanted with a restorative neuromodulation system (ReActiv8® - Mainstay Medical) and all patients showed atrophy of the lumbar multifidus on MRI. During the implant procedure two electrodes were placed at the L2 medial branch of the dorsal ramus and connected to the pulse generator. Patients were evaluated 6, 12 and 26 weeks after implant surgery.

Results: At baseline, average duration of low back pain was 9.3±6.2 years and average age was 45±10 years. Conservative treatment (pain medication, physical therapy, injections) failed in all patients. Low back pain NRS was 8.2±1.1. At last follow up (4.6±2.2 months) NRS had decreased to 3.6±1.6 (average reduction of 56%). Main aspects of quality of life which improved were walking, normal daily activities and sleeping.

Conclusions: In our "real world" case series, restorative neurostimulation provides clinical benefit to CLBP patients who are refractory to other available treatment options. Patient selection and an interdisciplinary approach (spine surgeon, pain therapist) is mandatory for good clinical outcomes in these patients.

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297. INS19-0345

REAL WORLD EXPERIENCE WITH HIGH FREQUENCY STIMULATION AT 10 KHZ IN CHRONIC BACK AND LIMB PAIN

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Introduction: Patients with chronic back and/or limb pain with failed conservative therapy are suitable candidates for spinal cord stimulation as an established treatment. High frequency stimulation at 10 kHz provides significant pain reduction without paraesthesia. In a randomized controlled trial the effectiveness of this new therapy was clearly shown. However, data on the commercial ("real-world") use of high frequency stimulation at 10 kHz are important to understand the safety and efficacy in a non-controlled study setting. Therefore, this study evaluated the "real-world" clinical results and complications in patients with chronic back and/or limb pain with high frequency stimulation at 10 kHz.

Materials/Methods: Preoperative assessment for correct indication was done for each patient by a neurosurgeon and a pain therapist. In a standard minimalinvasive procedure two leads were placed at C2-6 for cervical/and or arm pain and at T8-11 for lumbar and/or leg pain. Trial phase was 14 days and then the external parts of the leads were cut. IPG was implanted when pain reduction was > 50% during the trial. Patients were evaluated 6-8 weeks after surgery and then regularly each 3 -6 months.

Results: Overall 119 patients were trialed from 04/2016 to 09/2018. In 105 the trial was positive and IPG was implanted. Responder rate was therefore 88%. From the 105 patients 88.6% had a failed back surgery syndrome, 7.6% had no prior surgery, 1.9% had polyneuropathy and 1% had small vessel disease or migraine respectively. Back pain NRS decreased from 8.5 preoperatively to 3.0 (-65%) at last follow up. Same was seen for limb pain which decreased from 7.5 to 2.9 (-61%). Complications included 3 infections during the trial and 3 IPGs had to be corrected due to skin perforation after time (n=2) and pocket pain (n=1). No lead breakage was observed.

Conclusions: In our "real world" data, high frequency stimulation at 10 kHz was safe and showed good clinical results with significant reduction of pain. We propose an interdisciplinary approach (spine surgeon, pain therapist) in order to achieve favorable results for these chronic pain patients.

Objectives

References

1 Kapural 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. Neurosurgery. 2016;79:667-677.

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298. INS19-0379

CONTROLLING SPINAL CORD ACTIVATION DURING DELIVERY OF SCS THERAPY IN PATIENTS WITH HIGH DEGREE OF MOVEMENT IN THE SPINAL CANAL

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Introduction: Spinal cord stimulation (SCS) is a highly effective therapy for the treatment of chronic neuropathic pain and consists of delivering electrical stimuli to the spinal cord via electrodes implanted in the spinal canal. As the spinal cord is subject to substantial movement within the spinal canal, stimuli at constant amplitude will have varying effects on spinal cord activation (*Br J Anaesth*. 2008;101:804-9; *Eur Spine J*. 2012;21:2450-5). In some patients, these variations can affect activation even at rest (ie, heartbeat, breathing) and lead to uncomfortable sensations due to under- and overstimulation, which leads patients to adjust their stimulation (Horch K, Kipke D. *Neuroprosthetics: Theory and Practice*. 2017;8:710-61). Data demonstrating how a closed-loop SCS system, employing evoked compound action potential (ECAP) recording to measure spinal cord activation, responds to variations in spinal cord position with respect to the stimulating electrode are presented.

Materials/Methods: Spinal cord activation patterns (ECAP measurements) of patients identified in the Avalon trial (ACTRN12615000713594) reporting a pulsing sensation at rest, with constant-current (ie, open-loop fixed-output) stimulation, were reviewed. Spinal cord activation patterns while receiving open-loop stimulation were then compared to patterns with closed-loop stimulation (automatic adjustment of the current to maintain stable activation levels) enabled.

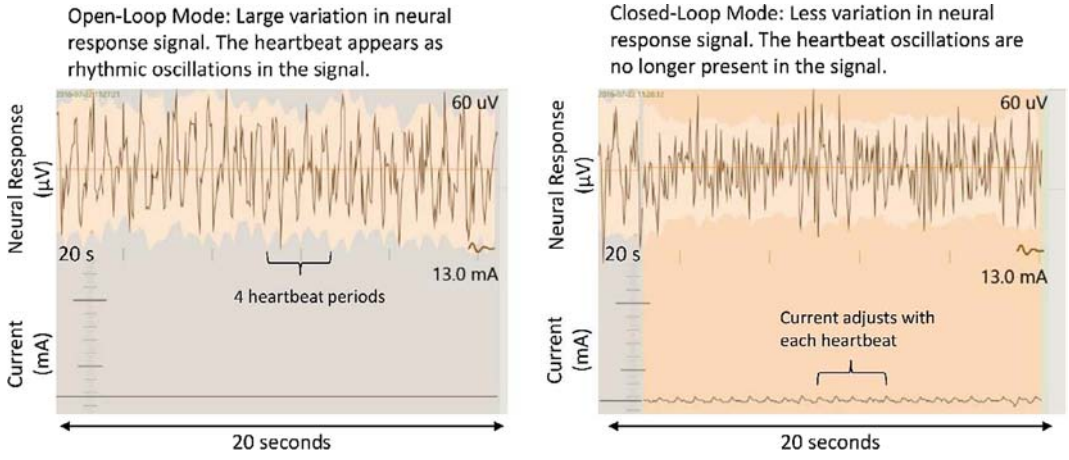
Results: The perceived pulsing sensation is reflected in the patient's spinal cord activation as oscillations in amplitude. In some cases, the level of activation can triple with each oscillation. The frequency of amplitude modulation was within the range of heart beat, fitting prior reports on spinal cord pulsations (*Eur Spine J*. 2012;21:2450-5; Horch K, Kipke D. *Neuroprosthetics: Theory and Practice. 2017;*8:710-61). Closed-loop stimulation reduced the amount of amplitude variation and translated into a decrease or elimination of pulsating sensation for the patient (Figure). Breathing has been observed to have a similar effect on both spinal cord activation and the patient's perception of intensity.

Discussion: There is a large degree of variation observed in some patients from normal physiological processes, even at rest. These variations could have an impact on the long-term efficacy of SCS.

Conclusions: ECAP recording facilitates quantification of spinal cord activation variations resulting from normal physiological processes, and closed-loop stimulation can provide a more reliable delivery of SCS therapy than any fixed-output system.

Objectives

1. ECAP recordings can be used to quantify variations in spinal cord activation
2. Physiological processes greatly affect spinal cord activation with SCS in some patients
3. Closed-loop SCS decreases spinal cord activation variation resulting from normal physiological processes



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299. INS19-0410

THE CORRELATION OF EPIDURAL FIBROSIS WITH EPIDUROSCOPIC AND RADIOLOGICAL IMAGING FOR CHRONIC PAIN AFTER BACK SURGERY

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Introduction: Epidural fibrosis has been implicated in the etiology of persistent pain after back surgery. Epidural fibrosis can be detected by conventional radiological methods, but these methods are insufficient to reveal the presence of epidural adhesions. The appearance of the epidural cavity with the epiduroscope is one of the best method to visualize the spinal cavity without damaging the anatomical structures. The aim of this study was to evaluate the correlation between the type and number of surgery and the degree of fibrosis in epiduroscopic and magnetic resonans imaging in patients FBSS.

Materials/Methods: A total of 61 patients (41 females, 20 males) with persistent low back pain after back surgery who accepted epiduroscopic imaging were included in the study. The mean age of the patients was 58.9 and the weight average was 79.2. The inclusion criterias were; VAS> 4, over 18 years of age, who underwent low back pain and/or radicular pain for at least 6 months despite lumbar surgery and conservative treatment. The patients were compared according to the fibrosis detected in epiduroscopic imaging and the degree of fibrosis detected in MR imaging. Epiduroscopic epidural fibrosis grading was evaluated using a four level grading system based on appearance and resistance to epiduroscope advancement. MRI epidural fibrosis grading was performed by a radiology specialist physician according to the modified Ross method.

Results: The incidence of advance and severe fibrosis (grade 3-4) at MRI and epiduroscopic imaging increases as the number of surgeries performed increases and the scope of the surgery expands. The conventional MRI and epiduroscopic imaging have similar findings in detecting advanced and severe (grade 3-4) fibrosis.

Discussion: In this study epiduroscopy is a more sensitive method in detecting mild and moderate (grade 1-2) fibrosis. Therefore, it should be kept in mind that epidural fibrosis may be the source of pain in normal MRI and treatment should be performed accordingly.

Conclusions: In the present study, we conclude that MRI is not very sensitive to detect epidural fibrosis in patients with chronic pain. On the other hand, with epiduroscopy, even low grade epidural fibrosis can be detected.

Objectives

the etiology of chronic pain after back surgery
diagnostic effect of epiduroscopy on epidural fibrosis
diagnostic effect of MRI on epidural fibrosis

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300. INS19-0243

NOVEL SURGICAL PADDLE LEAD PLACEMENT FOR SPINAL CORD STIMULATION VIA A MINIMAL INVASIVE APPROACH: SUB-SPINOUS LAMINECTOMY (SSL)

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Introduction: We present a novel minimal invasive microsurgical midline approach allowing for precise placement of paddle leads whilst fully preserving paraspinal muscles and spinal stability. SSL is commonly used for multilevel decompression in cervical spinal canal stenosis.

Materials/Methods: Fluoroscopy is used to identify T10. A two centimeter skin incision is placed over the tip of the spinous process. The supraspinous ligament is split in the midline. The spinous process is then split using a sharp and thin osteotome under fluoroscopy until the posteriopr rim of the arch of the lamina is reached. Both halves of the spinous process are broken laterally and are detached from the lamina. A gelpi retractor is used to open a working channel with a diameter of 2 – 3 cm. The caudal margin of the T10-lamina is removed in the midline and up to 1 cm on both sides using either a high speed drill or a punch under the microscope. After removal of the yellow ligament with 2 or 3 mm wide punches the dura and the epidural space are accessible. Paddle lead electrodes are now easily introduced into the spinal canal and advanced up to several centimeters. Fluoroscopy is used to confirm midline lead placement. After removal of the gelpi retractor the two halves of the spinous process are brought into contact and are sutured together with the supra spinal ligament.

Results: At time of abstract submission 15 patients had undergone this procedure with uncomplicated intraoperative handling of electrodes. There was virtually no blood loss and only minor postoperative local pain. No adverse events occurred. All patients had excellent pain area coverage and consecutive pain reduction during trial. There was no lead displacement.

Discussion: Spinal Cord Stimulation (SCS) has become a well established method for treatment of chronic pain with significant pain relieve for example in back and leg pain. Surgical leads show advantages like better coverage of multifocal pain areas, less energy consumption and lower dislocation rates. However, surgical leads usually have to be implanted via an invasive surgical procedure involving uni- or bilateral muscle detachment and partial laminectomy. This minimal invasive approach completely spares the paraspinal muscles (no detachment, no devascularization, no denervation) while providing an ideal exposure of the epidural space for precise placement of surgical leads resulting in only minor postoperative local discomfort.

Conclusions: Surgical lead placement via a microsurgical sub-spinous laminectomy (SSL) approach has shown to be a safe procedure.

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301. INS19-0153

A COMPREHENSIVE ALGORITHM FOR MANAGEMENT OF NEUROPATHIC PAIN

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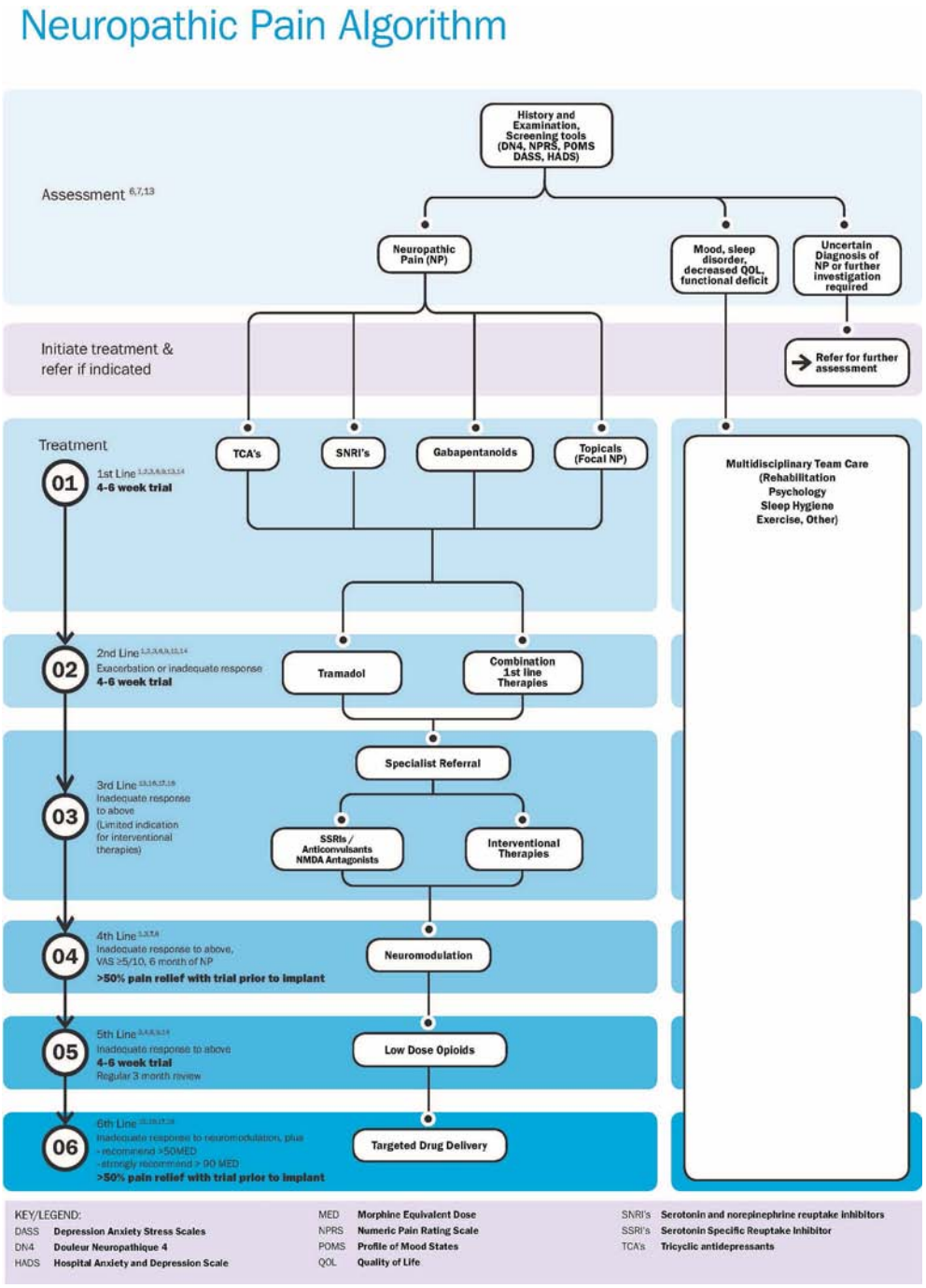
Introduction: Neuropathic pain is highly debilitating, difficult to diagnose and only partially responsive to nearly all treatment. A multidisciplinary, structured stepwise approach is needed to decrease pain and attain an acceptable quality of life for patients. We propose a treatment algorithm



to guide the primary physician through a step by step time limited treatment process.

Materials/Methods: Available literature was identified through a search of the United States National Library of Medicine's Medline database, PubMed.gov. References from identified published articles also were reviewed for relevant citations.

Discussion: This article presents a comprehensive treatment algorithm for chronic neuropathic pain based upon coalescence of international treatment guidelines and best practices recommendations. Additionally, the authors clarify the role of neuromodulation as the treatment of choice for neuropathic pain after the failure of conservative treatments, non-opioid pharmacologic management and interventional procedures. Low dose opioids are recommended as 5th line after failure of neuromodulation due to the limited duration of efficacy and the significant risk of side effects.

Conclusions: The presented treatment algorithm provides clear-cut tools for the assessment and treatment of neuropathic pain based in international guidelines, published data and best practices recommendations. It clarifies the role of neuromodulation and distinctly defines the benefits and limitations of the current pharmacological therapies at our disposal. Additionally, it provides an easy-to-follow visual guide of the recommended steps in our algorithm for primary care and family practitioners to utilize.

Objectives

1. Be familiar with examination methods and tools for assessment and differential diagnosis of neuropathic pain.

2. Understand the progression of non-pharmacological, pharmacological and neuromodulation treatment options for chronic neuropathic pain.

References

None

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302. INS19-0286

CERVICAL SPINAL CORD STIMULATION TREATMENT FOR BRACHIAL PLEXUS AVULSION INJURY COMPLICATED BY COMPLEX SEVERE REGIONAL NEUROPATHIC PAIN

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Introduction: Chronic neuropathic pain is one of the most important and severe intractable complication due to brachial plexus avulsion, seen in 26-90 %. Commonly, they present with burning pain, atrophy of upper extremity and vasomotor symptoms. Interventional treatment modalities like dorsal root entry zone lesioning, stellate ganglion blockade, and neuromodulation such as spinal cord stimulation (SCS) are used for treatment.

We presented 2 cases of cervical epidural SCS insertion for traumatic upper extremity brachial plexus avulsion injury due to their severe chronic neuropathic pain, Previous unsuccessful interventions, repeated stellate ganglion blocks, transcutaneous electrical nerve stimulation, and opioid medication, were performed at other clinics.

Materials/Methods: **Case 1:** 66-year-old man was referred for management of severe, intractable pain in his left upper extremity resulting from a brachial plexus avulsion injury after a motor vehicle accident 14 years ago. He suffered from chronic neuropathic pain in his left upper extremity radiating from the neck to all fingers of the left hand. He had 3/5 muscle motor deficit at his left upper limb and left C4-5-6 roots hypostesis. Epidural SCS was placed affecting his left C4,5,6 root levels. He experienced immediate amelioration of pain symptoms, and the patient's pain score decreased from 7/10 to 2/10 on the VAS during 3 year follow- up

Results: Case 2: 24-year-old man was referred for management of severe, intractable pain at his right upper extremity resulting from a brachial plexus avulsion injury after an motorbike accident 3 years ago. He suffered from chronic neuropathic pain at his right upper extremity from wrist and forearm radiating to all fingers of the right hand. He experienced flaccid paralysis of his right upper limb, and right C7,C8,T1 hyperalgesia. The patient underwent epidural SCS operation at C5,6,7 root level. He experienced immediate amelioration of pain symptoms, and the patient's pain score decreased from 8/10 to 1/10 on the VAS during 2.5 year follow- up.

Conclusions: SCS is an effective treatment model for deafferentation pain and complex regional pain syndrome secondary to brachial plexopathy refractory to pharmacotherapy. SCS not only reduces pain, improves quality of life, reduces analgesic consumption, but may also result in significant cost savings over time.

Objectives

SCS is an effective treatment model for deafferentation pain

References

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303. INS19-0303

PERCUTANEOUS COMPUTED TOMOGRAPHY-GUIDED TRIGEMINAL TRACTOTOMY-NUCLEOTOMY FOR INTRACTABLE PAIN CONTROL

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Introduction: Percutaneous spinothalamic tractotomy is a not usual but suggested viable treatment option for patients with intractable neuropathic facial pain d to malignancy, postherpetic neuralgia, glossopharyngeal neuralgia, geniculate neuralgia, and refractory trigeminal neuralgia. Especially, malignancy related and postherpetic neuralgia are severe and difficult pain syndromes to treat and is occasionally associated with facial allodynia and hyperalgesia. Tractotomy has a durable success rate of greater than 80% for pain control.

Materials/Methods: We reported a retrospective study of 11 cases suffered from intractable facial pain and underwent percutaneous CT-guided spinothalamic tractotomy. The contrast agent is administered via lumbar puncture 20 minutes before the operation. The patient kept in the Trendelenburg position before admission to the CT unit. Patients were awake and cooperative throughout the procedure to facilitate observation of neurologic functions, and no general anesthesia had been given. CT-guided percutaneous tractotomy performed in the prone position. Plastic-hubbed 20-gauge needles specially designed for CT-guided procedures used under local anesthesia and a tractotomy needle inserted from the C1-occiput region 5 to 7 mm lateral from midline. The target was 3 mm anterior to the posterior aspect of the spinal cord and 5 to 6 mm lateral to the midline at the first cervical segment. Target-needle and -electrode relations visualized using CT guidance (Figure 1). Electrode was inserted into the needle. Electrical stimulation was used to confirm the localization.

Results: There were 11 patients, 7 males, 4 females. The age of the patients ranges 49 to 79 years. The most common aetiology was herpetic neuralgis (4 carcinoma, 5 postherpetic neuralgia, 1 trigeminal dizestesia, 1 geniculate neuralgia). Preoperative VAS scores were ranged from 4 to 10, and decrease to 0 -3 after the tractotomy. Transcient ataxia during first 4 or 5 days was detected at all patients. There was no permenant complication.

Discussion: Medically intractable severe pain presents an enormous challenge, especially at the end stage of cancer patients or postherpetic neuralgia patients.

Conclusions: In an effort to expand upon the current guidelines for management of intractable pain of these patients, we have presented a 11 series of patients.

Objectives

CT-guided pain procedures should be used efficiently by neurosurgeons in the treatment of intractable pain

References

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304. INS19-0359

SPECIFIC NEUROPATHIC PAIN SUBGROUPS DETECTED BY VALIDATED QUESTIONNAIRES PREDICT RESPONSE TO SPINAL CORD STIMULATION

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Introduction: A trial of spinal cord stimulation (SCS) is recommended prior to definitive implantation of SCS system.[1] There is a lack of data on specific presentations of NP symptoms that are more likely to abate with SCS.

Table 1. Comparison of data between the two SCS groups: Trial success and failure. Values are numbers (percentages) or means (± SD).

	Trial success (n= 42)	Trial failure (n= 22)	p-value
Baseline			
Mean DN4 score (0-10)	6.85 ± 1.95	6.32 ± 2.24	0.359
Mean NPSI Scores (Total 0-100; Subgroups: 0-10)			
Total	57.1 ± 19.94	57.8 ± 23.92	0.903
Superficial spontaneous burning pain	6.61 ± 2.66	7.4 ± 2.76	0.290
Deep spontaneous pressing pain	4.49 ± 3.49	5.07 ± 3.58	0.548
Paroxysmal pain	6.21 ± 2.75	5.94 ± 3.36	0.752
Evoked pain	5.24 ± 3.02	4.43 ± 3.42	0.358
Paresthesia / dysesthesia	6.68 ± 2.69	7.68 ± 2.29	0.166
End of SCS trial			
Mean DN4 score (0-10)	4.13 ± 2.62	6.11 ± 1.64	0.006
Mean NPSI Scores (Total 0-100; Subgroups: 0-10)			
Total	25.86 ± 18.97	44.00 ± 27.86	0.006
Superficial spontaneous burning pain	2.26 ± 2.63	5.89 ± 2.51	<0.001
Deep spontaneous pressing pain	2.15 ± 2.27	3.74 ± 3.64	0.047
Paroxysmal pain	2.65 ± 2.49	4.76 ± 3.52	0.011
Evoked pain	2.34 ± 2.16	3.49 ± 3.50	0.138
Paresthesia / dysesthesia	3.41 ± 2.82	5.58 ± 3.72	0.017

This retrospective study evaluated specific phenotypes of NP that were associated with success of SCS trial.

Materials/Methods: Data from patients who had undergone SCS trials at our hospital between July 1, 2017 to November 30, 2018 was accessed after approval from the Institutional REB. Based on the definition of trial success as a minimum of 50% reduction in pain intensity from baseline with either or both SCS modes (tonic or paresthesia-free; both applied for 4 days each), trials were classified as "success" or "failure". Data from two validated questionnaires for NP was also accessed – Douleur Neuropathique 4 (DN4; a screening questionnaire) and Neuropathic Pain Symptom Inventory (NPSI; a questionnaire designed to evaluate the different symptoms of NP over time).[2] Data was compared using appropriate statistical tests at baseline and at the end of the SCS trial between and within the two groups.

Results: 64 patients underwent SCS trials with a trial success rate of 66%. The mean DN4 and total NPSI scores at the end of the SCS trial were significantly lower in patients who had a successful compared to those with a failed trial (Table 1). There was a significant reduction in superficial spontaneous burning, deep spontaneous pressing, paroxysmal, and paresthesia/dysesthesia subtypes of NPSI in patients who had a successful compared to those with a failed trial. All subtypes of NPSI score reduced significantly in patients with SCS trial success whereas only the superficial spontaneous burning and paresthesia/dysesthesia subtypes of NPSI reduced in patients who had a SCS trial failure.

Discussion: Patients with deep spontaneous pressing, paroxysmal, and evoked pains may not respond to SCS. Further research and evaluation of long-term outcomes are required to compare effects of tonic and paresthesia-free SCS modes on different subgroups of NP.

Conclusions: Use of validated tools for phenotyping NP can help increase success rate of SCS trials.

Objectives

1. Incorporating validated tools to evaluate subgroups of NP can help improve success rate of SCS.
2. Use of validated tools to evaluate NP yields insights into phenotypes more likely to respond to SCS.
3. Tonic and paresthesia-free modes of SCS may differ in their impact on different NP phenotypes.

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305. INS19-0357

PULSE DOSING OF 10 KHZ PARESTHESIA-INDEPENDENT SPINAL CORD STIMULATION PROVIDES SAME EFFICACY WITH SUBSTANTIAL REDUCTION OF DEVICE RECHARGE TIME

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Introduction: Rechargeable spinal cord stimulation (SCS) systems, while requiring periodic transcutaneous recharging, have enabled new powerful stimulation strategies. High Frequency 10 kHz paresthesia-independent spinal cord stimulation (10kHzSCS) has demonstrated statistical and clinical superiority over traditional, low-frequency paresthesia-based SCS in relief of chronic back and leg pain. While 10kHzSCS patients in commercial practice report over 85% satisfaction with typical daily device recharge times of 20-40 minutes [Unpublished data on file], reducing this duration would be welcomed, if efficacy is maintained. The purpose of this study is to assess the ability of percent pulse dosing (%PD=alternating 10kHzSCS ON and OFF times) to reduce device recharge time while maintaining efficacy.

Materials/Methods: Permanently-implanted subjects successfully using 10kHzSCS at 100%PD to treat back pain with or without leg pain for >3 months were enrolled in an institutional review board approved multicenter study. After a 1 week baseline period of documenting their pain twice-daily using a 0-10 numerical rating scale (NRS) using 100%PD of their self-identified "favorite" program, all subjects were reprogrammed to 14%PD and completed another NRS diary for 7-10 days. If subjects preferred 14%PD to 100%PD, they next were programmed to 3%PD; otherwise, they were programmed to 50%PD; in either case, subjects used this next program while completing a pain diary for another 7-10 days. After these initial %PD evaluations, each subject entered a 3 month uncontrolled observational period where the subject was requested but not limited to use their most preferred %PD program; all subjects had the option to return to their 100%PD program. At the end of 3 months, the subject completed a 7 day NRS diary and indicated a final %PD program preference. Study endpoints included %PD preference, mean diary NRS by %PD, and minutes of daily charging.

Results: Twelve subjects have completed the study to date. Four subjects preferred 3%PD, four preferred 14%PD, one preferred 50%PD, and three preferred 100%PD. Average daily charge durations: 3% PD=8.6$\pm$0.5min, 14%PD=14$\pm$7min, 50%PD=33$\pm$3.3min, 100% PD=38.6$\pm$6.5min. Average back pain scores were 3%PD=1.8$\pm$1.4, 14% PD=2.0$\pm$1.7, 50%PD=4.1$\pm$0.7, 100%PD=1.7$\pm$1.4, all P>0.1 from 100%PD. In general, subjects chose preferred %PD based on similar or reduced NRS compared to Baseline 100%PD.

Conclusions: In this prospective feasibility study, 75% of 10kHzSCS responders appeared to maintain efficacy and reduce device charging times an average of 64% using <100%PD. These trends suggest that 10kHzSCS therapy may be successfully employed in a majority of responders with device charging times approximately 30% shorter than traditional SCS.

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306. INS19-0166

PROTOCOL FOR A PROSPECTIVE, RANDOMIZED SINGLE-BLINDED CROSSOVER STUDY COMPARING HIGH-FREQUENCY 10,000 HZ AND BURST SPINAL CORD STIMULATOR THERAPIES

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Introduction: Three main modes of spinal cord stimulation (SCS) are used to treat various pain conditions: conventional tonic stimulation (30-120 Hz), burst technology that sends packets of electrical pulses (500 Hz), and high-frequency stimulation that is a tonic, sub-perception stimulation (>1,000 Hz). 10,000 Hz high-frequency and burst SCS have both been associated with potential improved efficacy and patient outcomes compared to traditional tonic SCS.[1,2] Limited research directly comparing the two therapies makes choosing between the technologies challenging. This study aims to 1) compare improvements in pain and patient satisfaction between 10,000 Hz high-frequency and burst SCS in patients suffering from axial back pain and 2) describe characteristics that make a patient more likely to benefit from one therapy over another.

Materials/Methods: This prospective, randomized single-blinded crossover study will include those age 22-75 with primarily axial back pain refractory to treatment with conservative therapy. Patients will undergo both a burst and 10,000 Hz high-frequency SCS trial over a 9-day period. Patients will randomly receive one therapy during the trial's first 4 days, followed by 24-hours of no stimulation, after which the alternative therapy will be utilized for the remaining 4 days.

Results: The primary outcome is VAS scores for back and leg pain at baseline, after SCS trial 1, before SCS trial 2, and after SCS trial 2. A paired t-test will be used to determine statistical differences in VAS. Secondary outcomes include percentage changes from baseline VAS scores and patient therapy preference assessed using an independent sample t-test. A sample size of 56 patients was deemed adequate.

Discussion: Current studies comparing burst and 10,000 Hz high-frequency SCS are limited by small sample sizes and lack of a crossover trial, leaving physicians with limited information when choosing between therapies. Our study is unique as all patients will receive trials of both SCS technologies. Results will offer invaluable information on patient perspectives and pain improvement to clarify the distinction between these therapies.

Conclusions: This study will allow interventional pain physicians to better understand which patients may benefit from specific SCS therapies, improving patient selection and clinical outcomes.

Objectives

1. Improve understanding of protocol design for spinal cord stimulator therapy research.
2. Describe barriers and facilitators to recruitment and enrollment of patients in a comparative SCS trial at a tertiary care center.
3. Gain insight into preliminary results comparing 10,000 Hz high-frequency and burst spinal cord stimulation.

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307. INS19-0148

ALTERNATIVE WAVEFORMS WITH A WIRELESS SPINAL CORD STIMULATION(SCS)SYSTEM YIELDING IMPROVED OUTCOMES FOR CHRONIC NEUROPATHIC PAIN

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Introduction: After decades of standardized SCS by conventional low frequency stimulation within the last 8 years new stimulation paradigms were established. Numerous studies have proven that high frequency stimulation techniques achieved improved results. Also during the last years new hardware developed and new wireless techniques with the alternative of conventional as burst and as different forms of high frequency stimulation offer the possibility of comparing these different techniques in an equal group of patients with pain and failed back surgery syndrome without the incidence of discomfort by battery and cables.

Materials/Methods: In the last years we treated up to 80 patients each year with 10K high frequency stimulation as our standard regimen of patients with chronic neuropathic pain of the lumbar and cervical region. We compared 2 equal samples of 14 subjects who had the choice between a standard 10 K SCS and a wireless system with burst,HD stimulation with 1500HZ and 10000HZ. In recent studies we found as other groups a superiority concerning VAS, ODI, SF 26 and our tread mill test with 10 K. In contrary to the results of the e.g. KAPURAL study the incidence of pocket pain and discomfort by the cable and extensions was markedly higher as publicated.

Results: in contrary as expected the two groups with an follow up of 6 months revealed comparable, nearly identical results in both groups. There were concerning our criteria with burst and high frequency stimulation (1500) no difference in the wireless group. Patient comfort and satisfaction however was significantly better in the wireless group. Here no mentionable differences between subjects treated with burst or high density. There was one electrodes dislocation in the wireless group and one infection with explantation in both groups.

Discussion: New insights and techniques such as novel waveforms have been reported to alleviate refractory neuropathic pain with superior results compared to conventional waveforms. The hardware of SCS devices has been pretty much unchanged over decades. New technology is needed to optimize trial procedures, improve patients experience, increase safety while reducing the costs and still retaining its positive results.

Conclusions: Our limited study shows the potential of wireless SCS technique. Subjects showed equal results in both groups while reporting better comfort with wireless system. New hardware solutions combined with a novel range of waveforms will lead to increased efficacy and comfort while limiting rates of complication.

Objectives

10 K and wireless technology for SCS, failed back surgery syndrome

References

No

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308. INS19-0375

LONG-TERM RESULTS FROM THE AVALON STUDY – FEEDBACK-CONTROLLED SCS USING EVOKED COMPOUND ACTION POTENTIALS

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Introduction: Currently marketed SCS systems operate in an open-loop configuration: stimulation is set to a fixed-output and delivered to the neural target without sensing or adjusting to the nerves' response. A new SCS system uses evoked compound action potential (ECAP) recordings in a real-time closed-loop feedback algorithm that automatically adjusts stimulation intensity to maintain ECAP amplitude within a therapeutic window. The effectiveness of this system for pain relief is measured using Visual Analogue Scale (VAS), quality of life (QoL; EuroQol instrument [EQ-5D-5L]), level of function (Oswestry Disability Index [ODI]), and medication changes through 12 months.

Materials/Methods: Seventy subjects with chronic pain were enrolled in this study. Fifty subjects were implanted with a closed-loop SCS system (ACTRN12615000713594). Post-implantation subjects were followed over 12 months to assess therapy effectiveness and safety.

Results: At 12 months, 35 of 43 (81.4%) subjects experienced ≥50% reduction in overall VAS pain, and 53.5% had ≥80% reduction (Table). Of the lower back pain subjects, 76.9% and 56.4% experienced ≥50% and ≥80% reduction in lower back VAS pain, respectively. Leg pain responded similarly well to the therapy. At 12 months, 88.4% and 76.7% of subjects experienced a clinically important change in EQ-5D-5L and ODI, respectively (Table). These results are sustained or improved from 3- and 6-month results. The average Morphine Equivalent Units (MEU) changed from 47.8 at baseline to 25.4 at 12 months, with 68.8% of subjects reducing or discontinuing use of opioid (Table).

Discussion: The majority of subjects (53.5%) experienced more than 80% pain relief at 12 months. The feedback-control mechanism in this device uses ECAP measurements to provide consistent stimulation at comfortable levels for the subject. Maintaining this constant level of spinal cord activation may be the driver of the excellent long-term outcomes of this study. This study continues to monitor the outcomes for subjects through a 2-year follow-up period. A multicenter, double-blind, randomized, controlled trial is currently underway in the United States (clinicaltrials.gov: NCT02924129) to investigate the difference in efficacy of closed-loop stimulation versus open-loop stimulation.

Conclusions: This study demonstrates long-term efficacy of closed-loop SCS in treating overall and lower back pain, improving QoL, function, and reduction in MEUs for subjects with chronic pain. The study is ongoing through 24-month follow-up.

Objectives

1. Sustained or improved pain reduction efficacy.
2. Increased elimination or reduction in MEUs.
3. QoL and function improvements.

Table. QoL, function, medication changes, and VAS responder rates over time.

	3 Month	6 Month	12 Month
EQ-5D Index Score Minimally Important Difference from Baseline (≥0.074)[a]	36/45 (80.0%)	40/46 (87.0%)	38/43 (88.4%)
ODI Minimum Detectable Change From Baseline (reduction ≥10%)	31/44 (70.5%)	31/44 (70.5%)	33/43 (76.7%)
MEUs Reduction or Elimination From Baseline[b]	20/33 (60.6%)	22/35 (62.9%)	22/32 (68.8%)
Overall VAS ≥80% Reduction (high responder)	19/45 (42.2%)	24/46 (52.2%)	23/43 (53.5%)
Overall VAS ≥50% Reduction (responder)	36/45 (80.0%)	36/46 (78.3%)	35/43 (81.4%)
Lower Back VAS ≥80% Reduction (high responder)[c]	22/41 (53.7%)	21/42 (50.0%)	22/39 (56.4%)
Lower Back VAS ≥50% reduction (responder)[c]	31/41 (75.6%)	32/42 (76.2%)	30/39 (76.9%)

[a]Walters SJ, Brazier JE. *Qual Life Res*. 2005;14:1523. https://doi.org/10.1007/s11136-004-7713-0.
[b]Subjects not taking opioids at baseline excluded from analysis.
[c]Subjects with VAS <60mm at baseline excluded from analysis.

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309. INS19-0092

HIGH FREQUENCY SPINAL CORD STIMULATION (HF-SCS) AT 10 KHZ FOR THE TREATMENT OF NEUROPATHIC LIMB PAIN FROM PAINFUL DIABETIC NEUROPATHY

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Introduction: Data from the Centers for Disease Control and Prevention estimate there are currently 29 million people in the United States living with diabetes, and another 86 million with prediabetes, resulting in $245 billion in healthcare costs and lost productivity.[1] Approximately 20% of patients with diabetes will develop painful diabetic neuropathy (PDN),[2] a debilitating, progressive chronic pain condition that significantly impacts the patient's quality of life. Neither pharmacological treatments nor low frequency spinal cord stimulation (SCS) has provided significant, long-term pain relief for PDN patients.[3, 4, 5] This study aims to document the value of HF-SCS at 10 kHz in addition to conventional medical management (CMM) compared with CMM alone.

Materials/Methods: In a prospective, multicenter, randomized controlled trial (SENZA-PDN), 216 subjects with PDN will be assigned 1:1 to receive HF-SCS at 10 kHz combined with CMM or CMM alone after appropriate institutional review board (IRB) approvals. Key inclusion criteria include: 1) diagnosis of PDN for at least 12 months, 2) average pain intensity of ≥5 cm (on a 0-10 cm visual analog scale [VAS]) in the lower limbs, and 3) an appropriate candidate for SCS. Key exclusion criteria include: 1) large and/or gangrenous ulcers, and 2) average pain intensity of ≥3 cm on VAS in the upper limbs. Along with pain VAS, neurological assessments, health-related quality of life, sleep quality, and patient satisfaction will be captured. Subject follow-up will last for 24 months.

The primary endpoint comparing responder rates (≥50% symptom relief) and safety rates between the treatment groups will be assessed at 3 months. Several secondary endpoints will also be reported on.

Results: Enrollment in the SENZA-PDN study commenced in 2017 and is expected to be complete in 2019.

Discussion: Randomized, controlled study would help in providing evidence for the efficacy of 10 kHz SCS treatment for PDN

Conclusions: The SENZA-PDN study will be the largest RCT conducted using SCS in subjects with PDN. This prospective, multicenter study will determine whether HF-SCS at 10 kHz improves clinical outcomes, health-related quality of life, and is a cost-effective treatment for PDN.

Objectives

To document the value of HF-SCS at 10 kHz in addition to conventional medical management (CMM) compared with CMM alone

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310. INS19-0277

COMPARISON BETWEEN HIGH FREQUENCY SPINAL CORD STIMULATION (HF-SCS) AND BURST STIMULATION FOR THE TREATMENT OF PATIENTS WITH FAILED BACK SURGERY SYNDROME (FBSS): A CASE SERIES

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Introduction: Our retrospective data collection aims to compare pain and functional state outcomes in a group of fourteen patients suffering from FBSS and treated with HF-SCS or with Burst therapy.

Materials/Methods: Fourteen patients with FBSS were assesses as suitable for SCS therapy and assigned to Burst stimulation or to HF-SCS, on a random basis.

All patients presented an average baseline VAS score of 8 and were assuming analgesic, FANS, antidepressant and antiepileptic medications.

After trial phase, all patients reported a pain relief ≥ 50% for their predominant pain; therefore, they proceeded with permanent implant.

Therapy parameters were set as per table below, following the standard protocol:

After permanent implant, patients were assessed for their pain intensity, drug intake, sleep disturbance, disability level, satisfaction and global perception of change at 3 and 6 months and compared with baseline values.

Table 1.

Parameters	values	
	HF-SCS	Burst DR
Lead positioning	T8-T10	paresthesia-guided
Stimulation frequency	10K Hz	40Hz frequency containing 5 spikes at 500Hz
Stimulation intensity	1.5 – 3.0 mA	1.5 – 3.0 mA
N° of active poles	2	2

Table 2.

Low Back pain drop in %:	Leg pain drop in %:
HF-SCS 45%	HF-SCS 65,5%
Burst Stimulation17%	Burst Stimulation 54%

Measure	Outcome
Pain-related drug consumption	No patients increased their analgesic use. Almost 79% reduced and 43% completely dismissed any drug intake
Sleep disturbance	Positive downward trend in sleep disturbance for all patients
Satisfaction	Only one patient declared no change/satisfaction related to SCS therapy
Global impression of change	Only one patient declared no change/satisfaction related to SCS therapy

Results: Here below we report some of the key results at 6 months from permanent implant:

Discussion: HF-SCS and Burst therapies represent a valid alternative for the management of the persistent post-spine surgery pain, refractory to traditional approaches.

Conclusions: The results of this retrospective data collection at 6 months show that patients with FBSS pain benefit more from HF-SCS than from Burst Stimulation in terms of pain relief, quality of life and global satisfaction.

Objectives

To investigate long-term

Results: to highlight any relevant statistical difference between the two therapies

to identify well-consolidated patient selection criteria for further future data collection

References

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2- Kapural, Leonardo et. Al. Novel 10-kHz High-frequency 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 Vol 123 No4, Oct 2015.

Poster Presentations - May 27 - May 30
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311. INS19-0081

USE OF ACCELEROMETRY AS AN EDUCATION TOOL FOR SPINAL CORD STIMULATION

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Introduction: An accelerometer measures speed, tilting motion, and orientation. Select neurostimulator platforms contain accelerometry within the implanted pulse generator, offsetting uncomfortable variations in stimulation amplitude with positional changes. Previously, a remote programmer was required to adjust amplitude to avoid uncomfortable stimulation. Select systems detect positional changes, automatically adjusting amplitude to avoid unpleasant stimulation. Additionally, positional habits and activity trends are recorded, giving patients, providers, and technicians individualized programming settings. Because this capability is unavailable before implant, we designed this study to determine whether a commercial external accelerometer could serve as an educational tool before implant, to enhance awareness of body positioning, and to understand whether information can be correlated to systems with internal accelerometry data after implant.

Materials/Methods: Single-center, prospective, non-randomized, observational, exploratory pilot study, N =10, with 8 month duration. Primary objective was to determine if utilization of a commercial external accelerometer prior to and during neurostimulator trial could serve as an educational tool to aid in activity behavior and pre-operative goal achievement after SCS permanent implantation. Secondary objectives include 11-point Numeric Pain Rating Scale and Oswestry Disability Index. Additionally, we compared the commercial external accelerometer data to accelerometer data from the implanted RestoreSensor® IPG and compared data to the 7-day Physical Activity Recall (PAR) patient diary.

Results: Total of 16 patients were enrolled; however, five patients did not move forward with implant after SCS trial as they did not meet criteria, one patient died during study from unrelated issues, and one was lost to follow up at three months. Of nine remaining patients, 8/9 met personal pre-operative goals, 8/9 met investigator goals, and 8/9 were globally satisfied with progress, participation. Additionally, PAR revealed that activity levels dropped during months 1-3 after implant, but returned to, or exceeded baseline at 6 months, consistent with our practice of limiting activity until 3 month post-surgical follow-up.

Discussion: External accelerometer obtained detailed information regarding patient positioning. Pre-implant data included activity behaviors before and during SCS trial. Patients reviewed data to decide whether to pursue SCS implant. Data was shared to enhance awareness of body positioning and impact on severity-quality of pain to aid in postoperative goal-setting.

Conclusions: We theorize that study helped patients better understand activity levels, positioning trends for setting realistic goal setting, expectations.

Objectives

1) Understanding accelerometry
2) Setting realistic SCS goals with patients
3) Understanding effect of body position on pain

References

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312. INS19-0132

RANDOMIZED CONTROLLED CLINICAL TRIAL DESIGN TO STUDY THE EFFECTS OF DTM-SCS IN TREATING INTRACTABLE CHRONIC BACK PAIN

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Introduction: A multicenter prospective feasibility study was conducted to evaluate Differential-Target Multiplexed spinal cord stimulation (DTM-SCS). In this study, trialing of DTM-SCS achieved significantly greater back pain relief and responder rate than conventional SCS. DTM-SCS uses multiple pulsed signals that are spatially and temporally combined. Glia constitute the majority of cells in neural tissue and play an important role in the establishment and maintenance of chronic pain. In chronic pain, the balanced homeostasis of neuro-glial interactions is disrupted. It is known that neurons and glial cells behave differently when exposed to electrical pulses. We hypothesize that multiplexing electrical signals, differentially targeting glia and neurons, may have beneficial impact on chronic pain relief. A randomized controlled trial (RCT) with long-term follow up has been designed and initiated to confirm the results of the feasibility study.

Materials/Methods: This is a randomized, controlled, multi-center study comparing DTM-SCS approach to standard SCS approach. Key inclusion criteria are: ≥5 cm VAS in back pain with moderate to severe leg pain, and candidate for SCS with stable pain medication. Key exclusion criteria are: other active implants, contraindications for SCS, and mechanical spine stability. Informed and consented subjects meeting eligibility criteria are randomized 1:1 to the two treatment groups in a parallel assignment. Subjects undergo a therapy trial as per standard of care. Those with a successful trial can elect to have a permanent SCS device implanted. Primary endpoint is percentage of responders (subjects with ≥50% pain relief) to therapy at 3 months.

Results: The RCT has been designed with two parallel arms and statistically powered to allow for robust comparison of the two SCS approaches.

Discussion: To reduce potential bias, programming for standard SCS is conducted by the device manufacturer's representatives and DTM-SCS by sponsor's (Stimgenics) representatives. To better assess the benefit of DTM-SCS, comparison of the percentage of Responders between the test and control groups in a statistical test of superiority will be performed.

Conclusions: Since DTM-SCS achieved significantly greater back pain relief and responder rate than conventional SCS in a feasibility observational study, a larger, long-term RCT has been designed to confirm the results.

Objectives

Introduce DTM-SCS for treating chronic back pain.
Compare DTM-SCS and standard-SCS therapies.
Evaluate RCT design to further study DTM-SCS.

References

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Spine - Pain

313. INS19-0046

BURST SPINAL CORD STIMULATION: POOLED ANALYSIS OF REAL-WORLD EVIDENCE AND OUTCOMES DATA

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Introduction: Burst spinal cord stimulation (SCS) has emerged as an important new waveform for treating chronic pain. The literature base for burst SCS is growing, but it is difficult to draw a single conclusion for its effectiveness across the variety of study designs, follow-up durations, and endpoints that have been employed. This report pooled the findings across all burst SCS trials to date.

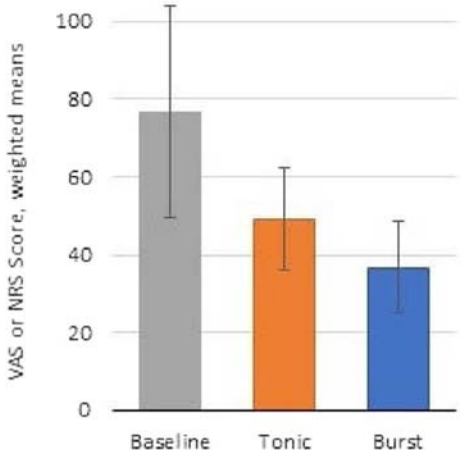
Materials/Methods: Articles were identified and selected from the literature according to replicable methodology for systematic reviews. Effectiveness data – pain scores and patient-reported outcomes (PRO) ratings – were weighted by study sample sizes and pooled. The effects of burst SCS were compared against values at baseline and with tonic SCS. For PROs, published population norms were used for comparison.

Results: Fifteen articles (combined N=427) were included. The weighted pooled mean pain rating across articles at baseline was 76.7 (±27.4). With tonic SCS, this was reduced to 49.2 (±12.9), and with burst SCS it was further reduced to 36.7 (±11.6), a 12.5-point difference between tonic and burst values (figure).

Pooled, weighted ratings on multiple PROs showed that psychometric scores improved with treatment and approached non-pain population norms. Furthermore across studies, 65% of subjects stated a preference for burst SCS.

Discussion: For pain intensity ratings as well as psychometric assessments of function, quality of life, and the emotional experience of pain, burst SCS had incremental benefits over tonic SCS. This suggests that burst SCS may be mediated by medial thalamo-cortical pathways. Importantly, these pooled analyses incorporated all available published evidence. Future research in burst SCS may benefit from adopting consistent design elements.

Conclusions: This report confirms that there is ample evidence for burst SCS as a valuable intervention and also increases support for use of this



waveform in chronic pain treatment algorithms. This report appears in a recent supplement to Pain Medicine (1). Abbott supported this work.

Objectives

Upon review of this abstract, delegates will be able to discuss results for burst SCS across the literature.

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Poster Presentations - May 27 - May 30
Spine - Pain

314. INS19-0170

BURST SPINAL CORD STIMULATION: SPINAL AND SUPRASPINAL MECHANISMS OF ACTION

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Introduction: Spinal cord stimulation (SCS) utilizing Burst stimulation patterning has been shown to be superior to low-frequency, tonic SCS. In many ways this stimulation pattern represents a mechanistic departure from other stimulation patterns such as high-frequency and low-frequency tonic stimulation.

Materials/Methods: Multiple structured database queries (MedLine, EMBASE, Google Scholar) and article back-searches were conducted to identify the relevant literature and experimental findings for results integration and interpretation. Data from recent conference presentations were also included for completeness and to ensure the most up-to-date scientific information was incorporated. Both human and animal data were targeted in the search to provide a translational approach in understanding the clinical relevance to the basic science findings.

Results: Burst SCS demonstrates the ability to, in some cases, evoke increased responses in spinal neurons and pathways that regulate somatic pain processing. Neurophysiologic processing of afferent sensory information is also differentially affected by Burst SCS when compared to other stimulation patterns in humans. Computational modeling and in vivo electrophysiological studies have demonstrated that not only is the Burst pattern important in the evoked physiological responses, but also the Burst signature influences how spinal structures in the dorsal column and horn respond. Last, supraspinal structures are also differentially modulated, likely from the patterned effects in the spinal cord.

Discussion: Burst spinal cord stimulation likely provides pain relief via multiple mechanisms of action at the level of both the spinal cord and brain. The specific waveforms and temporal patterns of stimulation both play a role in the responses observed. Differential modulation of neurons in the dorsal horn and dorsal column nuclei are the spinal underpinnings of paresthesia free pain analgesia. The Burst stimulation pattern also produces different patterns of activation within the brain when compared to tonic stimulation. The latter may have implications for not only the somatic components of chronic pain but also attentive and affective processing.

Conclusions: Multiple mechanisms likely underlie the clinical effects of Burst SCS. The range from enhanced effects in the dorsal horn of the spinal cord to differential effects in the brain.

Objectives

1. Audience will understand contemporary thoughts on MOA in Burst SCS
2. Burst SCS mechanisms will be contrasted with other SCS stimulation patterns
3. Audience will better understand how Burst SCS mechanism may play a role in the clinical outcomes with this therapy

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315. INS19-0338

T12 DORSAL ROOT GANGLION STIMULATION TO TREAT AXIAL LOW BACK PAIN: PROPOSED MECHANISM OF ACTION AND LITERATURE REVIEW

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Introduction: Dorsal root ganglion neurostimulation (DRG-SCS) has been demonstrated to be effective in treating various refractory chronic pain syndromes and has shown promise recently for the treatment of discogenic low back pain (LBP) via L2 DRG lead placement. We previously performed T12 DRG-SCS in 17 consecutive patients with predominantly axial LBP. At an average of 8 months follow-up there was an average LBP relief of 81%. Improvements in physical and mental functioning, disability and quality of life far surpassed improvements seen in traditional DC-SCS. Based on these results in a patient population with diverse LBP etiology, T12 DRG may be the optimal location for DRG-SCS to cover the low back**.**

Materials/Methods: A review of the literature was conducted to assess an anatomical and neurophysiological basis for T12 DRG-SCS in LBP treatment. Over 300 papers were full-text reviewed and more than 135 (>95% preclinical) were deemed relevant and included in a narrative review manuscript. The condensed findings of this manuscript are presented in this abstract.

Results:

Discussion: DRG-SCS at the T12 level in our case series showed a high level of promise for the treatment of severe LBP. A literature review led us to hypothesize that the low back fibers leave their individual spinal levels and travel in Lissauer's tract. Inhibition of LBP occurs at the T8/9 level by the incoming cutaneous fibers of the T12 spinal nerve when they converge with the low back fibers through a mechanism similar to that seen

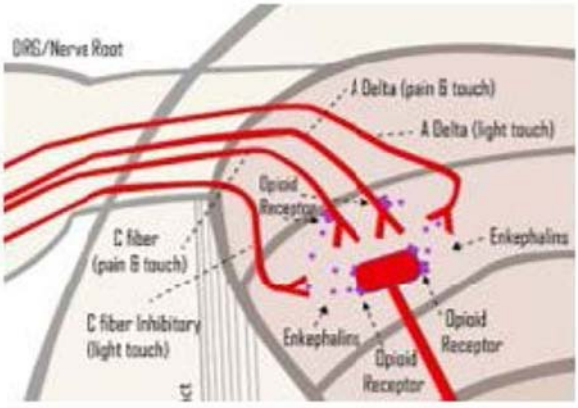
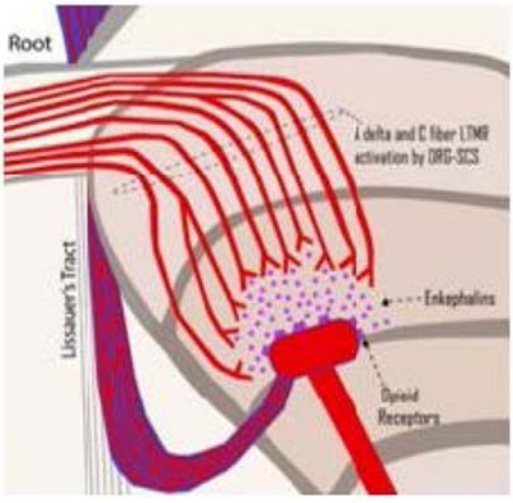


Figure 1: Light touch sensation in the normal state

In the normal state, A delta and C fiber low threshold mechanoreceptor (LTMR) are stimulated by light touch. Light touch is coded as a low frequency of action potentials as the sensation is relayed to the dorsal horn. This afferent input causes the release of enkephalin from the afferent terminals, which in turn can cause pre and post synaptic inhibition, as well as making the brain aware and the pleasant sensation.

Figure 2: Proposed mechanism of T12 DRG-SCS for LBP.



The T12 spinal nerve innervates the soft tissue of the low back. Low back cutaneous sensation through the T12 spinal nerve enters the spinal cord at the lower T10 vertebral level. Via Lissaur's tract the fibers enter the dorsal horn at approximately the T8-9 level. The deep lumbar structures are diffusely innervated at each vertebral level. Afferent fibers somatotopically organized in dorsal horn and converge onto second order neurons. Based on our clinical observations and current existing research we hypothesize that these converged low back pain transmitting neurons then travel rostrally to the T8/9 level where they enter the dorsal horn at the same level as the T12 fibers enter. Thus, by targeting T12, the afferent fibers would inhibit or modulate the deep lumbar neurons processing LBP, in a process similar to somatovisceral inhibition. Very low frequency stimulation (<20Hz) of A delta and C fiber low threshold mechanoreceptors activates inhibition by an enkephalin mediated system to inhibit the pain signal. The confluence of these anatomical pathways may also help explain why certain regions on the dorsal surface of the spinal cord seem to be "sweet spots" for dorsal column stimulation and high-frecuency SCS.

in somatovisceral inhibition. T8-9 level is also the most common location for DC-SCS for LBP coverage, DRG–SCS at the T12 level may provide a more direct inhibition of the nerve fibers of the deep lumbar structures as compared to traditional SCS. A-delta and C fiber very low frequency stimulation (<20Hz) activating enkephalin mediated pre and post synaptic inhibition is likely mechanism for the inhibition of the pain signal.

Conclusions: Compared to traditional SCS, T12 DRG-SCS may provide a more effective inhibition of pain fibers conducting nociceptive, as well as neuropathic, nerve traffic. By using very low frequency stimulation, we are applying a low dose, targeted application of electrical current to achieve these results.

Objectives

1. To apply results of 12 DRG-SCS case series to current literature to identify a potential mechanism of action.
2. Compared to conventional SCS, T12 DRG-SCS may be able to address both neuropathic and nociceptive elements of LBP more effectively.
3. Compare DRG-SCS MOA to other types of SCS.

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316. INS19-0339

T12 DORSAL ROOT GANGLION SPINAL CORD STIMULATION TO TREAT CHRONIC LOW BACK PAIN: A CASE SERIES

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Introduction: Dorsal root ganglion spinal cord stimulation (DRG-SCS) is a neuromodulation technique for treating chronic neuropathic pain syndromes. Results from recent case series and prospective studies have demonstrated that DRG-SCS may be effective in the treatment of other pain syndromes that may be considered to have non-neuropathic components and characteristics (e.g. nociceptive). Recent studies have demonstrated the efficacy of DRG-SCS for discogenic low back pain (LBP) at the L2 level. There is no prior literature determining which level would be optimal for capturing a more diverse population of LBP patients.

Materials/Methods: Patients presenting with LBP refractory to other treatments in a private pain management practice were considered for neuromodulation therapy. 19 patients were implanted after a successful DRG-SCS trial, including 7 patients who had a history of lumbar fusion, 7 with laminectomy w/o fusion, and 4 who had failed prior stimulator trials. Per standard clinical procedures, changes in pain intensity, disability, general health status and quality of life were collected by using the visual analogue scale (VAS), Oswestry Disability Index, EQ-5D index scores and the SF-36 health survey, respectively. Data was collected prior to device implantation and at 1, 3, 6, and 12 months following DRG-SCS therapy initiation.

Results: 19 patients with predominantly axial LBP with or without a secondary component of lower extremity pain were implanted with a DRG-SCS system at T12 to target the low back. Last follow-up times varied from 2 to 11 months with an average of 6.0 months. More than 80% of the patients showed a pain relief of 70% or more, with an average LBP relief of 81% at last follow-up (figure 1). Moreover, remarkable improvements in physical and mental functioning, disability and quality of life were demonstrated.

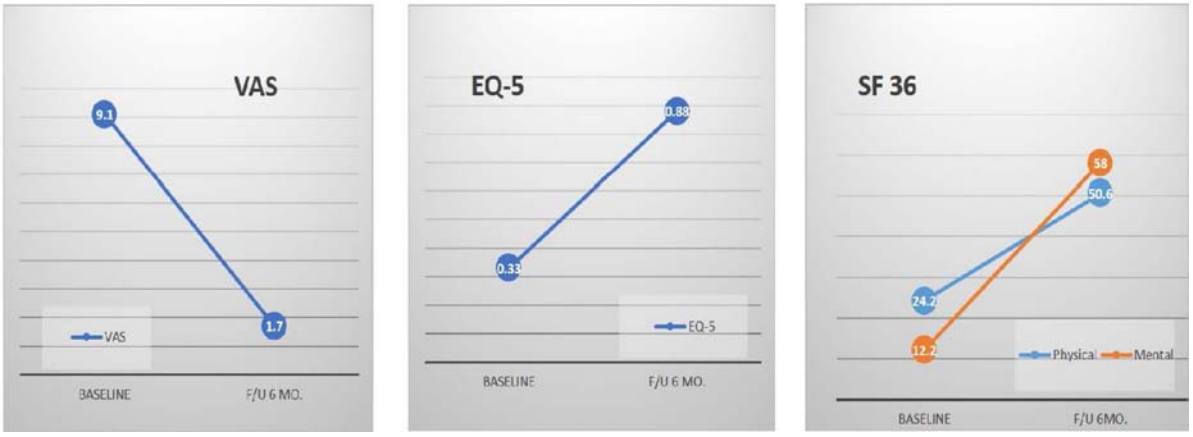
Discussion: T12 DRG-SCS appears to be an effective and more encompassing treatment option for chronic axial LBP.

Conclusions: Preliminary results of T12 DRG-SCS are demonstrating greater pain relief and improvements in disability and quality of life in chronic axial LBP than previous methods of stimulation. Larger prospective studies using this approach are warranted.

Objectives

1. T12 DRG-SCS can be used to treat chronic axial LBP.

Figure 1. Mean VAS scores, EQ-5D general health status score, and SF-36 quality of life scores in the case series. Pre-implant (baseline) and last follow-up post-implantation scores are depicted.



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317. INS19-0322

CORRELATION BETWEEN PAIN REDUCTION WITH SPINAL CORD STIMULATION AND HEALTH RELATED QUALITY OF LIFE MEASURES

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Introduction: Health related quality of life (HRQOL) measures are increasingly being utilised by healthcare funders to evaluate cost-effectiveness of therapies. The UK's National Institute for Health and Clinical Excellence has identified EQ-5D as the preferred measure.[1] However, the relationship between chronic pain and quality of life is complex.[2] The purpose of this study was to measure the correlation between average pain reduction, perceived pain reduction and quality of life measured by EQ-5D.

Materials/Methods: Baseline Brief Pain Inventory (BPI) and EQ-5D questionnaires were completed by patients. These were repeated at six months in addition to perceived percentage pain reduction. Pearson's and Spearman's correlation were used to determine correlations with BPI average pain reduction, EQ-5D index score and EQ-5D VAS.

Results: Complete data was available for 35 patients. All patients had back and leg pain due to failed back surgery syndrome and were implanted with a sub-perception stimulation device.

There was only moderate association between BPI average pain reduction and perceived pain reduction (r= 0.71).

There was moderate association between BPI average pain reduction and EQ-5D (r= 0.53) but could only explain 29.57 % of the variance. In comparison, perceived pain reduction explained 44.94 % of the variance (r= 0.67).

There was moderate association between BPI average pain reduction and EQ-5D VAS (r= 0.5) that explained 25% of the variation. In comparison, perceived pain reduction explained 48 % of the variance (r= 0.69).

Both perceived pain reduction (rs = 0.46, p= 0.005) and BPI average pain reduction (rs = 0.42, p= 0.01) were associated with change in EQ-5D VAS. Neither BPI average pain reduction (rs= 0.27, p= 0.12) nor perceived pain reduction (rs= 0.32, p= 0.06) were associated with change in EQ-5D index score.

Discussion: EQ-5D index score and EQ-5D VAS score might measure different aspects of quality of life in relation to SCS therapy. This needs to be considered when determining cost-effectiveness.

Conclusions: The applicability of EQ-5D to SCS therapy needs to be explored. Perceived pain reduction performs better than BPI average pain reduction as a measure of effectiveness.

Objectives

Understand

1. Relationship between perceived improvement and pain scores
2. Effect of SCS on HRQOL
3. Limitations of HRQOL

References

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318. INS19-0140

DIFFERENTIAL INVOLVEMENT OF SPINAL CYTOCHROME P450C17 AND 3B-HYDROXYSTEROID DEHYDROGENASE IN PERIPHERAL NERVE INJURY-INDUCED NEUROPATHIC PAIN: ROLE OF ASTROCYTE SIGMA-1 RECEPTORS

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Introduction: We have demonstrated that spinal sigma-1 receptors (Sig-1Rs) play an important role in the development of peripheral neuropathic pain. However, there is limited understanding of the role that the neurosteroidogenic enzymes, which produce endogenous ligands of Sig-1R, play during the development of neuropathic pain.

Materials/Methods: We examined whether sciatic nerve injury increases the expression of neurosteroidogenic enzymes, cytochrome P450c17 and 3β-hydroxysteroid dehydrogenase (3β-HSD), which modulate the expression and/or activation of Sig-1Rs leading to the development of peripheral neuropathic pain.

Results: Chronic constriction injury (CCI) of the sciatic nerve induced a significant increase in the expression of P450c17, but not 3β-HSD, in astrocytes of the ipsilateral lumbar spinal cord dorsal horn at postoperative day 3. Intrathecal administration of the P450c17 inhibitor, ketoconazole during the induction phase of neuropathic pain (days 0 to 3 post-surgery) significantly reduced the development of mechanical allodynia and thermal hyperalgesia in the ipsilateral hind paw, while administration of ketoconazole during the maintenance phase (days 14 to 17 post-surgery) had no effect on the developed neuropathic pain. In contrast, administration of the 3β-HSD inhibitor, trilostane during the induction phase had no effect on the development of neuropathic pain, while administration of trilostane during the maintenance phase facilitated the CCI-induced mechanical allodynia. Sciatic nerve injury increased astrocyte Sig-1R expression as well as dissociation of Sig-1Rs from BiP in the spinal cord at day 3 post-surgery. These increases were suppressed by administration of ketoconazole, but not by administration of trilostane. Co-administration of the Sig-1R agonist, PRE084 restored the development of mechanical allodynia originally suppressed by the ketoconazole administration. However, ketoconazole-induced inhibition of thermal hyperalgesia was not affected by co-administration of PRE084.

Discussion: Collectively these results demonstrate that early activation of P450c17 modulates the expression and activation of astrocyte Sig-1Rs, ultimately contributing to the development of mechanical allodynia induced by peripheral nerve injury. In contrast, activation of 3β-HSD during the maintenance phase plays an important role as the control mechanism to reduce mechanical allodynia.

Conclusions: These novel findings provided evidence that expands our understanding of the mechanisms underlying the induction and maintenance of neuropathic pain and further suggest the possibility of targeting P450c17 as a therapeutic approach to preventing the development of mechanical allodynia associated with peripheral nerve injury.

Objectives

Sciatic nerve injury increases P450c17 expression in astrocytes of the lumbar spinal cord dorsal horn.

P450c17 modulates the CCI-induced increase in astrocyte Sig-1R expression.

Sig-1R plays an important role in the P450c17-induced development of mechanical allodynia.

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319. INS19-0037

EFFECTS OF ANODAL TRANSCUTANEOUS SPINAL DIRECT CURRENT STIMULATION ON CHRONIC NEUROPATHIC PAIN AFTER SPINAL CORD INJURY: A PILOT STUDY

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Introduction: Several neurophysiological studies have shown modulating effects of tsDCS on nociceptive signal processing in healthy people. The first modeling study of tsDCS, conducted by Parazzini et al., showed that the current density and electric field tended to be primarily directed longitudinally along the spinal cord. Furthermore, the position of the reference electrode influenced current density distribution. Spinal tDCS with the reference electrode over the head vertex could act both at the spinal level and at the brain level.

Materials/Methods: A single-blind crossover design was used to investigate the effect of single sessions of both anodal and sham tsDCS (2 mA, 20 min) on chronic neuropathic pain in a group of ten volunteers with complete motor cervical spinal cord injury. The active electrode was placed over the spinal process of the tenth thoracic vertebra and the reference electrode was placed at the top of the head. Pre- to post-tsDCS intervention changes in pain intensity (numeric rating scale, 0–10), patient global assessment, and present pain intensity were assessed before and after the tsDCS session (immediately post-stimulation, and at 1 and 2 h post-stimulation).

Results: Comparing the pre- to post-treatment difference between the active and sham tsDCS groups, the Wilcoxon signed-rank test showed no significant differences in pain intensity, patient global assessment, or present pain intensity. Pain intensity, patient global assessment, and present pain intensity tended to improve by 1, 0.5, and 0.5 points, respectively, after stimulation, as assessed using a mixed effects model.

Discussion: This was a preliminary study to evaluate the neuropathic pain reducing effects of tsDCS in patients with spinal cord injury. We tried to extend the results of a previous modelling study of neuropathic pain after spinal cord injury by using a montage with a reference electrode attached to the head vertex. However, our data demonstrated that, at least in this subject group, chronic neuropathic pain after spinal cord injury was not improved by a single 20 min session of tsDCS.

Conclusions: The results suggest that a single session of anodal tsDCS with the montage used in this study does not have a significant analgesic effect in individuals with chronic cervical spinal cord injury.

Objectives

The objective of this study was to evaluate neuropathic pain in patients with spinal cord injury after the application of tsDCS.

References

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Poster Presentations - May 27 - May 30
Spine - Pain

320. INS19-0180

PRELIMINARY OBSERVATIONS IN A ONGOING TRIAL WITH MULTIMODAL WAVEFORMS

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Introduction: In the recent years the spinal cord stimulation was improved by new stimulation modalities like burst and KHz stimulation. The results published so far are encouraging but there is not a clear and unique approach on how and when to use them in a clinical practice (1). We report here the preliminary observations in an ongoing study during the trial phase.

Materials/Methods: Nineteen FBSS patients have been trialed and then implanted (if at least 50% pain relief was reached) with a SCS system capable of Illumina3D algorithm and multimodal waveform patterns (Burst3D, 1KHz and paresthesia-based). They all have been implanted with octopolar linear leads epidurally placed. During the trial phase they had the possibility to test in a random order three types of stimulation. At the end of the trial they could pick and use any of the modalities tested, also more than one. Part of these patients already reached 2-year followup.

Results: Among 18 patients enrolled, 17 succeeded in the trial phase and were implanted with permanent pulse generator. In terms of waveform response and preference we have observed that:

- 28% patients preferred only a subperception stimulation
- 33% preferred only a paresthesia-based stimulation
- 39% preferred at least two waveforms, to switch during the day and according to picks of pain.

Among this group, paresthesia-based stimulation was always chosen Globally we have observed that paresthesia-based was used by 72% total, even in combination with other waveforms.

Discussion: These preliminary data suggest an overall heterogeneous preference even among homogeneous patients (FBSS). However, we highlight that most of the patients still have good clinical outcomes with paresthesia-based stimulation and want the tingling sensation. Another interesting aspect is that a good part of the patients moved to a personal and flexible management of the SCS therapy using a combination of distinct programs according to the need.

Conclusions: According to this study results, the availability of different waveforms and the possibility to change them may address to a more personalized and efficient pain management.

Objectives

1. To evaluate a new SCS program usage approach with the availability of different waveforms.
2. To find out the best result in relation to the waveform
3. To find out the patient's preferred waveform

References

1. Duse et al, Effects of multiple waveforms on patient preferences and clinical outcomes in patients treated with spinal cord stimulation for leg and/or back pain. Neuromodulation 2018 in press

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321. INS19-0117

A MULTICENTER REAL-WORLD REVIEW OF 10 KHZ SPINAL CORD STIMULATION OUTCOMES FOR THE TREATMENT OF CHRONIC TRUNK AND/OR LIMB PAIN IN USA

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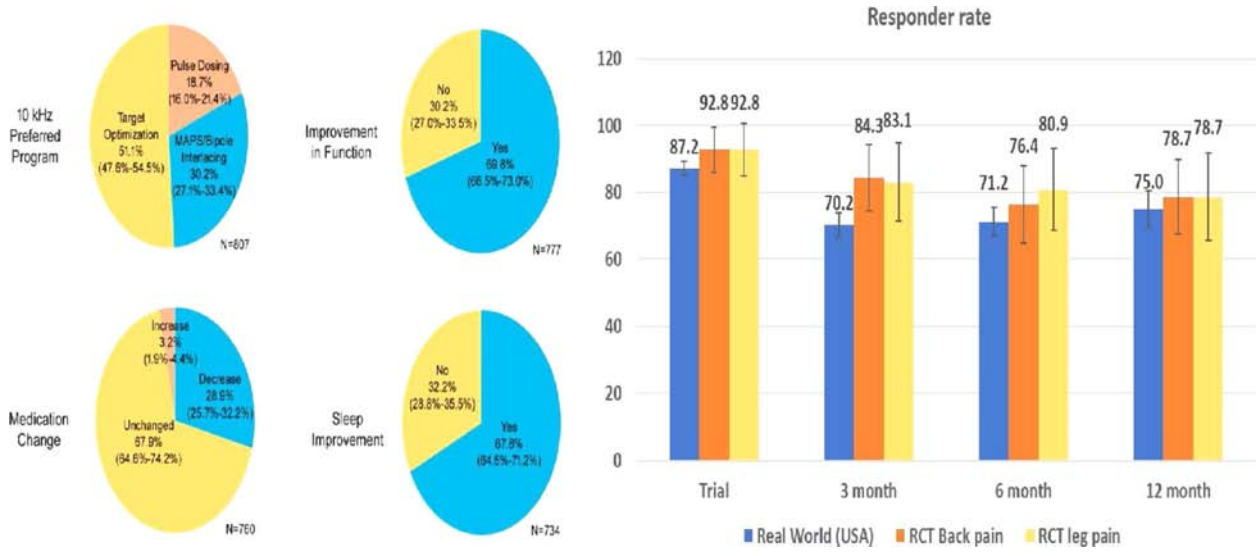
Introduction: High-frequency spinal cord stimulation (HF-SCS) at 10 kHz has proven to be efficacious in the treatment of chronic back and leg pain in a randomized, controlled, trial. However, large observational studies have yet to be published. Therefore, we performed a real-world, multicenter, retrospective, review of therapy efficacy in 1124 patients in USA with chronic trunk and/or limb pain.



Materials/Methods: Data were collected in a real-world environment and retrospectively sourced from a global database. Included patients were trialed and/or permanently implanted in USA with Senza™ HF-SCS at 10 kHz between April 2014 and January 2018. We evaluated responder rates at 3, 6, and 12 months post-implantation. Response was defined as ≥50% pain relief from baseline. A last visit analysis included responder rate along with overall change in function, sleep, quality of life, and medication intake versus baseline.

Results: Eighty-four percent of HF-SCS treated patients had both chronic back and leg pain. At least 70% of patients responded to therapy throughout 12 months of follow-up. The sustained response level was corroborated by the last visit value (72.0%). Most patients reported concomitant improvements in function (69.8%), sleep (67.8%), and quality of life (90.3%) at their last visit versus baseline (Figure 1). Twenty nine percent of patients reported decreased medication intake at their last visit.

Discussion: Results from the retrospective analysis of the real world data from USA are similar to the previously published findings from studies in back and leg pain patients.

Conclusions: Sustained and effective pain relief was experienced by >70% of HF-SCS at 10 kHz treated patients, consistent with the findings of a previously published randomized, controlled, trial (Figure 2). Our review provides complementary evidence to support the treatment of chronic back and leg pain with this therapy.

Objectives

To evaluate the efficacy of 10 kHz SCS in real world setting

References

None

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322. INS19-0214

CAN PULSE WIDTH PREDICT THE EFFECTIVENESS OF SUBPERCEPTION WAVEFORM IN CERVICAL SCS?

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Introduction: Finding the best optimal programming settings in spinal cord stimulation has always played a key role in therapeutic efficacy. Even with new subperception modalities like burst and 1 KHz stimulation, the titration of the stimulation patterns is dependent on amplitude, pulse width and rate, on top of the configuration of anodes and cathodes (1). We report some observations on waveform effectiveness on a series of five patients implanted with cervical SCS

Materials/Methods: Five patients with chronic cervical pain (mainly related to cerical radiculopathy), have been implanted with a SCS system capable of current steering, anatomical-based algorithm (Illumina™3D) for pain mapping and multimodal stimulation (burst and 1KHz) platform (Boston Scientific™, Valencia, CA). Three patients have been mplanted with dual octopolar linear leads, while two patients with a single 16-contact lead (Infinion™CX, Boston Scientific). They have been tested intraop with paresthesia based stimulation to find best configuration in pain coverage. Stimulation has been modeled in burst (4 pulses, same pulse width as paresthesia and 40 Hz inter-burst rate) or 1KHz (pulse width 40-130 microsec, rate 1KHz). Patients then reported program preference, pain relief by NRS, PDI and QOL. The best programming settings have been analyzed and compared.

Results: All patients underwent definitive SCS cervical implant reporting an average pain relief score by NRS of 3, PDI of 35 and QOL approx of 89 maintained after 24 months follow-up. Three patients preferred burst stimulation (with mean pulse width 600 microsec) while two patients preferred 1Khz stimulation (pulse width of 40 microsec and 130 microsec). Patients preferring burst program, reported multiple pain areas (cervical and lumbar) and 1 KHz program not effective

Discussion: We observed that patients preferring burst stimulation were the one with higher pulse width needed to cover pain areas (mean 600 microsec versus 150 microsec) and with multiple painful areas (cervical and lumbar). Therefore the value of the pulse width could be considered as a predictor element of the effectiveness of the sub-perception waveform.

Conclusions: Intraop paresthesia based test and in particular the setting of pulse width could be fundamental for predicting and optimizing the best modality of sub-perception waveform,.

Objectives

Observation of stimulation parameters in cervical subperception SCS

Evaluation of pulse width

Burst stimulation

References

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323. INS19-0045

UNIQUE CHARACTERISTICS OF THE DORSAL ROOT GANGLION AS A TARGET FOR NEUROMODULATION

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Introduction: The dorsal root ganglion (DRG) is a novel target for neuromodulation and DRG stimulation is proving to be a powerful tool in the treatment of chronic intractable neuropathic pain. Although the overall principle of conventional spinal cord stimulation (SCS) and DRG stimulation --in which an electric field is applied to a neural target with the intent of affecting neural pathways to decrease pain perception-- is similar, there are significant differences in the anatomy and physiology of the DRG that make it an ideal target for neuromodulation and may account for the superior outcomes observed in the treatment of certain chronic neuropathic pain states.

Materials/Methods: A narrative literature review was completed to highlight the anatomy of the DRG, its function in maintaining homeostasis and its role in neuropathic pain, and the unique value of DRG as a target in neuromodulation for pain.

Results: DRG cells are uniquely pseudounipolar neurons that conduct primary sensory afferent information. Evidence suggests that the DRGs are key sites of physiologic changes that occur with chronic pain, and as such may be good targets for pain management. Specifically, the capacity of the DRG to prevent pain signals that arise in the periphery from proceeding to the central nervous system may be compromised in neuropathy. This critical function can, however, be restored, with DRG stimulation (figure).

Discussion: Overall, the DRG is a critical structure in sensory transduction and modulation, including pain transmission and the maintenance of persistent neuropathic pain states. Unique characteristics including selective somatic organization, specialized membrane characteristics, and accessible and consistent location make the DRG an ideal target for neuromodulation. Because DRG stimulation directly recruits the somata of primary sensory neurons and harnesses the filtering capacity of the pseudounipolar neural architecture, it is differentiated from SCS, peripheral nerve stimulation, and other neuromodulation options.

Conclusions: Advantages exist for targeting the DRG as a neuromodulation intervention, including conservation of energy usage, focused and posture-independent stimulation, absent or limited paresthesia, and good clinical outcomes. This report appears in a recent supplement to Pain Medicine (1).

Abbott supported this work.

Objectives

Upon review of this abstract, delegates will be able to discuss the anatomic and physiologic characteristics that make the DRG an important target for neuromodulation and support the clinical outcomes observed.

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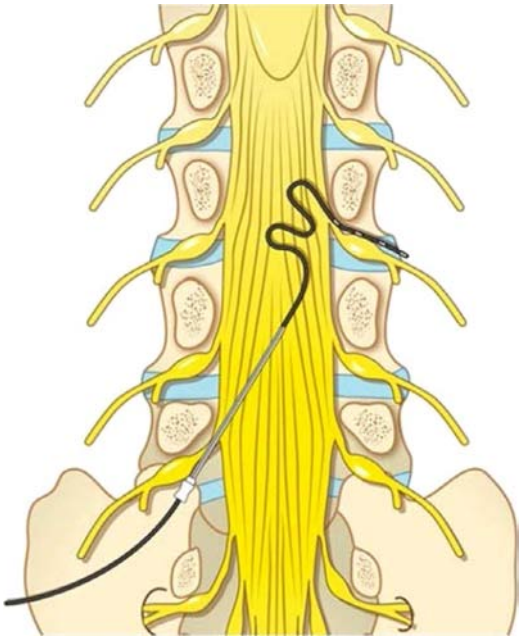

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324. INS19-0096

LARGE SCALE, REAL-WORLD SAFETY ANALYSIS OF DRG STIMULATION

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Introduction: Stimulation of the dorsal root ganglion (DRG) has been shown to be safe and efficacious in the treatment of chronic neuropathic pain. Results from the ACCURATE study demonstrated both safety and superior clinical efficacy in CRPS patients when compared to traditional spinal cord stimulation (SCS). This analysis was initiated to investigate the ongoing, post-approval safety of this therapy.

Materials/Methods: Manufacturer device vigilance and safety records for DRG stimulation (n=500+) and SCS (n=2000+) implants were analyzed and compiled to further assess device safety. Clinical safety data were stratified according to event type as well as rates. Data between therapies from the same manufacturer were compared, as well as rates reported in a prior pivotal RCT and the published SCS literature.

Results: DRG stimulation device complaint rates were lower or comparable to similar epidurally placed neurostimulation devices. Rates of complaints and events varied from 0.0-1.0% for DRG stimulation which was similar to the event rates in the pivotal ACCURATE clinical trial. The most common events were infection (1%) and CSF leaks (0.5%). Event rates were comparable to spinal cord stimulation by the same manufacturer. In comparison, adverse events ranged from 0-14% for spinal cord stimulation in the literature.

Discussion: Overall, in a large consecutive cohort, DRG stimulation demonstrated an excellent safety profile similar to previously reported adverse event rates. Similarly, the safety event rates were lower or similar to previously reported rates for SCS, further demonstrating the comparative safety of this neuromodulation technique for chronic pain treatment. These results are better than those published utilizing systems that are not specifically designed to be placed near, and stimulate, the DRG. Moreover, systems not designed to be placed near the DRG for prolonged periods show less efficacy and clinical utility than those specifically designed for DRG stimulation.

Conclusions: DRG stimulation continues to show an excellent safety profile in large-scale clinical use comparable or better than that described in the pivotal ACCURATE study and published literature.

Objectives

1. Provide up to date safety data on DRG stimulation
2. Confirm safety of the therapy since FDA approval
3. Provide comparative safety performance in comparison to other spinal stimulation therapies

References

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. Deer TR, Levy RM et al., Pain. 2017 Apr;158 (4):669-681 (ACCURATE Study)

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325. INS19-0136

A NEXT GENERATION, MINIATURIZED, BATTERY-FREE IMPLANTABLE SPINAL CORD STIMULATOR SYSTEM: DESIGN AND OUTCOMES

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Introduction: Over time multiple technological advancements in spinal cord stimulation (SCS) devices have introduced improvements to the therapy that have resulted in better clinical outcomes. Miniaturization of various system components has partly provided the basis for system improvements. We present a new miniaturized SCS system design and embodiment that is currently in clinical studies. A historical perspective on how technology advancement has helped to enable this miniaturized system, as well as mitigate prior system deficiencies, is discussed.

Materials/Methods: A review of technical and functional limitations of RF-based SCS systems is presented, identifying past system design issues. Application of modern-day usability engineering practices and advancements that have enabled miniaturization and system performance improvements will be discussed. Design elements that are incorporated into a new miniaturized SCS system will be described including implantable system elements, external RF-based power and bidirectional communication for active RF-power control.

Results: In the current system, a lead is either integrated (permanently attached to the implantable pulse generator; IPG) or ported (connects to a port in the IPG). The microelectronic design not only provides a small implant (<1.5 cc) but also a highly capable IPG. The IPG is powered by an RF induction method from an external device or "Therapy Disc." Unlike other externally powered devices that utilize a passive one-way delivery of power and commands to the IPG, the new system utilizes intelligent bidirectional communication between the IPG and Therapy Disc enabling dynamic control. A "system" approach enables the micro-size implantable IPG to deliver a variety of precisely controlled electrical stimulation therapy. The platform provides stimulation paradigms via a minimally invasive procedure without the risk of implanted batteries and the recurring need for replacement. With much of the intelligent function housed in the external wearable unit, feature upgrades to improve the patient experience can be completed through software and firmware updates.

Discussion: Advancements in electronic miniaturization, design engineering and wearable technology such as dermal adhesives have provided a foundation for improved system design and performance. Prior ergonomics and clinical research findings have been encouraging and ongoing clinical studies are validating longer-term system performance and clinical utility.

Conclusions: A new, miniaturized, battery-free SCS has potential advantages that may address unmet needs in chronic pain patients.

Objectives

The attendee will learn of an engineered system to miniaturize the device size, improve wearability, and choose candidates.

References

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326. INS19-0312

EFFICACY OF BURST SPINAL CORD STIMULATION NEURAL DOSING IN DE-NOVO PATIENT: PRELIMINARY ANALYSIS

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Introduction: Burst spinal cord stimulation (SCS) is a stimulation paradigm that has shown to provide superior efficacy when compared to traditional tonic stimulation. BurstDR neural dosing consists of delivery of intermittent dose of Burst stimulation, with stimulation off period in between. Preliminary evidence supports that the therapeutic efficacy of burst neural dosing results in a similar clinical outcome compared to standard burst stimulation. In this study, we aimed to evaluate the therapeutic efficacy of different burst neural dosing patterns in patients with chronic intractable pain.

Materials/Methods: The study is a prospective, open label, multicenter, feasibility trial with follow-up periods at 1,3 and 6 months. At the start of the trial phase, patients were programmed with a standard neural dosing stimulation pattern (30 second stimulation on, 90 seconds stimulation off). At the end of the SCS trial, all subjects that experience at least 50% pain relief using the neural dosing Burst stimulation paradigm will be considered for further participation in the study and be provided with four additional neural dosing programs with higher stimulation off periods. Pain intensity (Visual Analog Scale), quality of life (EQ-5D), disability (Oswestry Disability Index), pain catastrophizing (Pain Catastrophizing Scale), satisfaction (Patient Global Impression of Change), and medication usage will be assessed at baseline, after SCS trial and at the 1-, 3- and 6-month follow up.

Results: Currently, 53 patients (34 females) have enrolled in the study with an average overall visual analog scale (VAS) score of 76.6+ 15.4. Forty-two patients have completed the trial with an average end-of-trial overall VAS score of 32.1+24.9 (58% pain reduction; $p<0.001$). Twenty-eight of 42 patients (67%) who completed the trial achieved at least 50% of pain relief and moved on to the permanent phase. Using the Oswestry Disability Index (ODI) score, patients, on average, reported an improvement from 54.5+16.1 at baseline to 35.8+23.6 at the end-of-trial ($p<0.0001$). Quality of life and pain catastrophizing all yielded similar improvements from baseline. Presently, patients are distributed across all available neural dosing programs.

Discussion: Although preliminary, our results show that patients can achieve comparable and effective pain relief while using longer OFF periods in their neural dosing programs, potentially prolonging battery life of their devices

Conclusions: The use of neural dosing could provide an additional parameter, complementing stimulation intensity, that can be titrated and leveraged to provide optimal pain relief particularly in cases when efficacy wanes over-time.

Objectives
Evaluate Neural Dosing in Burst Stimulation
Evaluating Burst stimulation
Programming optimization

References
None

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327. INS19-0077

COMPLEX REGIONAL PAIN SYNDROME AND FAILED BACK SURGERY SYNDROME WITH FAILED HIGH FREQUENCY SPINAL CORD STIMULATION SALVAGED WITH ARTHRODESIS REVISION SURGERY AND BURST THERAPY

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Introduction: Complex regional pain syndrome (CRPS) is a disabling form of constant and intense chronic pain involving a limb. Failed back surgery syndrome (FBSS) is chronic back pain following back surgery. After failing medical therapy, spinal cord stimulation (SCS) can be attempted. Burst stimulation is a novel concept applied recently to treat chronic pain through SCS. The waveform is delivered in packets and made up of closely spaced high-frequency electrical impulses followed by an inter-burst interval. The impulses are thought to travel to the thalamus to treat sensory, affective, and attentional components of neuropathic pain by targeting both the somatosensory cortex and the limbic system. A case of FBSS and CRPS, who failed to have prolonged relief with high frequency SCS, was treated successfully with a combination of arthrodesis revision and SCS burst therapy.

Materials/Methods: A 50-year-old-female presented one-year after L5-S1 posterior instrumentation and posterolateral arthrodesis for spondylolisthesis with disabling Type-I CRPS of her left foot and back pain.

Results: A T9-T10 high-frequency-10 kHz SCS-trial followed by permanent paddle lead placement at T9-10 provided more than 50% foot pain relief resulting in improved range of motion. However worsening back pain and pseudoarthrosis mandated a revision of her prior arthrodesis 6-months after SCS-surgery. Postoperative improvement in back pain was noted but her left leg pain became worse despite SCS-reprogramming. 2-months later, she underwent placement of a different paddle lead at T12 and a new pulse generator using burst therapy. This resulted in complete resolution of foot pain. She remains pain-free five-months post-operatively.

Discussion: In selected patients with FBSS and CRPS, revision of arthrodesis combined with SCS may be needed to achieve adequate pain relief. In this case of CRPS, SCS using burst therapy at T12 was superior then high frequency stimulation at T9-10 for foot pain relief.

Conclusions: Patients presenting with FBSS and CRPS can benefit from a combination of arthrodesis revision and SCS to achieve a good outcome.

Objectives

-In patients with prior lumbar arthrodesis, persistent back pain after SCS treatment can be secondary to pseudoarthrosis and fusion revision surgery may be needed.

- When CRPS pain relief from SCS is lost overtime, changing to a different system or revising the placement of the paddle lead may offer better outcome.

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328. INS19-0078

CENTRAL NEUROPATHIC PAIN AND COMPLEX REGIONAL PAIN SYNDROME FOLLOWING BRACHIAL PLEXUS INJURY TREATED SUCCESSFULLY WITH DORSAL ROOT ENTRY ZONE LESIONING

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Introduction: Refractory pain resulting from brachial plexus injury is debilitating both physically and mentally. Current treatments have limited efficacy and are often resistant to medication, which can lead to narcotic dependency. Dorsal root entry zone (DREZ) lesioning may serve as a valuable alternative for managing this condition. We present a case of post-brachial injury refractory pain that failed spinal cord stimulation (SCS) but was treated successfully with DREZ.

Materials/Methods: A 36-year-old male with chronic complete right brachial plexus injury from multiple nerve roots avulsion following a motorcycle accident presented with chronic narcotic dependence. His severe pain in the C6, C7, C8, and T1 distributions was disabling despite neuropathic pain medication and escalation of narcotic use.

Results: A trial of conventional SCS was failed due to poor topographical coverage. Two years later the pain intensity worsened and a second SCS trial with placement of a paddle lead using burst therapy was attempted. Initial pain relief was partial and lasted less than 3 days. A week later, SCS paddle lead removal and C5 to T1 right DREZ lesioning with C4 to T1 laminoplasty was carried out. Using a 2 mm insulated neurotomy electrode, 83 lesions were made at 75°C for 15 seconds. Five months postoperatively, 50% pain improvement and decreased narcotic consumption was noted.

Discussion: SCS should remain the first surgical treatment option for refractory brachial plexus pain, DREZ lesioning can achieve significant pain relief with low morbidity. A paddle lead SCS trial can be attempted if DREZ is considered as a second treatment option.

Conclusions: When faced with refractory brachial plexus injury pain, a SCS paddle lead trial can be attempted first. If the trial fails, removal of the paddle lead can be done in the same setting of DREZ lesioning.

Objectives

-Medical management of brachial plexus injury pain can lead to narcotic dependence.

-SCS is the first line surgical option for this condition.

-Placement of a paddle lead for SCS trial can be attempted if, DREZ lesioning is considered as a salvage option.

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329. INS19-0178

FIRST EXPERIENCE IN SCS WITH COMBINATION THERAPY AND NOVEL ALGORITHM FOR DORSAL HORN MODULATION

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Introduction: The treatment of chronic intractable pain has been optimized in the years using a personalized and multimodal combination of drugs and interventional approaches. We report here our preliminary experience in Spinal Cord Stimulation with a new programming approach which simultaneously combines different waveforms and uses a new mapping approach modelled to recruit the dorsal horns instead of dorsal columns (1).

Materials/Methods: Up to now 5 patients with diagnosis of Failed Back Surgery Sindrome, Cervical and Lumbar Spinal Stenosis, baseline pain of 9 NRS scale, have been trialed with a SCS system capable of combination of different waveforms at the same time. The possible stimulation modalities are Microburst, higher rate, tonic and a novel algorithm to modulate the dorsal horn. The percutaneous leads implanted are octopolar linear leads or 16-contact leads. The patients have been followed up for 1 month. The lead placement was decided according to pain areas and paresthesia test (2 patients with cervical and lower limbs pain, 4 patients with low back and legs pain).

Results: The preliminary data consist on a reported average pain relief of 57% in terms of NRS score. All the patients passed the trial phase and have been implanted with a permanent pulse generator. Regarding the best combination of waveforms preferred by the patients we have: - 5 combinations with DHM and tonic or microburst - 1 combinations of microburst and higher rate. The patients with multiple pain areas have a dedicated waveform for each pain district.

Discussion: Although these are preliminary results, the usage of a new approach in SCS with combination therapy seems to report positive and encouraging clinical outcomes, already at trial phase and with an apparent quicker wash-in period. These patients will be then followed up in the upcoming months to monitor the long-term results.

Conclusions: Preliminary clinical data suggests that combination therapy may be considered as a new approach to SCS aligned with the strategy of other pain treatments aimed at optimizing and personalizing pain therapy.

Objectives

Evaluate a new SCS programming approach with combination therapy

References

Outcomes Using an SCS Device Capable of Delivering Combination Therapy (Simultaneous or Sequential) and Advanced Waveforms/Field Shapes, Metzger, INS European chapter poster 2018

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330. INS19-0183

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)

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Introduction: The evidence for effectiveness and cost effectiveness of a screening trial being conducted before a final implant of spinal cord stimulation (SCS) remains unclear. The aim of the TRIAL STIM RCT is to assess the clinical utility and cost effectiveness of such screening trials.

Objectives: The TRIAL-STIM Study aims to assess the diagnostic performance, clinical outcomes and cost-effectiveness of a screening trial prior to full implantation of a SCS device vs no screening trial.

Materials/Methods: This is a superiority, parallel-group, three-centre, randomised controlled trial in patients with chronic neuropathic pain with a nested qualitative study and economic evaluation. The study takes place in three UK centres: The James Cook University Hospital, Middlesbrough, Basildon and Thurrock University Hospitals NHS Foundation Trust; and Leeds Teaching Hospitals NHS Trust. A total of 100 adults undergoing SCS implantation for the treatment of neuropathy were included. Subjects were recruited from the outpatient clinics of the three participating sites and randomised to undergo a screening trial prior to SCS implant or an implantation-only strategy in a 1:1 ratio. Allocation was stratified by centre and minimised on patient age (≥ 65 or < 65 years), gender, presence of failed back surgery syndrome (or not) and use of high frequency (or not). The primary outcome measure is the numerical rating scale (NRS) at 6 months compared between the screening trial and implantation strategy and the implantation-only strategy.

Secondary outcome measures include diagnostic accuracy, the proportion of patients achieving at least 50% and 30% pain relief at 6 months as measured on the NRS, health-related quality-of-life (EQ-5D), function (Oswestry Disability Index), patient satisfaction (Patients' Global Impression of Change) and complication rates.

A nested qualitative study was carried out in parallel for a total of 29 of the patients recruited in each centre to explore their views of the screening trial, implantation and overall use of the SCS device. The economic evaluation will take the form of a cost–utility analysis.

Results: we will present the up to date state of recruitment

Discussion: The TRIAL-STIM Study is a RCT with a nested qualitative study and economic evaluation aiming to determine the clinical utility of screening trials of SCS as well as their cost-effectiveness. The economic evaluation will estimate the cost-effectiveness of a screening trial and implantation strategy versus implantation only strategy. A two-stage economic model will be developed with extensive deterministic and probabilistic sensitivity analysis.

Poster Presentations - May 27 - May 30
Spine - Pain

331. INS19-0323

HIGH FREQUENCY SPINAL CORD STIMULATION (HF-SCS) AT 10 KHZ FOR THE TREATMENT OF CHRONIC PAIN RESULTING FROM SPINAL CORD INJURY

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Introduction: Most research in spinal cord injury (SCI) with neuromodulation techniques has been performed with low-frequency spinal cord stimulation (SCS). Literature reviews don't find sufficient evidence supporting the use of low-frequency SCS in SCI[1]. Promising results were observed in SCI patients treated with high-frequency SCS (HF-SCS) at 10 kHz[2,3]. The goal of this prospective, feasibility study is to evaluate the safety and effectiveness of HF-SCS for the alleviation of chronic neuropathic pain in patients with SCI.

Materials/Methods: Subjects with chronic, intractable pain of ≥5 cm (visual analog scale-VAS) in pain area directly related to SCI were enrolled in a prospective, single-center study following ethics committee approval. Other key criteria were: injury at cervical/thoracic/lumbar/sacral level, the American Spinal Injury Association Impairment Scale (ASIA) of A-D and neuropathic pain. Subjects were trialed with HF-SCS at 10 kHz with percutaneous epidural leads. Subjects with successful trial (≥50% pain relief) were implanted with a Senza system (Nevro Corp., Redwood City). Safety and effectiveness endpoints were captured up to 12 months post-implant.

Results: As per latest analysis, 10 of the 16 enrolled subjects underwent a trial implant; scar tissue and fusion material precluded lead placement in 2 subjects and 5 had a successful trial (62.5% success rate). Three procedure related adverse events were reported. For subjects with a permanent implant baseline mean (SD) pain scores (primary area) of 8.8±0.9 cm (N=4) improved to 2.2±1.9 cm (N=4) at end of trial, 3.1±1.8 cm (N=4) at 1 month follow-up, 5.4±4.3 cm (N=4) at 3 months follow-up, 5.5±4.5 cm (N=3) at 6 months follow-up, 2.1±0.2 cm (N=2) at 9 months follow-up and 2.3±1.0 cm (N=2) at 12 months follow-up. ASIA for one subject was reclassified from an A (baseline) to B at the 3, 6 and 12 month visits due to an improved sensory function.

Discussion: Additional data on disability grading, functionality, spasticity, spasms, quality of life and sleep will also be presented.

Conclusions: This study provides promising preliminary results with HF-SCS at 10 kHz in SCI patients.

Objectives

Please see introduction.

References

1. Lagauche et al. The chronic neuropathic pain of SCI: which efficiency of neuropathic stimulations? *Ann.Phy.Rehab.Med*. 52 (2009) 180-187.

2. Sisson et al. Sustained pain relief and functional improvement in SCI patients treated with HF-SCS at 10 kHz: Two Case reports. Abstract & Poster, NANS congress 2018.

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Poster Presentations - May 27 - May 30
Spine - Pain

332. INS19-0163

ANALYSIS OF DORSAL COLUMN RESPONSE TO TRADITIONAL AND NEW SUB-PERCEPTION SCS FIELD SHAPES

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Introduction: Sub-perception SCS (Spinal Cord Stimulation) therapy has become an important therapeutic modality along with paresthesia-based SCS for the treatment of chronic pain. Traditional sub-perception SCS uses a simple-bipole as the electrode configuration for stimulation, where the cathode and anode are typically ~8mm apart. Novel field-shapes have been developed and deployed using independent current sources with the goal of preferentially modulating dorsal horn (DH) elements aligned with the field while minimizing activation of other targets like Dorsal Columns (DCs). In this analysis, we compare DC responses to the traditional bipole and the novel rostrocaudal (RC) field-shape used in sub-perception SCS using computational modeling and experimental preclinical data.

Materials/Methods: Parallel modeling and experimental studies were performed as an on-going effort to understand the targets that are recruited by SCS therapies. A finite element model was used to determine the voltage distribution across the spinal cord and to establish the voltages effect on neuronal models representing DC and IINs (Inhibitory Interneurons) from superficial DH. Outputs from the model were assessed for both field-shapes (8mm-bipole and RC field-shape). Swine were implanted epidurally with SCS leads powered by an External Trial Stimulators following IACUC/AWA standards. CAPs (Compound Action Potentials) produced in response to the two field-shapes were analyzed to compare trends in DC recruitment based on responses to each field.

Results: Modeling results predict the novel RC field-shape increases DC activation thresholds compared to the 8mm-bipole by 38%. Consistent with model predictions, the magnitude of experimentally measured CAPs generated by the RC field-shape were 35%-40% smaller than CAPs generated by the 8mm-bipole at fixed stimulation settings. The model also predicts that IIN activity is increased from baseline using both field shapes, but the novel RC field increases IIN activity over a 4-mm greater extent than the simple-bipole using the same stimulation settings.

Discussion: The novel RC field-shape developed from model-based design yielded experimental CAP results consistent with expectations. Next steps include experimental evaluation of model predictions regarding IIN activity.

Conclusions: Neural engineering techniques can be used to engage intriguing candidate neural targets, such as IINs in the DH, as they are revealed through increased mechanistic understanding.

Objectives

- Consistency of model's predictions for DC activation was evaluated experimentally using CAP activation.
- Experimental validation of model-predicted field effects on DH elements is necessary.

References

2018 Pyles et al., INS EU Congress

Poster Presentations - May 27 - May 30
Spine - Pain

333. INS19-0294

BURST STIMULATION AS ALTERNATIVE FOR RESCUING PATIENTS WHO NO LONGER RESPOND TO TRADITIONAL SPINAL CORD STIMULATION

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Introduction: Despite the fact that patients usually undergo successful trial stimulation phases before receiving a permanent stimulation system, some fail to keep a sufficient level of relief months or years after the initial implantation. In recent years, new SCS modalities have appeared which may serve as rescue for such patients.

Materials/Methods: Consecutive patients in which traditional tonic stimulation had failed to maintain long-term pain relief, and who had expressed their intention to have the system explanted, agreed to undergo a "retrial" stimulation phase with Burst stimulation [1].

The implanted leads and/or subcutaneous extensions were disconnected from the implanted pulse generator (IPG) and connected to an external trial stimulator by means of one or two percutaneous temporary extensions.

A standard Burst Stimulation program (40 Hz inter-burst, 500 Hz intra-burst frequencies, 1000 µs pulse width, pulse amplitude 60% below perception threshold), was loaded into the trial system and the patient was sent home for a trial period that ranged from 1 to 4 weeks.

After the trial, all patients chose either to have a new Burst IPG or complete explantation of the SCS system.

Results: 11 patients (6 male, 5 female, age 51±22) were re-trialed. All of them had been implanted in our hospital with tonic SCS systems with initial significant relief that lasted for 2.5 (0.4-10.0) years. 8 patients (82%) regained significant relief and received a new IPG. After 12 (0-42) months of follow-up after retrial with Burst stimulation, patients refer 73% (56%-88%) relief and are very satisfied (n=6) or satisfied (n=2) with the new system. Specific data for each individual patient can be seen in Table 1.

Discussion: Reasons for long-term decrease of SCS efficacy are not well known and may include evolution of the disease and tolerance to the therapy. Some new stimulation waveforms probably feature different mechanisms of action and may serve as rescue to such patients. In any case, if tolerance has any impact on the decline of relief, stimulation systems capable several waveform types would be a good option to overcome tolerance.

Conclusions: In this small cohort, Burst stimulation regained relief and satisfaction for a majority of patients, although it is unknown how long will this relief last with the new system.

Objectives

Burst Spinal Cord Stimulation
SCS non responding patients.
SCS Retrial

References

[1] Hou S et al: A Systematic Evaluation of Burst Spinal Cord Stimulation for Chronic Back and Limb Pain. Neuromodulation 2016; 19: 398–405

PATIENTS RETRIALED WITH TONIC DR STIMULATION

Patient	Initial Diagnosis	Sex	Age Years	NRS Basal	Pain Location	Years w/tonic	Weeks Retrial	Months FU	Satisf. w/Burst	NRS Post	Relief w/Burst
1	FBSS	F	48	9.0	LEGS/LOW BACK	1.0	4	5,5	VERY SATISFIED	3	67%
2	FBSS	M	55	9.0	LEGS/LOW BACK	1.0	3	0,6	VERY SATISFIED	4	56%
3	FBSS	F	45	9.0	LEGS/LOW BACK	0.4	4	4,1	VERY SATISFIED	2	78%
4	FBSS	M	44	9.0	LEGS/LOW BACK	2.2	4	42,6	SATISFIED	4	56%
5	FBSS	M	54	7.0	LEG/LOW BACK	2.4	3	7,9	VERY SATISFIED	1	86%
6	EPENDIMOMA RESECTION	F	43	8.0	FEET/DORSAL	4.2	2	21,4	VERY SATISFIED	2	75%
7	PVD	M	45	8.0	LEGS	1.4	4	23,7	SATISFIED	2	75%
8	CRPS I	F	45	9.5	LEGS	3.0	4	4,1	VERY SATISFIED	2	79%
9	CEREBROVASCULAR CCIDENT	M	48	8.5	LEGS	10.0	4	10,7	VERY SATISFIED	1	88%
10	POST-HERPETIC NEURALGIA	F	73	10.0	CHEST/ARM	0.6	4	UNSUCCESSFUL RETRIAL, SYSTEM EXPLANTED			
11	CRPS I	M	61	8.0	ARM	1.5	4	UNSUCCESSFUL RETRIAL, SYSTEM EXPLANTED			

Poster Presentations - May 27 - May 30
Spine - Pain

334. INS19-0299

EVOLVING COMPLEX PAIN MANAGED WITH SPINAL CORD STIMULATION, SUBCUTANEOUS STIMULATION AND BURST STIMULATION SUCCESSIVELY

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Introduction: Long-term treatment of complex pain syndromes, with two or more anatomical pain regions distant from each other, ethiological diversity and evolution over time, represents a challenge for the pain specialist and very often must be addressed with equally different and evolving solutions.

Materials/Methods: Female patient treated in our Pain Unit since January 2009 (age 39), referred to us by the Neurosurgery Service with neuropathic pain in lower limbs and right T7-T8 intercostal region after intermedullary spinal cord ependymoma surgery.

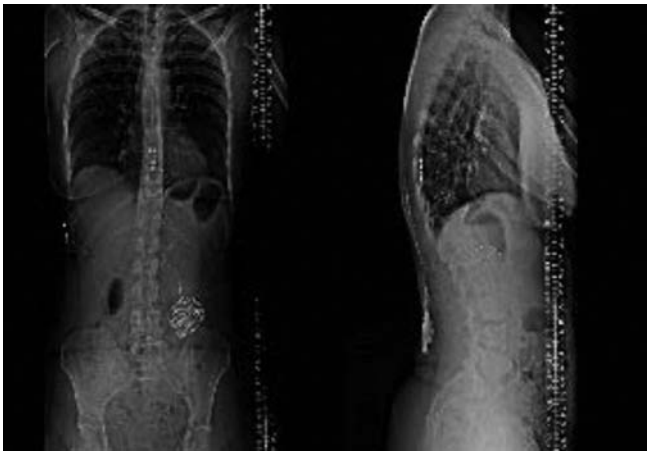
In November 2012, a 5-column 16-pole paddle lead was implanted at T9-T10 level with acceptable coverage of both pain areas during the implant. However, in the course of the trial phase it was observed that, despite good relief in lower limbs, coverage could not be achieved in the ribs region, so it was decided to add a subcutaneous lead during the permanent implantation procedure.

The system provided adequate therapy up to October 2016. After this date the patient referred that she couldn't increase stimulation amplitude without producing painful paresthesias. For this reason, Burst stimulation was tested in a trial phase, and the permanent pulse generator was then replaced in February 2017.

Results:

Since the change of stimulation waveform, the patient has recovered and exceeded the maximum degree of relief achieved with tonic stimulation so far, maintaining such relief and a high degree of satisfaction after 20 months of follow-up.

Discussion: Adapting neurostimulation therapies to the changing needs of patients with complex and/or evolving pain patterns is important to maintain a constant level of relief. In this particular patient, the early addition of a subcutaneous lead and the change (years after) of burst stimulation, were important adaptive steps to overcome evolving issues of her pain syndrome.



Conclusions: Burst Stimulation may re-capture relief and satisfaction in patients with complex, evolving pain syndromes.

Objectives

Mixed lead configurations for complex pain picture

Adapting SCS therapies for evolving pain syndromes

Burst stimulation as rescue for SCS non-responders

References

[1] Pajuelo A et al. From tonic to burst: re-capturing pain relief. Poster presented at the International INS Congress (2015)

Abejón D, Pajuelo A: Burst Stimulation with Hybrid Spinal Cord/Subcutaneous Lead Stimulation System: A Case Study. Poster presented at the International INS Congress (2015)

Poster Presentations - May 27 - May 30
Spine - Pain

335. INS19-0189

PLACEBO- AND SHAM-CONTROLLED TRIALS IN IMPLANTED NEUROMODULATION INTERVENTIONS FOR PAIN: EVIDENCE AND IMPLICATIONS

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Introduction: Clinical research of neuromodulation for pain is growing in sophistication, with the previous decade seeing multiple well-designed randomized controlled trials employing active treatment comparators. A small number of studies have employed control via placebo (no electricity output) or sham (very small electricity output). This has become easier with the recent advent of advanced waveforms that do not create a percept, because active treatment would be indistinguishable from control. The extent of the placebo effect, in which clinical response occurs in the absence of treatment, are not yet well-characterized in neuromodulation for pain, nor are the putative differences in outcomes for placebo vs. sham controls.

Materials/Methods: A systematic review of the literature was performed. Placebo- or sham-controlled studies of chronically-implanted neuromodulation technology for pain were included. Pain ratings were compared for placebo-controlled and for sham-controlled trials.

Results: 18 studies were included: 9 for SCS (n=183 [total subjects included]), 2 for peripheral nerve (field) stimulation (n=35), and 7 for headache (n=360).

For SCS and PN(f)S, the results of 24 experiments across 11 studies were compared. Active treatment reduced pain relative to pre-implant baseline levels. With placebo treatment, pain returned. In contrast, with sham treatment, pain remained controlled (see figure). This trend was apparent for stimulation that produced paresthesias as well as sub-perception stimulation (e.g., burst and high-frequency SCS). Similar trends were observed in headache data.

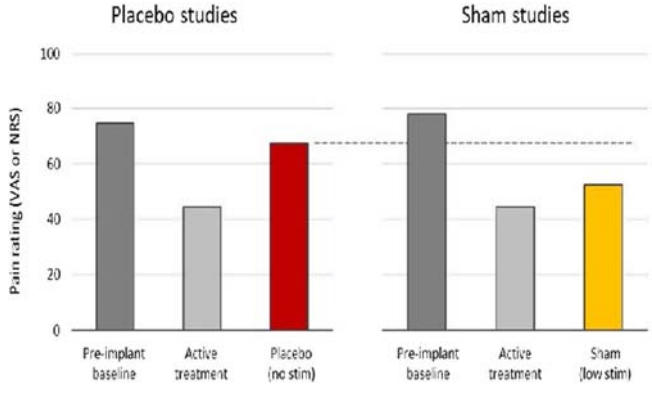
Discussion: Neuromodulation treatments for chronic pain have repeatedly demonstrated superior analgesia versus placebo. This may not, however, be the case for sham controls. The approach used for the control group (no stimulation versus low-levels of stimulation) appears to have a substantial impact on the control group response. These results substantiate the effectiveness of neuromodulation therapy and draw attention to important design considerations in studies involving these therapies.

Conclusions: Care needs to be taken in using sham controls when studying neuromodulation devices in the treatment of chronic pain. Further study may be needed to understand nuanced dose-response relationships in the neural targets, as well as the impact of psychological context on placebo or sham responses. Without such knowledge, these controls may impose uncontrolled and unintended effects that potentially impact study outcomes.

Objectives

Placebo and sham controls may have different outcomes in neuromodulation trials.

Careful study design and conduct must be employed.



Poster Presentations - May 27 - May 30
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336. INS19-0358

10 KHZ HIGH-FREQUENCY SPINAL CORD STIMULATION FOR CHRONIC THORACIC PAIN: A MULTICENTER CASE SERIES AND A GUIDE FOR OPTIMAL PARESTHESIA-FREE LEAD PLACEMENT

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Introduction: Historically, chronic thoracic back pain has been difficult to treat. Conservative measures and spinal interventions are only modestly successful as treatments and surgical options carry significant risks. Paresthesia mapping has proven difficult and uncomfortable, which has halted the advancement of study for spinal cord stimulation. This multicenter, retrospective case series suggests that paresthesia-free spinal cord stimulation with 10 kHz high-frequency therapy (HF-SCS) for thoracic back pain may reliably and sustainably reduce pain scores, offer anatomically-based stimulation targets, improve function, improve sleep, and decrease opioid requirements.

Materials/Methods: A multicenter, retrospective review was conducted for patients with thoracic back pain treated with HF-SCS implantation. Patients had lead placement between T1-T6 vertebral levels. Records were reviewed for stimulation location, pain scores at time of implantation and at 1, 6, and 12 months post-implant. Functional improvement, improved sleep, or decreased pain medication usage following implantation were also recorded.

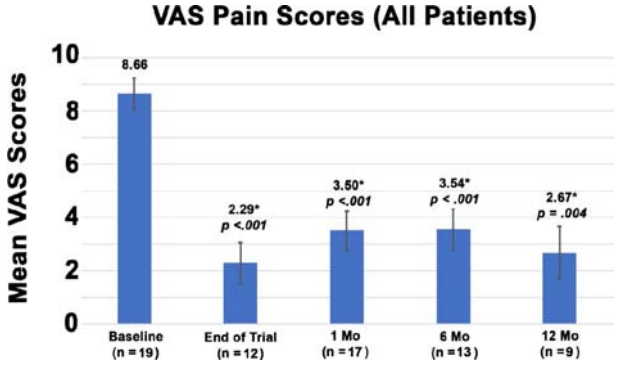
Results: 17/19 patients (89.5%) demonstrated response to therapy (>50% reduction in VAS relative to baseline). These results were sustained at 1, 6, and 12 months post-implant, with variable follow-up. Patients also reported functional improvement (17/19), improved sleep (14/19), and reduction in pain medication usage (9/19). 10/19 (52%) reported their greatest pain relief with stimulation over the T2 vertebral body and 5/19 (26%) over the T1 vertebral body. Together, 15/19 (79%) had their greatest relief with stimulation over either the T1 or T2 vertebral bodies There were 10 patients who failed to follow-up consistently at each time point.

Discussion: The responder rate suggests that significant pain relief from thoracic back pain can be achieved with HF-SCS. Despite biases and inconsistent follow-up, these findings may signify a substantial advancement in SCS application. With HF-SCS, paresthesia-free pain management is possible for this difficult-to-treat population. The sustained pain relief seen in every patient reporting at 12 months invites further study for durability. These findings suggest that anatomic target stimulation can be identified and reproduced for treatment of thoracic back pain with HF-SCS. These results also suggest that HF-SCS therapy for thoracic pain improves functionality, improve sleep, and decrease opioid use.

Conclusions: HF-SCS provided significant and sustained relief of thoracic pain. Patient functionality, sleep, and opioid use were all improved. This case series provides an anatomically-based approach for target stimulation for thoracic pain. The results found here should inspire further study of HF-SCS in the treatment of chronic thoracic pain.

Objectives

To evaluate efficacy, stimulation targets, and quality outcomes of HF-SCS therapy for chronic thoracic pain.



Poster Presentations - May 27 - May 30
Spine - Pain

337. INS19-0097

A PROSPECTIVE CLINICAL TRIAL TO ASSESS HIGH FREQUENCY SPINAL CORD STIMULATION (HF-SCS) AT 10 KHZ IN THE TREATMENT OF CHRONIC INTRACTABLE PAIN FROM PERIPHERAL POLYNEUROPATHY

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Introduction: Current treatment options for neuropathic pain are primarily pharmacological with limited effectiveness and sometimes intolerable side effects[1]. Based on documented long-term pain relief seen in previous studies, we hypothesized that paresthesia-independent, high frequency SCS (HF-SCS) at 10 kHz may provide effective pain relief for neuropathic pain[2,3].

Materials/Methods: Twenty-eight subjects with chronic, intractable pain of ≥5 cm (on a 0-10 cm visual analog scale) of the upper or the lower limb from PPN were enrolled in a prospective, multi-center study following IRB approval. Each subject was implanted with two epidural leads spanning C2-C6 or T8-T11 vertebral bodies for upper limb pain and lower limb pain, respectively. Subjects with successful trial stimulation were implanted with a Senza system (Nevro Corp., Redwood City, CA). Interim 12-month results are presented as mean±95% confidence interval in the permanent implant population.

Results:

A total 28 subjects were enrolled in the study; majority of the subjects presented with lower limb pain (n=27). Common diagnoses include idiopathic polyneuropathy (n=15) and painful diabetic neuropathy (PDN, n=9). Twenty-two of the 26 subjects (84.6%) trialed had a successful trial and 18 received a permanent implant (declined to proceed to the permanent implant-3, withdrawn by investigator-1). Five procedure related adverse events or serious adverse events were reported. In addition to improvements in pain and disability (Table 1) and impression of change (Table 2), neurological assessment demonstrated either sensory, motor or reflex improvements in 12, and 14 subjects at end of trial and 3 months, respectively.

Discussion: Neuropathic pain is difficult to treat and there are not many options available for patients. The results from the current study are in line with previously seen results from studies in back and leg pain patients.

Conclusions: HF-SCS at 10 kHz resulted in clinically meaningful improvements in pain scores, disability and interference measures in subjects with PPN that were sustained over long-term follow-up with concomitant improvements in subjects' neurological status.

Objectives

The goal of this study is to document the safety and effectiveness of HF-SCS at 10 kHz in treatment of chronic intractable pain from peripheral polyneuropathy (PPN).

References

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Table 1. Pain and disability outcomes for study subjects (mean±95% CI). Responders had at least 50% pain relief from baseline.

		Baseline	3 months	6 months	12 months
All subjects	Pain score (N; Responder rate)	7.5±0.7 (18, N/A)	1.9±0.3 (18; 78%)	2.2±0.8 (18, 78%)	2.8±1.5 (16, 69%)
PDN subjects		8.1±0.8 (8, N/A)	1.9±0.9 (8; 100%)	2.0±0.8 (8; 87%)	2.1±1.7 (7; 86%)
Pain disability index		38.7±7.9 (18)	21.6±6.6 (18)	18.4±7.5 (18)	22.0±7.7 (14)
Pain interference (McGill Pain Questionnaire)		4.8±0.7 (18)	1.8±0.7 (18)	N/A	2.1±0.9 (15)

Table 2. Global Impression of Change (GIC) for study subjects

		Better/Great deal better (n/N)
Physician-rated	3 months	78% (14/18)
	12 months	80% (12/15)
Subject-rated	3 months	83% (15/18)
	12 months	80% (12/15)

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338. INS19-0122

ASSESSMENT OF CHRONIC PAIN PATIENT OUTCOMES USING A NEUROMODULATION SYSTEM CAPABLE OF MULTIPLE WAVEFORMS AND PROGRAMMING MODALITIES IN AUSTRALIA

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Introduction: Treatment of chronic pain is inherently challenging given the subjective nature of pain that uniquely manifests within each patient. Different neuromodulatory approaches such as spinal cord stimulation (SCS), peripheral nerve stimulation (PNS), peripheral nerve field stimulation (PNFS), occipital nerve stimulation (ONS), and sacral nerve stimulation (SNS) may help address this variability. In addition, patients can increasingly customize their own treatment using a variety of available stimulation modalities and/or waveforms with the use of an anatomically-guided neural targeting algorithm. This report presents a real-world, case series examination of a wide group of patients using a neuromodulation system capable of providing multiple neurostimulative modality options.

Materials/Methods: This is a multicenter, observational case series of patients implanted with a multiple waveform neuromodulation system (Precision or Precision Spectra, Boston Scientific) conducted at six sites in Australia as part of an ongoing retrospective chart review evaluation of outcomes for chronic pain (Clinicaltrials.gov identifier: NCT01550575). Assessments collected include baseline characteristics (demographics, medical history, pain diagnosis) and pre- and post-implant outcomes.

Results: Data from 51 subjects (76% PNS, 24% SCS), at last follow-up of 315 days (mean) has been reported. Among these subjects, a 4.2-point reduction in overall pain at their last follow-up was reported (7.2 [baseline] to 3.2 [mean last follow-up], $p < 0.0001$). Additional data is being collected and will be presented.

Discussion: It is proposed that a system capable of providing multiple waveforms and/or field shapes can enable the attainment of substantial, long-term pain relief. Studies are needed however to further understand the impact of personalized therapy on the outcomes of chronic pain patients.

Conclusions: This real-world, case-series examination reports pain reduction outcomes within a diverse group of patients using a neuromodulation system capable of providing multiple waveform and other stimulation programming options.

Objectives

1. To report pain relief scores (NRS) in patients implanted with an SCS device capable of providing multiple neurostimulative modality options for use in the treatment of chronic pain.

2. To report the use of various programming/modality options from patients implanted with an SCS device capable of providing multiple neurostimulative modality options for use in the treatment of chronic pain.

3. To report baseline characteristics of patients implanted with an SCS device capable of providing multiple neurostimulative modality options for use in the treatment of chronic pain.

References

NA

Poster Presentations - May 27 - May 30
Spine - Pain

339. INS19-0098

SPINAL CORD STIMULATION AT 10 KHZ FOR THE TREATMENT OF CHRONIC FOCAL NEUROPATHIC POST-SURGICAL PAIN

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Introduction: Chronic post-surgical pain (CPSP) is one of the most prevalent etiologies of neuropathic pain (1). Pre-clinical evidence from high frequency SCS (HF-SCS) at 10 kHz demonstrated an inhibitory effect on projection interneurons in the superficial layers of dorsal horn. We hypothesized that HF-SCS at 10 kHz may provide effective pain relief in focal CPSP conditions.

Materials/Methods: In this multicenter, prospective study subjects with chronic, intractable pain of ≥5 cm (on a 0-10 cm visual analog scale [VAS]) of the trunk, upper or the lower limb from CPSP and at least a score of 4 in the Douleur Neuropathique 4 questionnaire were enrolled following IRB approval. HF-SCS at 10 kHz is designed to deliver electrical stimulation for the treatment of chronic intractable pain of the trunk and/or limbs [2]. Chronic focal neuropathic pain of the trunk or the limbs post-surgery is, thus, an on-label indication for this therapy. Significant spinal stenosis, epidural scarring or symptoms of myelopathy were causes for exclusion. Subjects were implanted with two epidural leads spanning appropriate vertebral bodies as determined by the location of pain and were implanted with a Senza system (Nevro Corp., Redwood City, CA) if they had successful trial stimulation (≥40% pain-relief). Safety and effectiveness endpoints were captured up to 12 months post-implant. Interim 6-months results are presented as mean±95% confidence interval in the permanent implant population.

Results: Monitored data was available for 27 enrolled subjects, with 17 presenting lower extremity pain, 2 upper extremity pain, and 8 trunk pain. Twenty-five subjects had successful trial (92.5% trial success rate) and received a permanent implant. Baseline pain scores and pain disability index of 7.9±0.6 cm (n=25) and 41.6±6.2 (n=22) improved to 1.2±0.4 cm (n=25), 1.8±0.7 cm (n=23), 1.2±0.8 cm (n=24), 1.7±0.8 cm (n=16) and 20.9±6.3, 11.8±4.4, 10.7±4.7 at the end of trial, 1-, 3-, and 6-month follow-ups, respectively. Meaningful improvements were also reported in all domains of McGill Pain Questionnaire including affective scores (Table 1) and 3-item pain and sleep questionnaire (Table 2).

Discussion: Results from this study are in line with previously reported data from patients with back and leg pain.

Conclusions: Results using HF-SCS 10 kHz to treat chronic focal neuropathic pain following surgical intervention are promising and demonstrate that a midline epidural lead placement may effectively treat this condition.

Objectives

To test the efficacy of 10 kHz SCS for focal CPSP patients.

References

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Table 1. Domain scores for short form McGill Pain Questionnaire (SF-MPQ-2)

	Total Score	Continuous Pain	Intermittent Pain	Neuropathic Pain	Affective Descriptors
Baseline	5.03±1.03	5.97±1.08	5.42±1.13	4.60±1.21	3.68±1.47
3 Months	1.13±0.54	1.49±0.75	1.15±0.50	0.95±0.46	0.87±0.56

Table 2: Three-item pain and sleep questionnaire

	Trouble falling asleep due to pain	Awakened from sleep (night)	Awakened from sleep (morning)
Baseline	6.95±1.05	6.79±1.01	7.83±0.99
3 Months	1.99±1.03	1.79± 0.83	1.94±0.94

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340. INS19-0155

COST SAVINGS ASSOCIATED WITH SYSTEMIC OPIOID ELIMINATION FOLLOWING INITIATION OF INTRATHECAL DRUG DELIVERY FOR TREATMENT OF CHRONIC PAIN IN THE UNITED STATES

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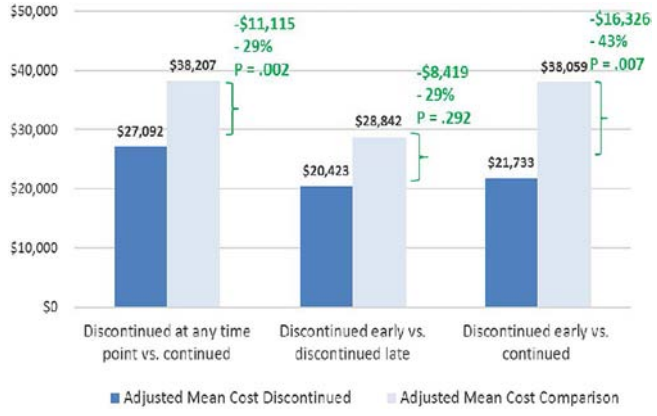
Introduction: The intrathecal drug delivery system (IDDS) provides an alternative means of pain control for patients with chronic intractable pain, with studies showing reduced or eliminated need for systemic opioid therapy (termed "opioids" hereafter).[1-3] This study evaluates the cost savings associated with opioid elimination following start of IDDS therapy from a US commercial payor perspective.

Materials/Methods: This retrospective database analysis used the U.S. Truven MarketScan® Research Databases (2011-2016). We identified patients with chronic pain that were newly implanted with IDDS. Patients were defined as discontinuing opioid therapy if they had a final prescription fill with the days' supply ending during baseline (pre-IDDS), 30-day washout following IDDS implant, or up to 365 days follow-up; otherwise patients were considered "continued". Discontinuation during baseline or washout were defined as "early" opioid discontinuation. Total medical + pharmacy insurer payments ("costs") were adjusted in generalized linear models (GLM) controlling for demographic and clinical characteristics.

Results: 631 patients met inclusion criteria, with 43.3% discontinuing opioid therapy, among whom 11.4% were considered "early" discontinuers. Total costs over one-year post-washout follow-up were 29% lower among patients discontinuing vs. continuing opioids ($27,092 vs. $38,207, P = .0117). Opioid prescriptions accounted for 17% of decreased cost. Savings associated with early discontinuation vs. continuation were -$16,326, suggesting an additional $5,211 in savings relative to late discontinuation. Index through follow-up costs were equivalent among discontinuers vs. continuers due to the upfront pump insertion cost incurred in each group. When considering the mean IDDS insertion cost ($17,986) relative to post-washout follow-up savings associated with opioid discontinuation anytime (early or late), financial break-even would occur at 19.4 months; whereas break-even would occur at 13.2 months among patients discontinuing early.



Discussion: Results from this study suggest that not only is opioid discontinuation associated with meaningful costs savings in opioid prescriptions, but additionally in medical visits and other pharmacy costs. Early discontinuation is associated with even greater savings.

Conclusions: This study shows a cost savings associated with systemic opioid therapy elimination following initiation of IDDS. There remains opportunity to assist more patients in earlier and complete elimination of opioid therapy following IDDS.

Objectives

Summarize the proportion of patients discontinuing systemic opioids following start of IDD.

Evaluate costs associated with opioid discontinuation after IDD implant.

Assess the incremental financial impact of early vs later opioid discontinuation.

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Poster Presentations - May 27 - May 30
Spine - Pain

341. INS19-0292

THE EFFECT OF SPINAL CORD STIMULATION INTENSITY ON SOMATOSENSORY PROCESSING OF TACTILE STIMULI IN NEUROPATHIC PAIN

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Introduction: Spinal cord stimulation (SCS) is an effective treatment for intractable neuropathic pain. One mechanism underlying its therapeutic effects may be the inhibition of somatosensory processing. However, little is known of how SCS intensity modulates these effects. We sought to investigate the influence of modulating SCS intensity on neural responses to tactile stimuli in neuropathic pain.

Materials/Methods: Patients using SCS for neuropathic leg pain were recruited. They completed questionnaires assessing treatment response and pain intensity, and underwent electroencephalography (EEG) during 4 blocks of brushing on a pain-free leg. Blocks were ordered pseudo-randomly and modulated by SCS intensity: 'Therapeutic' (100%), 'Moderate' (66%), 'Low' (33%) and 'Off'. Changes in spectral power during brushing versus rest were calculated for each block. EEG data were processed in EEGLAB and FieldTrip. At this preliminary stage, group-level statistical analyses were not performed.

Results: Local ethical approval was obtained prior to study commencement. Twelve participants (5 female, 7 male) have completed the study to date. One participant was excluded due to incomplete data. SCS duration ranged from 1 month to 4 years (M = 22 months, SD = 20 months). Nine patients reported an improvement in pain symptoms from SCS. All patients showed a modulation of cortical oscillations during brushing as a result of SCS intensity. Visual inspection of topographic maps suggested a nonlinear trend, with the most pronounced change in power amplitude in 8-12 Hz and 16-24 Hz bands at moderate SCS intensities.

Discussion: Our preliminary findings suggest that SCS intensity has a graded, non-linear effect on cortical processing of innocuous somatosensory stimuli. This has implications for the method by which stimulation intensity is determined, particularly for paraesthesia-free stimulation which does not depend on perceived comfort. Further analysis upon completion of data collection will explore whether different stimulation patterns (i.e. traditional tonic or paraesthesia-free) have a divergent effect on somatosensory processing and will seek to identify the estimated sources of these effects.

Conclusions: The intensity of SCS may influence its effects on somatosensory processing. This has potential clinical applications to use EEG as an objective method to define the most effective parameters to relieve neuropathic pain.

Objectives

Demonstrate the effect of modulating SCS intensity on somatosensory processing of innocuous stimuli. Compare alternative stimulation patterns of SCS (i.e. traditional tonic or paraesthesia free) with regards to their impact on somatosensory processing and mechanisms of action. Identify the potential clinical implications of an objective tool to define effective parameters for SCS.

References

None.

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Spine - Pain

342. INS19-0172

A CASE OF ABDOMINAL PAIN AND ILEUS FOLLOWING SPINAL CORD STIMULATOR IMPLANTATION

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Introduction: Spinal cord stimulation (SCS) is a safe, reversible surgical treatment for chronic pain syndrome refractory to conventional therapy. Paddle lead are routinely used for the permanent implant because of the reduced risk of migration, lower energy requirements, and expanded coverage options. We report a patient with abdominal pain and ileus after undergoing spinal cord stimulator paddle lead placement.

Materials/Methods: The patient is a 71 year old female who presented with a history of multiple spinal surgery due to lumbar spinal stenosis. Though surgical intervention for lumbar spinal stenosis, she developed ongoing severe low back pain and left leg pain. She subsequently underwent a successful percutaneous SCS trial with greater than 50% relief of pain. The patient then had placement of paddle lead at levels T9-10 using tubular retractor under general anesthesia.

Results: In the immediate postoperative period, she complained of severe abdominal pain. She underwent full gastrointestinal, cardiac, and pulmonary workups, and no etiology was discovered. Immediately, she underwent removal of the paddle lead, with resolution of the abdominal pain. Post-operative day 2, the patient developed ileus. Ileus were transient and improved over the next two weeks.

Discussion: There are a few case studies that have described abdominal pain and ileus after spinal cord stimulator placement. The lateral placement of paddle leads can predispose patients to post-operative thoracic radiculopathy. Lateral placement of paddle leads should be avoided to prevent this problem. If there is spinal canal stenosis, performing a laminectomy can provide more space for safe electrode introduction.

Conclusions: Although a rare phenomenon, it is important to know that abdominal pain and ileus can be a result of thoracic radiculopathy or spinal cord injury during SCS lead placement.

Objectives

SCS complication

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Spine - Pain

343. INS19-0171

BURST SCS: HUMAN MECHANISTIC AND CLINICAL OUTCOMES

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Introduction: Burst spinal cord stimulation (SCS) utilizes a patterned stimulation paradigm that impacts neural function differently than other SCS stimulation approaches. Emerging human clinical evidence is demonstrating not only improved clinical outcomes but also mechanisms potentially underlying the unique characteristics of this approach to SCS.

Materials/Methods: A critical analysis of research restricted to human species (MedLine, EMBASE, Google Scholar) was conducted to provide an overview of both clinical outcomes from the highest levels of published evidence as well as basic research findings. To this end, the analysis is restricted to integrate human research findings both from a translational perspective.

Results: Burst spinal cord stimulation demonstrates greater pain relief over tonic stimulation in multiple studies in including blinded, sham-controlled, randomized trials. Burst stimulation can impact multiple dimensions of pain including both somatic pain as well as affective elements. Patient preference is weighted towards Burst over tonic due to the lack of paresthesias, increased pain relief and impression of change in condition. Human research has also confirmed that Burst SCS affects CNS sensory processing differently than other forms of SCS. This suggests that not only are the mechanisms underlying Burst SCS different but the Burst signature may play an important role in the evoked physiologic response.

Discussion: Burst stimulation has been shown to be statistically and clinically superior to tonic spinal cord stimulation, and may provide additional benefits through different mechanisms of action. Multiple RCTs, including the use of sham/placebo controls, have been published utilizing Burst SCS. These studies demonstrate that Burst SCS evokes significant, paresthesia-free pain relief that is superior to both placebo and tonic SCS. Basic human physiologic research also has demonstrated that Burst SCS evokes differential processing of sensory information which is consistent with the work published in non-human species as well. Further, high-quality controlled studies are warranted to elucidate not only basic mechanisms of burst SCS but also how this stimulation signature and pattern may more adequately address multiple affective dimensions of pain in varying patient populations.

Objectives

1. Audience will understand the clinical outcomes for Burst SCS reported in the literature.
2. Participants will understand other potential clinical benefits of Burst SCS outside of pain relief.
3. Audience members will understand the potential advantages Burst provides compared to tonic SCS.

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Spine - Pain

344. INS19-0244

BURST(ABLE) - A RETROSPECTIVE, MULTICENTER STUDY EXAMINING THE IMPACT OF BURST ON PAIN AND OPIOID CONSUMPTION IN THE SETTING OF SALVAGE TREATMENT AND "UPGRADE"

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Introduction: Loss of efficacy (LOE) is a well-known phenomenon associated with dorsal column spinal cord stimulation (DC-SCS), and is the leading cause of explant. Traditionally, there have been limited options to curb/reverse LOE as DC-SCS devices were typically restricted to tonic stimulation and its derivatives. Recent advances (i.e. high frequency and novel pulse trains) have decreased the incidence of LOE due to superiority of tonic therapy – LOE does still occur, albeit with less frequency. With the number of alternatives currently available, logic suggests that when LOE occurs to simply switch to a different therapy – however there is no data available to show efficacy. We present multicenter, retrospective study on patients who were switched to Burst as defined by De Ridder either as a "salvage" technique in the setting of LOE or in an attempt to "upgrade" an already successful SCS.

Materials/Methods: 307 patients with DC-SCS currently implanted from 7 independent pain practices were reviewed. All patients had their therapy switched to De-Ridder-Burst either through surgical revision (DR-S) whereby their current generator (IPG) was swapped for one that was capable of the burst waveform as defined by DeRidder, or in those cases where their current system was already Burst-DR capable and was simply activated (DR-ON). Some patients were failing their current device/therapy and the switch was made in attempt to "salvage" or restore their pain relief. Others were already succeeding with their DC-SCS and were switched in an attempt to "upgrade" their device for even more pain relief.

Results: The DR-S and DR-ON cohorts reported statistically significant reductions in NRS, percentage of pain relief and opioid consumption. Follow up extended out to 302.7 days post revision/upgrade in the DR-S cohort with 2.54 NRS reduction showing the improvement was sustainable. There was no statistical difference between the cohort that had their entire system replaced versus the cohort where adapters were used. When compared over time, DR-S reported larger reductions in pain/opioid consumption the earlier the revision was attempted. Subgroup analysis showed both DR-S and DR-ON restored treatment efficacy irrespective of time or the previous frequency/waveform.

Conclusions: LOE can be extremely destructive to a patient's physical and emotional well-being. Perhaps the most devastating consequence is relegating a patient back to a life of pain with no alternative but opioids. Our findings suggest that implementing Burst is a safe and effective option to treat LOE while reducing opioid medication needs regardless of the prior system.

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Spine - Pain

345. INS19-0248

DORSAL ROOT GANGLION (DRG) STIMULATION FOR CHRONIC PELVIC PAIN - A CASE SERIES

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Introduction: Chronic pelvic pain (CPP) is a complex neuropathic condition that is typically recalcitrant to most treatments, including spinal cord stimulation (SCS). Of all diagnoses for which SCS is used, CPP has the highest explant rate with the 2 more common reasons being inability to capture the affected area (pelvic/genital/perineal/anal) and unwanted paresthesias in unaffected areas. Contrary to SCS, dorsal root ganglion stimulation (DRGS) is able to provide predictable, targeted stimulation to focal areas of pain and does not rely on paresthesias to provide pain relief - thus rectifying the most common reasons for failure with SCS. We present 7 patients with intractable CPP, resistant to conventional treatment methods, all successfully treated with DRGS.

Materials/Methods: This case series includes 9 patients with severe, CPP (varying etiologies and locations of pain) that failed to respond to conservative and interventional pain treatments - in some cases SCS, as well. All 9 patients were successfully trialed > 5-days with DRGS using leads placed over the L1 and S2 DRG's (bilaterally in cases with bilateral CPP).

Results: All 9 patients had successful trials with DRGS (>50% pain reduction) and were subsequently implanted with the same L1/S2 arrays. Contrary to SCS, none of the patients reported loss of efficacy over time or unwanted paresthesias - to date none of the patients have been explanted. All patients reported significant pain relief, in some cases well over 1-year since the implant. The patients also reported reduction in opioid consumption as well as improvement in concomitant symptoms (i.e. sexual function, urination, and visceral sensations).

Conclusions: CPP is one of the most difficult pain conditions to treat. It is typically unresponsive to conservative and interventional treatments, alike, and is the highest rate of explant with SCS. Our case series demonstrates that the inability of SCS to adequately treat CPP has not been a failure of neuromodulation as whole, simply that stimulation of the dorsal columns is not the appropriate means of managing this particular syndrome. Additionally, not only does this case series demonstrate that DRGS is a potentially effective treatment for CPP, but that the targeting of the L1 and S2 levels would appear to the configuration of choice, regardless of differences in etiology or variations in the location of pain.

Objectives

1. Is DRGS an effective treatment for CPP?
2. Is L1/S2 an effective means for targeting the pelvic region?
3. Does DRGS rectify the deficiencies typically seen with SCS in the setting of CPP?

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346. INS19-0414

CAN MOTION SENSING NEUROSTIMULATORS BE USED TO ASSESS OBJECTIVE FUNCTIONAL OUTCOME OF SPINAL CORD STIMULATORS?

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Introduction: Spinal cord stimulators (SCS) have an established role for treatment of chronic neuropathic pain. There remains no objective marker for assessment of outcome of SCS. The new motion sensing stimulators have ability to capture the data of periods of activity and sleep for patients. We conducted a small study to determine if there is correlation between traditional recorded outcome of SCS and improvement of activity.

Materials/Methods: Total 20 patients who underwent spinal cord stimulator implant from November 2017 were included in the study. Indication for SCS was mainly failed back surgery syndrome (n=15) and Chronic regional pain syndrome (n=5). Baseline activity was recorded for one month when the stimulation was off. At 1st month follow up stimulator was switched on and activity recorded at 3 month (n=20) and 6 month (n=13) follow up. Pre and post implant VAS scores along with global perception of improvement was recorded for all patients.

Results: Out of the 20 patients, 19 patient activity data was available for assessment. The mean pain score VAS reduction was from 8.15 to 3.10 and mean global perception of improvement was 70.52%. Daily activity/mobility improved from 32.9 % baseline to 38.25% in 19 patients at 3 month follow up. At 6 months 13 patients showed sustained improvement of base line activity from 37.8 % to 41.07%. Statistical correlation of outcome was insignificant P Value- 0.2.

Discussion: Although spinal cord stimulators are beneficial for management of chronic pain, the exact evaluation of outcome remains uncertain due to subjective scoring of pain by patients. Various other co-factors, co morbidities influence the traditional outcome assessment. There remains no objective assessment to determine improvement of function achieved by pain relief.

Conclusions: In all our patients SCS was beneficial to reduce the pain scores. The global perception of pain relief perceived was around 70 % with good patient satisfaction. There was improvement noted in mobility/activity of patients recorded by motion sensor stimulator however it was too modest to be considered for using as a tool for outcome assessment of SCS.

Objectives

To determine whether motion sensing neuromodulation stimulator captured activity data can be used for assessment of SCS outcome.

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347. INS19-0411

NEUROSTIMULATION SURGERY IN THE TREATMENT OF POST-STROKE PAIN

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Introduction: The study is aimed to estimate the effectiveness of surgical neuromodulation methods in the treatment of patients with post-stroke pain syndrome.

The study is aimed to estimate the effectiveness of surgical neuromodulation methods in the treatment of patients with post-stroke pain syndrome.

Materials/Methods: Totally six patients with chronic post-stroke pain were included in the study. Gender profile was 5:1 (5 males and 1 female). Mean age was 64,3 y.o. (from 59 to 70 y.o.). Pain syndrome occurred after ischemic stroke in one patient and after hemorrhagic stroke in five patients. In four patients epidural electrodes were implanted on the motor cortex contralateral to the side of pain, Other two patients were implanted with epidural spinal electrodes at levels of cervical and lumbar intumescences (1 patient) and only lumbar intumescence (another 1 patient). We evaluated pain intensity (with 10-point visual analogue scale (VAS)) and quality of life due to pain (with modified form of Brief Pain Inventory) before surgery and in follow-up.

Results: All the patients with positive results of rTMS (with 50% and more pain relief), underwent implantation of electrodes for motor cortex stimulation. After implantation pain relief varied from 37,5% up to 90%. Statistically significant ($p<0,05$) improvement of daily activity, mood, general well-being, sleeping and self-care ability was achieved in all the patients. One patient developed purulent inflammation in subcutaneous pulse generator pocket and decubital ulcer over the place of connector implantation. Two patients underwent implantation of spinal epidural electrodes at the levels of cervical and lumbar intumescences. Basic pain intensity was 7 points by VAS with pain relief down to 4 points in the course of medical treatment. After implantation, pain relief was more than 50% (to 2 points by VAS).

Discussion: Neurostimulation can be a perspective method for pain treatment in patients with post-stroke pain.

Conclusions: Surgical neurostimulation may allow achieving stable pain relief.

Objectives

Further investigations are essential for more accurate evaluation of effectiveness for pain relief and safety.

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Spine - Pain

348. INS19-0413

SPINL CORD STIMULATION IN PATIENTS WITH SPINAL CORD INJURY

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Introduction: Spinal cord injury is one of the most significant public health issues in both developed and developing countries). Pain syndrome is common for these patients. Neuromodulation therapy is one of the most perspective methods in for pain treatment and rehabilitation.

Materials/Methods: We included 30 patients in our trial: 14 men and 16 women. All patients underwent implantation of spinal cord stimulation electrodes. The patients were evaluated using VAS, Ashworth scale and various neuropathic pain scales (DN4, Pain Detect, LANSS). The mean age of the patients was 32 years (from 17 to 63) and the mean disease duration was 8 years. The longest follow-up was 13 years (since 2005). Statistical analysis was performed using nonparametric methods (t-test, Wilcoxon test).

Results: 66,6% of the patients reported >50% reduction of pain during the trial period. 16,6% of the patients showed failed SCS trial). The average baseline VAS score was 9.78 points and decreased to 3.2 points. 16,6% of the patients showed failed SCS trial). The average baseline VAS score was 9.78 points and decreased to 3.2 points. Two patients demonstrated reduction of initial pain relief one year after surgery. The average Ashworth scale score decreased from 4,48 points to 2,1 points in a year ($p<0, 05$).

Discussion: In addition we found correlation between SCS efficacy and disease duration.

Conclusions: Spinal cord stimulation may be an effective method in the management of neuropathic pain syndromes but it requires careful patient selection.

Objectives

Further investigations are essential for more accurate evaluation of effectiveness for pain relief, indications, contraindications and safety.

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349. INS19-0404

PATIENT WITH FAILED BACK SURGERY SYNDROME AND INSTRUMENTED SPINE: IS INTRATHECAL DRUG DELIVERY SYSTEM A NON-INVASIVE THERAPY?

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Introduction: Neuro modulation technologies and techniques continue to evolve offering improved back pain management for patients with Failed Back Surgery Syndrome. Safety and efficacy of narcotics for treatment of nonmalignant pain, particularly chronic spinal pain, is a controversial topic. The Agency for Healthcare Research and Quality's Healthcare Cost and Usefulness Project reported up to a 40% increase in spinal fusions in the 7-year period from 1998 to 2004, and Deyo and colleagues reported that the rate of complex fusion procedures being performed for lumbar spinal stenosis increased 15-fold from 2002 to 2007. It has been reported, that spinal surgeries in the United States are at least 40% higher than any other country developed country.

Persistent or recurrent pain in the back/neck or limbs despite surgery or treatment to relieve pain has a failure rate as high as 20%.

It is our experience, that intrathecal therapy for pain and/or spasticity provides benefit for this particular patient population.

Materials/Methods: We did a retrospective chart review of FBSS instrumented patients, referred to us from other centers who failed their intrathecal therapy due to CSF leaks, catheters migrated and catheter infections during a 5 year period.

Results: Results: Patients charts were reviewed and compiled cause of failure of intrathecal therapy. All patients reported changes in NRS scores over time, with an initial decrease after implant, followed by a pre-revision increase. The most common reason for device revision was lack of, or complete loss of efficacy followed by complications such as infection that may require catheter and hardware removal, and CSF leaks. We will present our technique for open implantation vs. needle catheter placement to avoid complication related to complex spinal instrumented patients.

Discussion: Instrumented patient with failed back surgery syndrome represents a growing subgroup of patients.

Risks related to intrathecal drug delivery system are higher and are more likely to require an open technique.

Conclusions: IDDS is a viable option for instrumented patient with failed back surgery syndrome.

Objectives

1-recognize the augmentation of instrumented patients in the chronic pain population

2-identified and select the patient amenable to IDDS for pain relief

3-describe the different technique and the complications related to them

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350. INS19-0405

OPEN DORSAL ROOT GANGLION STIMULATION LEAD PLACEMENT: A TECHNICAL NOTE

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Introduction: Chronic neuropathic pain may be iatrogenic or post traumatic. Patients may have significant sleep disturbances, experience sociopsychological changes, along with significant physical limitations. A combination of pharmacological treatments along with physical therapy and nerve blocks may provide some pain relief.

In the following cases, the patient's pain remained chronic and intractable despite all interventional measures. Pre operatively, patients were screened for suitability for dorsal root ganglion stimulation.

Materials/Methods: We reviewed retrospectively 2 cases that required an open technique to place the DRG leads due to technical challenges placing them epidurally. We will discuss our technique for placement that may involve a foraminotomy along with a modified anchoring technique.

Results: Quality of life scores, VAS, and paresthesia mapping were recorded as baseline parameters, and further recorded post operatively to demonstrate pain improvement. Up to 4 percutaneous leads were placed epidurally at the dorsal root, but were removed during the trial, as they were unable to place them in the dorsal root due to foraminal stenosis, and epidural scaring. The patients were referred to our institution, at which time we opted for an open technique to place the leads.

Discussion: The open technique for DRG stimulation is a viable option for patient with chronic neuropathic pain, who are unable to have leads placed epidurally due complex pathology at the dorsal root foramen.

Conclusions: Patients amenable to DRG stimulation needs to have imaging allowing the surgeon to evaluate the need for an open technique.

Objectives

1-identify the patient that can benefit from DRG stimulation

2-define the anatomy that is likely to fail the percutaneous technique

3-describe the open technique to help patient amenable to DRG stimulation

References

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351. INS19-0400

BACK/ TRUNK PAIN CAN BE SUCCESSFULLY TREATED WITH PERIPHERAL NERVE FIELD STIMULATION

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Introduction: Back and trunk pain is a highly prevalent and disabling condition (1) that can be intractable to conventional medical management. Many patients are considered at this point for spinal cord stimulation (SCS), but some may not be appropriate candidates due to deformities of the spinal canal, extensive surgery preventing safe epidural access or scarring and adhesions in the epidural space. Here, we present a small cohort of such patients in which neuromodulation treatment was nevertheless achieved.

Materials/Methods: Six patients (4 men, 2 women) were evaluated for SCS for well-defined pain in the lower back and trunk. Ultimately, SCS did not proceed because extensive scarring related to multiple prior back surgeries made placement of epidural leads impossible. One patient had, in fact, previously failed an SCS trial. Instead, peripheral nerve stimulation (PNS) treatment was trialled. Pre-implant, the average pain was 7 on a standard 0-10 numeric rating scale, and all patients expressed pain-related impediments in function and quality of life.

Results: Patients were trialled with peripheral nerve stimulators with octad leads covering the most painful area. Stimulation was described to completely or adequately cover the painful regions. At the end of the trial, all the patients had successful trial with >50% improvement in pain and significant improvement in other parameters including mood, sleep, function and self-efficacy. All patients were satisfied with treatment and subsequently proceeded with permanent implant. One patient died due to causes unrelated to the pain or treatment.

Discussion: : These findings of PNS for chronic lower back pain are promising. Based on this, we recommend that a further multicentre trial be conducted for patients who are not suitable/high risk for SCS.

Conclusions: Subcutaneous peripheral nerve field stimulation has been reported to be an effective long-term treatment for chronic back pain (2), similar to our findings. PNS represents a minimally-invasive option that can be employed when traditional treatments cannot be employed. Future research should investigate the utility of this intervention.

Objectives

1. Back and trunk pain can be chronic and intractable.
2. SCS may be inappropriate in cases of extreme spinal scarring or deformity.
3. PNS represents another minimally-invasive option.

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352. INS19-0401

EFFECTIVE TREATMENT WITH BURST SCS IS INDEPENDENT OF PAIN-PARESTHESIA OVERLAP WITH TONIC PARAMETERS

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Introduction: Paraesthesia free sub-perception spinal cord stimulation (SCS) has emerged as a valuable new waveform for pain management. Despite its enthusiastic uptake, optimal programming protocols have not yet been developed. Conventional wisdom involves post-operative mapping of the leads with tonic stimulation, and based on the paraesthesia coverage achieved, selecting the ideal electrode configuration, frequency, pulse width and amplitude. Then, the electrode configuration is converted to the sub-perception parameters. Here, we present evidence to suggest that the mapping procedure may be unnecessary.

Materials/Methods: : Two women with post-laminectomy pain syndrome underwent SCS trials with bilateral octopolar leads. During the implantation procedure, leads were placed anatomically covering T7-10 in a staggered pattern. During post-operative programming, pain-paraesthesia overlap with perceptible tonic stimulation was tested for one patient; despite best attempts, the paraesthesia was perceived only in limited areas of pain. The other patient, due to a heightened emotional state, did not undergo tonic stimulation testing on the table. Both patients used BurstDR SCS with open bipoles for a two-week trial.

Results: Treatment reduced baseline pain from 8 (on a standard 0-10 numeric rating scale) to 2 for one patient and from 7 to 2 for the other. Both also reported improvements in function, mood, sleep and quality of life. Data for the first three months of treatment after implantation will be presented

Discussion: Post-operative mapping with tonic stimulation resulted in poor overlap in one case, and was not completed in a second case. Even so, excellent therapy with SCS was achieved in both cases. This suggests that the traditional model focusing on pain-paraesthesia overlap may not be necessary. Lead implantation by anatomic landmarks may be sufficient

Conclusions: Paraesthesia free Sub-perception spinal cord stimulation mimics the natural phasic patterns of activity in the brain, and impacts both the medial and lateral pain pathways (1, 2). The programming that delivers broad sub-perception coverage may be an effective treatment, even in the absence of conventional mapping procedures.

Objectives

Paraesthesias generated with tonic stimulation may or may not be useful indicators regarding the efficacy of SCS.

With Sub-perception SCS, anatomic landmarks may be sufficient to guide lead implantation.

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353. INS19-0402

RESOLUTION OF SEVERE POST-ELECTROCUTION NEUROPATHIC PAIN OF THE UPPER EXTREMITY WITH SPINAL CORD STIMULATION

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Introduction: Although severe accidental electrocution is often fatal, survivors may experience severe musculoskeletal injuries and chronic pain that may be refractory to conventional pain management interventions. Here, we present an unusual case that may establish a role for neuromodulation in treating this pain pathology.

Materials/Methods: A middle aged man sustained a high-voltage electrocution while working on his farm. His acute injuries resolved within weeks, but intense chronic neuropathic pain emerged in his neck and right upper limb. Prior to presenting to our clinic, the patient had tried many therapies including pharmacotherapy and exercise without meaningful improvement. He rated his pain as 8 on a standard 0-10 numeric rating scale and indicated that it nearly completely interfered with his ability to work, as well as his sleep, mood and quality of life. After failure of extensive cognitive rehabilitation, he was found suitable for trial of spinal cord stimulation (SCS).

Results: A two-week trial of cervical SCS was completed using two octad leads placed in the dorsal epidural space from C2-6 and using Paraesthesia free sub-perception stimulation. Pain relief of better than 50% was achieved. The patient also had significant improvement in sleep and mood along with functional improvement. With the stimulator off after the trial, the pain returned to its pre-stimulation levels. The patient had a successful permanent implant which is giving him an excellent relief of neuropathic pain.

Discussion: The published literature contains anecdotal reports of the development of chronic pain following electrocution trauma, all emphasizing its disabling and tenacious nature (1, 2, 3). As with most unusual conditions, optimal treatment algorithms for this type of pain etiology do not exist. In our experience, SCS is a reasonable option.

Conclusions: SCS can provide minimally invasive and reversible pain relief. Additionally, it is a drug-free option and may allow weaning of stronger analgesics, thus improving quality of life. Although more research is needed, SCS should be considered in post-electrocution neuropathic conditions.

Objectives

Neuropathic pain can develop after severe electrocution.

We describe successful early treatment of such a condition with SCS.

SCS should be considered in similar cases.

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354. INS19-0101

CASE-SERIES ASSESSMENT IN EUROPE OF A NEW PERCUTANEOUS SCS LEAD FOR MULTI-SITE AND/OR EVOLUTIVE PAIN PATTERNS

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Introduction: Advancements in Spinal Cord Stimulation (SCS) lead designs, when used in combination with new neural targeting technologies, are thought to be capable of supporting improved outcomes with SCS, including in patients with multi-site and/or evolutive (or changing) pain patterns over time. In this study, SCS clinical outcomes are assessed in chronic pain patients using a newly available lead with increased span and minimal spacing between electrodes (versus other traditional linear designs).

Materials/Methods: This is a multicenter, observational clinical study utilizing retrospective chart reviews at selected sites in Europe. We examined a series of chronic pain patients using a 16-contact lead designed for coverage of up to 3 vertebral levels with a 67 mm active span and 1 mm electrode spacing (Infinion CX, Boston Scientific). All patients were treated per standard of care and implanted with SCS devices (Boston Scientific) using neural targeting algorithms and capable of multiple stimulation waveforms.

Results: To date, data analyzed in 15 patients demonstrates a 68% improvement (change in NRS from baseline = 5.7 $\pm$ 1.7) in overall pain as reported at last follow up (mean 4.2 $\pm$ 5.7 months; $p < 0.0001$). Additionally, a high responder rate (≥50% improvement in overall pain scores) was reported post-trial and at last follow up. Eighty-seven percent of all patients (13 of 15) reported a pain score of 3 or less at last follow-up (baseline mean NRS = 8.3).

Discussion: These early results from this ongoing, multicenter, real-world cohort demonstrate significant improvement in overall pain with the use of recently introduced SCS system with new leads capable of addressing multisite pain and/or changing pain locations.

Conclusions: New lead designs offering greater adaptability may be important in reducing treatment failures and enhancing more personalized SCS treatment approaches. A 16-electrode lead with minimal contact spacing and longer vertebral span coverage represents another potential tool in the drive to achieve better and sustained SCS patient outcomes.

Objectives

To collect baseline demographics, pain score outcomes, and percent pain relief data in patients using a recently introduced SCS system with new leads capable of addressing multisite pain and/or changing pain locations.

References

NA

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355. INS19-0103

TARGETED NEUROSTIMULATION IN PATIENTS REPORTING CHRONIC FOCAL PAIN IMPLANTED WITH A SPINAL CORD STIMULATION SYSTEM CAPABLE OF MULTIPLE WAVEFORM PROGRAMMING OPTIONS

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Introduction: Recent studies evaluating Dorsal Root Ganglion (DRG) stimulation for focal pain report encouraging results (1); however, a high incidence of associated adverse events has been documented (2,3). Spinal Cord Stimulation (SCS) is thought to be a viable alternative as programming SCS to deliver stimulation to dorsal nerve roots has been reported to successfully treat focal pain (4). In this preliminary investigation, we report initial experience using SCS with precise neural targeting technology and sub-perception modalities to treat patients with focal pain.

Materials/Methods: This is an ongoing multicenter, consecutive, observational, case-series examination of patients reporting chronic focal pain implanted with a multiple waveform SCS system (Precision, Montage and Novi, Boston Scientific) with following capabilities: Multiple Independent Current Control (MICC), Anatomically-Guided (3D) Neural Targeting (3DNT, Precision Spectra only) and multiple available stimulation waveforms (including sub-perception programming). Pain relief outcomes (NRS) are being collected and analyzed at baseline and follow up.

Results: To date, 10 patients diagnosed with Complex Regional Pain Syndrome or other types of focal pain (e.g. Hernia, Neuropathy, DPN, etc) who were implanted with a multiple waveform SCS system for ankle, foot and/or upper limb pain have been assessed. Mean baseline NRS score was determined to be 8.5 (SD=1.2), and mean last follow up duration was 10 months (SD=5.3). A statistically significant improvement in mean overall pain was reported at last follow-up as indicated by a 47% reduction in NRS score (NRS = 4.5; $p < 0.001$) versus baseline. Additional data will be reported.

Discussion: This preliminary study reports initial findings investigating relief of chronic focal pain with a system capable of providing precise neural targeting capabilities and multiple waveform options, including sub-perception stimulation. This approach may therefore represent a viable alternative with reduced adverse effects.

Conclusions: This work will help support the study of Spinal Cord Stimulation using multiple programming options and neural targeting in patients suffering with chronic focal pain. Further follow up and analysis is planned.

Objectives

To report initial findings (demographics, pain scores, percept pain relief) investigating reduction of chronic focal pain with a system capable of providing precise neural targeting capabilities and multiple waveform options, including sub-perception stimulation.

References

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356. INS19-0168

OUTCOMES OF A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL UTILIZING A SPINAL CORD STIMULATION SYSTEM CAPABLE OF MULTIPLE NEUROSTIMULATION MODALITIES (COMBO STUDY)

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Introduction: Spinal Cord Stimulation (SCS) devices that enable personalized fine-tuning of stimulation parameters or waveforms offer the potential to address the variability among chronic pain patients. We endeavored to clinically investigate this system by evaluating the outcomes associated with use of multiple neurostimulation modalities as compared with conventional SCS settings alone in a prospective, randomized controlled trial.

Materials/Methods: COMBO is a prospective, multicenter, randomized controlled trial (RCT) with an adaptive design (Clinicaltrials.gov identifier: NCT03689920). The primary endpoint of the study is based on the proportion of subjects, permanently implanted with an SCS system capable of multiple neurostimulation modalities (Spectra WaveWriter, Boston Scientific), demonstrating ≥50% reduction from Baseline in average overall pain intensity at 3-month follow up. Additional endpoints will assess quality of life, disability etc. Adverse events will also be collected.

Results: Real-world data utilizing the same SCS System demonstrated, in a cohort of 312 subjects, a statistically significant improvement in overall targeted pain scores (NRS) at last follow up (7.3 [baseline] to 2.1 [last follow-up with mean 106 days]). This improvement was also noted at 3 and 12 months follow-up ($p < 0.0001$). Data collection and analysis using the same SCS system in this RCT are ongoing at up to 15 centers. Preliminary analysis to be presented.

Discussion: Outcomes of a prospective, randomized controlled trial offer the opportunity to provide Level 1 evidence related to the use of an SCS system capable of multiple neurostimulation modalities in the treatment of chronic pain, while minimizing bias and confounding effects resulting from differences in patient selection, demographic variables, investigator technique and/or patient management.

Conclusions: The COMBO randomized controlled trial will evaluate the clinical effectiveness of multiple neurostimulation modalities of SCS (versus conventional SCS settings) used in treatment of chronic pain.

Objectives

1. To evaluate pain intensity using a SCS system capable of delivering multiple neurostimulation modalities.

2. To evaluate patient quality of life as part of a randomized controlled trial assessing outcomes associated with individualized utilization of multiple neurostimulative modality options.

3. To evaluate patient satisfaction as part of a randomized controlled trial assessing outcomes associated with individualized utilization of multiple neurostimulative modality options.

References

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357. INS19-0169

EARLY CLINICAL EXPERIENCE USING A SPINAL CORD STIMULATION DEVICE CAPABLE OF MULTIPLE WAVEFORMS AND FIELD SHAPES FOR CHRONIC FOCAL LOWER LIMB PAIN

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Introduction: The effectiveness of neurostimulation for treatment of chronic pain is well established. Data on chronic focal pain relief is limited but has been reported using Dorsal Root Ganglion (DRG) stimulation.[1] However, a high incidence of adverse events associated with this technique has been documented.[2-4] Here, we present our early clinical experience using multiple waveforms as an alternative method for treatment of focal lower limb pain.

Materials/Methods: This is a retrospective, case-series evaluating patients with chronic focal lower limb pain, some of whom previously failed DRG stimulation. Patients were implanted with a neurostimulator capable of multiple field shapes and waveforms at variable amplitude, pulse width, and frequency (Precision Spectra WaveWriter, Boston Scientific).

Results: Recent reports using SCS to target focal pain, using leads placed through the sacral hiatus (L5/S1) reported a 6.3-point reduction in NRS ($p<0.0001$) was reported at last follow-up (mean =315.6 days) in a cohort of 9 patients. Outcome measures from our early clinical experience using standard SCS techniques for focal pain will be presented.

Discussion: Advancements in waveforms add to treatment options available for patients with focal lower limb pain, and the sub-group of patients who do not respond to DRG stimulation. Additionally, DRG stimulation may be associated with further risks in addition to a more complex procedure.

Conclusions: This small case-series demonstrates that neurostimulation using advanced waveforms is a viable option to treat focal lower limb pain. Additional, larger studies are warranted to further evaluate efficacy in this patient population.

Objectives

1. To assess focal pain outcomes in patients using an SCS system capable of multiple waveforms/field shapes.
2. To describe programming parameters in patients using an SCS system capable of multiple waveforms/field shapes.
3. To describe baseline characteristics of patients in this study who used an SCS system capable of multiple waveforms/field shapes.

References

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358. INS19-0194

TWO-YEAR FOLLOW-UP OF A CUSTOMIZED FIELD SHAPE USING SUB-PERCEPTION SPINAL CORD STIMULATION IN A REAL-WORLD, OBSERVATIONAL COHORT OF CHRONIC PAIN PATIENTS

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Introduction: Recently published data suggests that substantial pain relief can be achieved using sub-perception Spinal Cord Stimulation (SCS) within a wide range of frequencies and pulse-widths (1). Contrary to traditional SCS which requires paresthesia mapping, sub-perception SCS can rely on an anatomically-guided bipolar search along the lead until the best patient-specific outcome is determined (2). Here, we present 2-year real-world outcomes utilizing a novel sub-perception based SCS algorithm for customizing field shape based on patient-specific anatomy and lead placement.

Materials/Methods: This is an observational study of permanently implanted patients (up to N=15) assessed at a single center as part of an ongoing retrospective chart review of SCS outcomes for chronic pain (Clinicaltrials.gov identifier: NCT01550575). A customized field shape (CFS) algorithm was designed to engage anti-nociceptive terminals over a broader coverage area than a traditional 8 mm bipole. This algorithm delivers precise amounts of current through multiple independently-controlled contacts calibrated to each patient's unique anatomy and lead placement. A "sweet-spot search" was performed with CFS programs spanning vertebral levels T8-T10. At follow-up visits, patients were asked to score their pain intensity (NRS) when using a set of predefined CFS programs. Patients were assessed for the duration of time they were able to sit, stand and walk without unbearable pain. Additionally, duration of time (days) between charging sessions was calculated for each patient's preferred program.

Results: Preliminary results (n = 15) reported that pain was reduced on average by 68% (NRS = 2.7, Δ = 5.8) at six months, and by 72% at 1 year (NRS = 2.4, Δ = 6.1) (4). Longer term data for this cohort is ongoing. Final results will be presented.

Discussion: A customized field shape algorithm using sub-perception SCS programming is capable of providing effective pain relief, substantial improvement in functional mobility, and reduced patient charging.

Conclusions: Precise customization of stimulation field shape for each patient can facilitate long-term sub-perception pain relief while reducing patient charge burden.

Objectives

1. To assess sub-perception SCS pain relief utilizing a customized field shape algorithm.
2. To assess functional mobility utilizing a customized field shape algorithm.
3. To assess charging burden utilizing a customized field shape algorithm.

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359. INS19-0337

CLINICAL OUTCOMES IN PATIENTS USING A SPINAL CORD STIMULATION SYSTEM WITH MULTIPLE NEUROSTIMULATIVE MODALITIES FOR CHRONIC PAIN: INITIAL REAL-WORLD EXPERIENCE FROM EUROPE

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Introduction: Spinal cord stimulation (SCS) systems equipped with several available modalities of neurostimulation such as multiple advanced waveforms, customized field shape programming, and simultaneous or sequential pulse trains are designed to provide for robust customization of treatment for chronic pain using SCS. This capability is particularly relevant given the dynamic nature of chronic pain. Recent real-world observational data reported a mean 5.2-point reduction ($p < 0.0001$) in a cohort of over 200 subjects at their last follow-up (mean 3-months.) utilizing a recently launched SCS system (1). In this report, we describe our collection and analysis of clinical outcomes in patients implanted with an SCS system capable of delivering multiple modalities and/or waveforms.

Materials/Methods: This is an observational case-series of up to 35 patients conducted in Europe as part of an ongoing retrospective chart review evaluation of SCS outcomes for chronic pain (Clinicaltrials.gov identifier: NCT01550575). Patients were implanted with an SCS system (Precision Spectra WaveWriter, Boston Scientific) capable of combination therapy (either sequential or simultaneous), multiple waveforms and advanced field shapes, and waveform automation for treatment of low back and/or leg pain. Assessments collected include (but not limited to) baseline characteristics (demographics, medical history, pain diagnosis), procedural information (lead configuration, programming parameters), and pre- and post-implant pain and quality-of-life scores.

Results: To date, data analysis is currently ongoing. Results from the initial cohort of included patients will be presented.

Discussion: Evaluation of novel systems engineered with new technology designed to foster more personalized treatment approaches for chronic pain using SCS is key to establishing best treatment options. Real-world evidence studies are thus important to establish how these devices are utilized clinically and the outcomes associated with their use.

Conclusions: This European-based, observational case-series evaluation seeks to assess the real-world clinical outcomes of patients implanted with an SCS device capable of providing multiple neurostimulation modalities for use in the treatment of chronic pain.

Objectives

1. To report pain relief scores (NRS) in patients implanted with an SCS device capable of multiple neurostimulative modality options for use in treatment of chronic pain.
2. To report the use of various programming/modality options from patients implanted with an SCS device capable of multiple neurostimulative modality options for use in treatment of chronic pain.
3. To report baseline characteristics of patients implanted with an SCS device capable of multiple neurostimulative modality options for use in treatment of chronic pain.

References

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360. INS19-0113

TREATMENT OF CHRONIC ABDOMINAL PAIN WITH 10 KHZ SCS: EFFICACY RESULTS FROM A 12-MONTH PROSPECTIVE, MULTICENTER, FEASIBILITY STUDY IN PATIENTS WITH DIVERSE PAIN ETIOLOGIES

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Table 1

	Baseline mean (95% CI)	3 Month mean (95% CI)	12 Month mean (95% CI)	p value†
	n=24	n=22*	n=12**	
VAS (cm)	8.3 (7.4 - 9.1)	2.2 (1.3 - 3.1)	2.6 (1.4 - 3.8)	p<0.001
PDI	48.0 (41.8 - 54.2)	21.9 (15.5 - 28.4)	22.4 (13.8 - 31.0)	p<0.001
GAF	45.4 (38.8 - 51.9)	78.1 (71.2 - 85.0)	87.5 (78.4 - 96.6)	p<0.001
PGIC	% "Better" to a "Great Deal Better"	89.5 (66.9 - 98.7)	91.7 (61.5 -99.8)	
CGIC	% "Better" to a "Great Deal Better"	90.5 (69.2 - 98.8)	91.7 (61.5 -99.8)	
Satisfaction	% Satisfied or Very Satisfied	90.5 (69.2 - 98.8)	91.7(61.5 -99.8)	

*1 trial failure and 1 explant due to infection
** 58% reporting, expected completion December 2018
† one way ANOVA showed significant difference between baseline and 3 and 12M

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Introduction: Chronic abdominal pain (CAP) is a huge burden to our health care system, with the CDC reporting that the top reason for emergency room visits is abdominal pain (1, 2). The proportion that is refractory to pharmacological interventions, minimally invasive techniques, and surgical intervention is high, presenting a large unmet need. Published case series have shown SCS can be effective in treatment of CAP (3), but this is the first prospective multicenter trial to investigate this new indication for SCS.

Materials/Methods: Following Institutional Review Board approval, 24 subjects were enrolled and underwent temporary trial. The primary inclusion was abdominal pain that is refractory to conventional treatments, and exclusions included inflammatory and neurological diseases. Safety was assessed by neurological status and adverse events. Efficacy assessments included pain (visual analog scale [VAS]) (with ≥50% reduction considered a treatment success), disability, global assessment of functioning (GAF), global impression of change by both subject (PGIC) and clinician (CGIC), and satisfaction.

Results: Twenty-four CAP patients were enrolled and underwent temporary trial with 10 kHz SCS (19 female, 45±16 years). The main pain etiologies were gastroparesis/dysmotility (n=14), chronic post-surgical pain (n=9), chronic pancreatitis (n=5), abdominal wall pain (n=2). Percent Pain relief achieved in trial averaged 84% (95%CI 78-89). 23/24 (96%) subjects who underwent trial stimulation achieved ≥50% pain relief and were implanted. Two participants underwent an explant due to infection; one IPG was replaced. Responder rate (per protocol) was 82% (18/22) (95%CI 60-95) and 75% (9/12) (95%CI 43-95) at our complete 3 month and incomplete 12 month endpoints, respectively. All efficacy outcomes showed significant improvement at the 3 month endpoint, 73%, 54%, and 72% for VAS, PDI and GAF respectively (Table 1), with evidence of stable improvement to 12 months. In addition, the vast majority of subjects (>89%) self-reported to be "Better" to "A great deal better" and "Satisfied" or "Very Satisfied" at 3 and 12 months, and this was consistent with clinician reporting.

Discussion: Efficacy and patient satisfaction are comparable to findings from previous studies in chronic back and leg pain patients.

Conclusions: The results of this feasibility study show potential for good clinical efficacy in the treatment of chronic abdominal pain with multiple etiologies.

Objectives

To investigate the efficacy of 10 kHz SCS in patients with chronic abdominal pain.

References

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Poster Presentations - May 27 - May 30
Spine - Pain

361. INS19-0118

EFFECTS OF SPINAL CORD STIMULATION ON CHRONIC REFRACTORY PAINFUL GASTROPARESIS: A RETROSPECTIVE CASE SERIES ANALYSIS

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Introduction: There is mounting evidence supporting the therapeutic effect of spinal cord stimulation (SCS) in chronic abdominal pain (CAP), including some limited cases of refractory painful gastroparesis (1,2). This group represents a substantial portion of CAP sufferers, and one with few clinical options. We present a retrospective analysis of a consecutive case series of patients with a primary gastroparesis diagnosis who were trialed with SCS.

Materials/Methods: Electronic chart review found 26 consecutive patients (20 women and 6 men, average age 48 years) who underwent SCS trial for primary diagnosis of gastroparesis at our center. Data on pain scores, nausea, vomiting, utilization of opioids and patient satisfaction were extracted at baseline, close to 6 months after implant, and at the most recent long-term follow-up visit. Patients were separated into two groups based on the type of SCS, low frequency (Trad-SCS) and 10 kHz SCS, and outcomes were compared.

Results: Twenty-three of the 26 patients received >50% of pain relief during the trial, underwent SCS implant, and were followed for a mean of 41 months (range: 22-62 months post-implant). There were no infections or lead migrations. A significant reduction in pain, opioid use, and nausea/vomiting frequency were observed (Table 1). Patients also reported high levels of satisfaction. When queried, majority of the patients (20 or 87%) suggested that they will recommend the therapy to their friends. Comparing outcomes between subgroups, while the pain reduction was similar, the opioid use decrease was only significant for the 10kHz SCS group. In addition, days per month of nausea was significantly lower at follow-up in the 10KHz SCS group compared to Trad SCS.

Discussion: Profound improvements in pain scores, and reduction in frequency of nausea and vomiting were recorded in this retrospective study. Further studies are needed to elucidate the mechanism for the gastrointestinal symptom improvement and confirm these results.

Conclusions: This case series supports the use of SCS as a long-term treatment of documented painful gastroparesis of various causes.

Table 1

	Baseline mean (95% CI)	6 Month mean (95% CI)	Last Follow-up mean (95% CI)	p value[†]
	n=23	n=23	n=23	
VAS (cm)	8.7 (8.1 – 9.2)	3.3 (2.1 – 4.6)	3.2 (1.9 – 4.4)	p<0.001
MSO4 Equiv.	57.7 (34.3 – 81.0)	24.3 (8.9 – 39.7)	28.0 (12.3 – 43.8)	p=0.01
Nausea *	26.3 (22.3 – 30.3)	12.8 (7.3 – 18.3)	11.7 (6.4 – 17.1)	p<0.001
Vomiting*	52.4 (21.2 – 83.7)	23.2 (1.4 – 44.9)	20.3 (2.1 – 38.5)	p = 0.02

[†]paired t-test between baseline and Last Follow-up
*Frequency in units of events per month

Objectives

1. Present long term results of spinal cord stimulation in painful gastroparesis
2. Analyze both pain and nausea/vomiting outcomes
3. Compare outcomes with 10kHz to traditional SCS

References

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Spine - Pain

362. INS19-0263

OPTIMIZATION TECHNIQUES FOR HIGH FREQUENCY 10 KHZ SPINAL CORD STIMULATION MAINTAIN LONG-TERM OUTCOMES: RETROSPECTIVE ANALYSIS OF A RANDOMIZED CONTROLLED TRIAL

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Introduction: Candidates for spinal cord stimulation (SCS) typically undergo a 7-day trial of stimulation to determine if a permanently implanted pulse generator (IPG) is warranted to relieve their chronic intractable pain. Trial responses to low-frequency, paresthesia-based SCS (LF-SCS), however, have not historically been predictive of long-term outcomes. Historical studies have shown that, of LF-SCS patients who pass a 50% pain relief trial standard, 26% never achieve 50% relief with an IPG, and 13% report no relief with an IPG. High frequency 10kHzSCS has been shown to have better long-term maintenance of initial efficacy. In a retrospective analysis of randomized controlled trial data, we compared the ability of 10kHzSCS to sustain "excellent" trial responses over LF-SCS.

Materials/Methods: A total of 198 subjects with both back and leg pain were randomized in a 1:1 ratio to a treatment group across 10 comprehensive pain treatment centers. Of these, 171 passed a temporary trial and were implanted with an SCS system: 81 receiving LF-SCS and 90 receiving 10kHzSCS. An 'excellent' outcome was defined as a subject achieving at least 75% back pain relief. We analyzed how well these initially-excellent trial responses were maintained at 1- and 12-months post-implant. Programming in each arm of the study was optimized by the respective experts in applying the full range of each device's capabilities.

Results: The average percent pain relief (PPR) at end-of-trial was 69% for LF-SCS and 76% for 10kHzSCS. Twenty-one (27%) of LF-SCS subjects and 40 (45%) of 10kHzSCS subjects achieved an initially-excellent outcome of ≥75% back pain relief. At 1-month post-permanent implant, 29% of initially-excellent LF-SCS trial responders and 25% of initially-excellent 10kHzSCS trial responders saw a reduction in their back pain relief (30%-60% PPR). By 12 months, using a variety of therapy optimization techniques, 80% of initially-excellent 10kHzSCS responders had returned to excellent back pain relief, in contrast to only 17% of initially-excellent LF-SCS subjects.

Discussion: Reduction of pain relief after receiving an IPG has historically been a common LF-SCS phenomenon, and contributes to the poor predictive value of the LF-SCS trial.

Conclusions: We observed that initially-excellent 10kHzSCS trial results could be maintained over the long-term, at a four-fold rate versus LF-SCS. Post-IPG therapy optimization techniques such as target-optimization, pulse-dosing, multi-area pain sequencing, and bipole-interlacing allowed for individual customization of 10kHz therapy to each subject's needs.

Objectives (Please provide three educational objectives)
Understand:
-long-term outcomes of different strategies of SCS,
-ability of 10kHzSCS optimizations to maintain outcomes
-variance of outcomes in the post-implant period for SCS

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363. INS19-0242

EPIDURAL GRANULOMA AFTER INTRATHECAL PUMP IMPLANTATION IN SPINAL CORD

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Introduction: Since the 1990s, the procedures for insertion of an intrathcal delivery device have been performed on patients with cancer pain, intractable nonmalignant pain syndrome (1).

The procedure-related complications include meningitis, infection, migration, granulation formation. In this case, we report the case that the catheter was migrated to the epidural space and the granulation formation (2).

Materials/Methods: CASE REPORT

Results: A 55-year-old man with no specific medical history experienced pain in his neck and arm due to a motorcycle traffic accident. He underwent anterior interbody fusion, as well as cervical and cage insertion, under the diagnosis of central cord syndrome on MRI. In addition, MRI of the right knee was performed due to sustained knee pain 6 months after surgery, and menisectomy was performed as a result of medial meniscus posterior tear. However, even after surgery, systemic pain and edema were present, including left-sided foot and ankle pain. The patient was thus administered medication and neuroaxial block. However, intrathecal pump insertion was needed for persistent pain. The test was performed whether morphine was effective in reducing pain, and the catheter was inserted into L1-2 interlaminar space, without any specific side effects. The catheter advanced to T10 (Figure 1). 7.71 per day mg of morphine was injected through the pump. At 22 months after intrathecal pump insertion, the patient exhibited weakness in both lower legs. As time passed, walking became difficult, and the pain persisted continuously on the left side. Later, T-L spine CT was performed to identify granulomas with contrast media. A catheter-induced granuloma had developed in the 4.7-cm extradural layer and cord compression was suspected. Subsequent removal of the granuloma and intrathecal pump revision were performed (Figure 2). After the procedure, the patient's pain was reduced, and the patient was followed up by outpatient observation.

Discussion: same as Conclusions Conclusions Intrathecal delivery is useful for cancer pain or uncontrolled pain, but we should remain aware of the possibility of complications. When using drugs such as morphine or hydrophone sufentanil, the dose or concentration should be lowered, and patient symptoms should be checked frequently, to prevent sudden increase in pain or other neurologic symptoms. Finally, it is important to consider MRI, CT, or myelography (3).

Objectives

1. to report complication od intrathecal pump delivery device
2. note on confirming the above contents
3. effort to reduce complication

References

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364. INS19-0364

INCREASED RISK FOR PARESTHESIA AND LEAD MIGRATION IN TOBACCO SMOKERS PATIENTS WITH SPINAL CORD STIMULATORS

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Introduction: Spinal Cord Stimulator (SCS) therapy is used for varying types of chronic pain where conservative approaches have failed. Given the increasing attention regarding the safety and efficacy of these devices and their expanding range of clinical applications, more studies are needed to determine the viability of these devices in clinical practice. The purpose of this study is to further our prior investigations in determining the safety and the rate of the most common complications of SCS therapy considering Body Mass Index (BMI) and smoking status.

Materials/Methods: After Advocate IRB approval, a retrospective study of prospectively collected data of 106 SCS implants performed at the Advocate Illinois Masonic Medical Center over a two-year period was conducted. Safety and effectiveness of SCS treatment were analyzed according to smoking status and BMI classification. The SPSS 22.0 statistical software was used to analyze the collected data.

Results: The average age of included patients was 55.8 $\pm$ 13.8 years. There were 61 non-smokers, 30 current smokers, and 12 former smokers. All patients were followed up between 20 and 30 months (average 25.3). All patients had significant pain improvement ($p< 0.001$) compared to their baseline. The average pain score reduction using a Numerical Rating Scale (NRS) was 63.3%. There was no difference in the effectiveness of SCS regardless of the BMI and smoking status. In our study, we identified that 5.7% of the study participants developed superficial skin infections, 8.5% presented with lead migration, and 16% reported uncomfortable paresthesias and dysesthesias, while 3.8% reported a loss of effect. Thirty-four percent of the patients required SCS revision. Thirteen percent of the patients underwent explantation of the SCS with a significant correlation with tobacco use ($x2$ $p<0.001$). There was an increase in the frequency of uncomfortable paresthesias and dysesthesias in smokers ($x2$ $p=0.004$) and these patients were more likely to require revision of the SCS ($x2$ $p=0.03$). Uncomfortable paresthesias and explantations were less frequent in former smokers than in current smokers.

Discussion: There was no difference in complication rates in obese patients.

Conclusions: Results of our study show that tobacco smoking increases the risk of complications such as paresthesias and dysesthesias, leading to explantation and treatment failure. Furthermore, there was no increased risk of complications in obese patients.

Objectives

1. describe possible complications of spinal cord stimulators
2. list all risks of complications in tobacco smokers
3. list all possible complications in obese patients

References

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365. INS19-0365

CAN WE HAVE MORE USEFUL INFORMATION FROM MANDATORY PSYCHOLOGICAL TESTING PRIOR TO SPINAL CORD STIMULATOR IMPLANTATION

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Introduction: Chronic pain is extremely prevalent and creates a significant burden on healthcare costs. The ongoing opioid crisis has urged clinicians to seek new nonpharmacological treatments for pain. Neuromodulation via spinal cord stimulator (SCS) implantation has proven to be an effective and cost-efficient treatment modality providing exceptional pain relief for some patients. Psychological screening is currently a mandatory requirement by insurance companies prior to the procedure to identify any unstable psychiatric disorders. This study was conducted to assess the usefulness of psychological evaluation data in the prediction of SCS outcomes.

Materials/Methods: We obtained Advocate Healthcare Institutional Review Board approval to retrospectively collect and evaluate the data from patients who had permanent SCS implantation in our hospital. Psychological screening data were obtained from an electronic health record system or by contacting mental health providers. We selected only those that used one of the quantifiable tests Beck's Depression Inventory-2 (BDI-2), Minnesota Multiphasic Personality Inventory-2 (MMPI-2) and Battery for Health Improvement (BHI-2). The data were evaluated with SPSS software-version 25.

Results: Total study sample size included 105 patients (68 females), a mean age of 56.3 years (range: 29-88 years). Based on our criteria and availability of the psychological screening records, we were able to collect the following data: BDI-2 scores for 35 patients, MMPI-2 scores for 21 patients, and BHI-2 scores 17 patients. The rest of the assessing mental health professionals used other non-standardized tests. Based on BDI-2 scores we have grouped the patients in 4 groups: normal, mild mood disturbance, borderline depression, moderate depression. Early analysis showed a correlation between BDI-2 scores and pain difference between pre-procedural and 12 months follow up pain score, 0.44 ($p=0.046$).

Discussion: Currently, psychological screening is performed as one of the mandatory steps required by the insurance industry prior to performing SCS trials and permanent implantation. Early results of this study show some correlation between the psychological evaluation and pain outcomes. It is important to note that of the 105 subjects in this study, psychological evaluation data was accessible only for one-third of patients.

Conclusions: Preliminary results of the study indicate that psychological evaluation is considered to be promising in terms of SCS outcome prediction, however, this process lacks standardization and the data is not being used up to it's potential.

Objectives

1. describe the role of psychological testing prior to SCS
2. describe correlation between chronic pain and depression
3. list factors that might influence the effectiveness of SCS

References

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Poster Presentations - May 27 - May 30
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366. INS19-0430

INTRATHECAL OPIOID THERAPY DONE CORRECTLY - A CASE REPORT THAT MANIFESTS THE ESSENCE OF INTRATHECAL OPIOID TREATMENTS.

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Introduction: The intrathecal application of morphine has been established as the most effective way to treat chronic pain. The guidelines of the International Neuromodulation Society have helped to bring standards to the treatment. Nevertheless, if the basic principles are not followed, even such a potent treatment is bound to fail.

Materials/Methods: We report the case of a patient who developed complications after the implantation of an intrathecal pump system. X-ray and MRI investigations were performed. An MRI-compatible intrathecal morphine pump was implanted.

Results: A 61-year old woman with FBSS, VAS 8-9/10 since 2008, presented to our clinic. In 2010 an intrathecal catheter-pump system was implanted. The initial intrathecal morphine dose was 1mg/die. The pain was reduced to 5/10, though later the initial good effect faded and the MSI Dose was increased. In 2017 the patient developed a new neuropathic pain in the genital and perianal region. A MSI dose of 12mg/die and Pregabalin up to 300 mg/die didn't offer any pain relief. No MRI scan or other diagnostic was performed prior to her visit to our department. Our X-ray revealed a misplacement of the intrathecal catheter in the sacral region. MRI imaging of the lumbosacral spine revealed a granuloma located around the catheter tip with pressure on the sacral roots as the cause of the neuropathic pain. A new intrathecal catheter and a new constant flow pump with variable profile were implanted. The tip of the new intrathecal catheter was placed at T5. Part of the old intrathecal catheter was left due to the risk of injury to the sacral nerves. The intrathecal morphine dose was reduced to 1mg/die. Postoperatively the pain was reduced down to VAS 3/10. Pregabalin was gradually reduced and stopped. The MSI dose is still 1mg/dies.

Discussion: The intrathecal opioid therapy is still the most effective pain treatment in neuromodulation. When basic principles and guidelines are followed, pain relief can be achieved without an increased risk of a complication.

Conclusions: Placement of the intrathecal catheter is essential in the effectiveness of the treatment. The appearance of neuropathic symptoms should always alert us of the possibility of a granuloma.

Objectives

The intrathecal application of morphine is an effective way to treat refractory chronic pain. When therapy is performed according to the INS guidelines, the anticipated pain relief can be achieved without an increased risk of a complication. The appearance of neuropathic symptoms should always alert us of the possibility of a granuloma.

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367. INS19-0164

DORSAL ROOT GANGLION STIMULATION IN THE TREATMENT OF NEUROPATHIC PAIN AFTER PERIPHERAL NERVE INJURY OF UPPER AND LOWER EXTREMITIES – THREE-YEARS FOLLOW-UP IN 21 PATIENTS

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Introduction: Neuropathic pain after peripheral nerve injury (PNI) is usually chronic and hardly responds to common analgesics. Sleep disorders, anxiety and depression are common comorbidities. The quality of life is even more impaired in patients with neuropathic pain than in chronic non-neuropathic pain. The drugs proven to be effective against neuropathic pain in controlled trials are not tolerated by many people due to the side effects, and even the best of these drugs has a number needed to treat between 6 and 10. Dorsal root ganglion (DRG) stimulation has been shown to be effective in treating neuropathic pain. Here, we present 36 months clinical outcomes resulting from our experience with DRG stimulation in treating chronic neuropathic pain after PNI of upper and lower extremities.

Materials/Methods: 25 patients trialed a DRG stimulation system for their PNI and 21 patients were subsequently implanted if results were positive (defined as ≥ 50% pain relief). 5 patients had suffered a lesion of nerves of the upper extremity, 16 patients had damaged nerves of the lower extremity. Pain, quality of life, mental and physical function and drug usage were assessed at baseline (prior to implant), 3-, 6-, 12, 18-, 24- and 36-months post-permanent implant using Visual Analog Scale (VAS), Quality of Life Impairment by Pain Inventory (QLIP), and Short Form-12 (SF-12) mental (MCS) and physical (PCS) health composite score evaluations, Medication Quantification Score III, and morphine equivalent calculations, respectively. Implant related complications were also documented. The statistical processing was performed with SPSS® statistics 22.

Results: A total of 21 patients (52.5 ± 14.2 years; 13 female) with a definite neuropathic pain component [painDETECT questionnaire (PDQ) = 24.9±4.9] were implanted with the DRG system.

Discussion: DRG stimulation seems to be really effective in providing pain relief, improving quality of life, physical and mental status and reducing medication (including opioids) in patients with chronic neuropathic pain after PNI. Limitations of the study include the small sample size and d the retrospective design. Larger, randomized, prospective clinical trials are needed to confirm this observation.

Conclusions: Summarizing, chronic neuropathic pain after peripheral nerve lesion can be successfully treated by DRGS with good long-term results. The pre-interventional multidisciplinary diagnostics including pain analysis or quantitative sensory testing is the key to long-term therapeutic success.

Objectives

The data demonstrates the effectiveness (providing pain relief, improved life quality, reduced drug usage), reliability and safety of DRG stimulation in patients suffering from chronic neuropathic pain after PNI.

References

none

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368. INS19-0173

THORACIC SPINAL EPIDURAL HEMATOMA AFTER FUNCTIONAL DIAGNOSTICS AND PULSED RF APPLICATION USING EPRF-MULTIFUNCTIONAL-ELECTRODE - CASE REPORT AND POSSIBLE CONSEQUENCES FOR DAILY PRACTICE IN NEUROMODULATION

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Introduction: Most SCS complications are mechanical-related issues, such as lead migration, leadfracture,andequipmentfailure[1]. Biological complications are rare and includeeinfection,seroma, cerebrospinal fluid leak, spinal cord trauma, and spinal epidural hematoma (SEH). In one study, Levy et al. reported the incidence of SEH to be 0.014% for epidural catheter placement and 0.19% for SCS[2]. A more recent review of over 8,300 patients found the overall incidence of SCS associated SEH was 0.71%[3].

Materials/Methods: We report on a 63-year-old male patient who developed a SHE after applying a ePRF-multifunctional electrode (PE) (OMT GmbH & Co. KG Frittlingen, Germany) for the diagnosis and application of eRF in cervical radiculopathy. About 4.5 hours after the procedure the patient complained of severe pain in the lumbar region and numbness in both legs. An MRI of the thoracic and lumbar spine performed immediately after showed a multilevel epidural hematoma with an extent from the level Th2 to Th11 with compression of the spinal cord. Emergency surgery was carried out within 60 minutes. A decompression and evacuation of hematoma was performed via hemilaminectomy at three levels Th5, 8 and 10. Epidural AV malformations were conspicuous intraoperatively, which retrospectively confirmed by histological examination.

Results: On the morning of the first postoperative day, no neurological deficit was detectable. The further course was uneventful, the patient could be mobilized without complications and was discharged from hospital on the 6th postoperative day.

Discussion: Our case emphasizes the need for extreme caution and careful patient selection in performing epidural intervention such as application of a diagnostic PE or SCS-electrodes. To our surprise, epidural AV malformation seemed to be the cause of the hematoma in the presented case. This malformation was not detectable in pre-interventional diagnostic MRI.

Conclusions: Consequently, in the case of pain and increasing neurological deficits after manipulation in the epidural space, there is a compelling need for immediate imaging diagnostics and in the case of epidural hemorrhage there is a need for immediate decompression.

Objectives

We advocate the use of MR imaging prior to spinal interventional procedures in generally. Careful consideration should also be given to patients with abnormal hematologic or coagulation studies, and for patients on anti-platelet medications or anticoagulants. Close neurological monitoring of patients for 72 hours must be demanded, so that we do not support the outpatient implementation of such interventions.

References

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Poster Presentations - May 27 - May 30
Spine - Pain

369. INS19-0174

TREATMENT OF CHRONIC POST-SURGICAL KNEE PAIN AFTER TOTAL KNEE ENDOPROSTHESIS WITH DORSAL ROOT GANGLION STIMULATION (DRGS) – RETROSPECTIVE ANALYSIS AFTER 36 MONTHS

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Introduction: The total knee endoprosthesis (TEP) procedure can often result in chronic post-surgical neuropathic pain [Complex Regional Pain Syndrome type II (CRPS II)] due to damage of the infrapatellar branch of the femoral nerve[1]. Dorsal root ganglion stimulation (DRGS) has been shown to be effective in treating neuropathic pain after peripheral nerve damage [2,3]. Here, we present clinical outcomes resulting from our experience with DRGS in treating chronic post-surgical knee pain.

Materials/Methods: DRG leads (Abbott-St. Jude, Plano, TX) were implanted in the L3 and L4 foramen in patients with chronic post-surgical pain resulting from the TEP procedure. Subsequent to a successful trial (defined as ≥ 50% pain relief), patients were implanted with a permanent DRG system. Pain, quality of life, mental and physical function and opioid and antineuropathic drug usage were assessed at baseline (prior to implant), 3-, 6-, 12-, 24- and 36 months post-permanent implant using Visual Analog Scale (VAS), Quality of Life Impairment by Pain Inventory (QLIP), and Short Form-12 (SF-12) mental (MCS) and physical (PCS) health composite score evaluations, Medication Quantification Score and morphine equivalent calculations, respectively. Implant related complications were also documented. Complications related to the implantation were documented. The statistical processing was performed with SPSS® statistics 22.

Results: A total of 9 patients (66.4 ± 16.0 years; 6 female) with a definite neuropathic pain component [painDETECT questionnaire (PDQ) = 25.6 ± 4.9] were implanted with the DRG system. Compared with baseline, scores in all domains improved significantly (*$p<0.05$) after 3 or at latest 12 months and were maintained out to 36 months. There were 2 lead migrations through the evaluation period.

Discussion: DRG stimulation seems to be really effective in providing pain relief, improving quality of life, physical and mental status and reducing opioid usage in patients with chronic post-surgical neuropathic pain resulting from TEP. Larger, randomized, prospective clinical trials are needed to confirm this observation.

Conclusions: Neuromodulating therapy via DRG stimulation leads to greatly improved pain control and a distinct improvement in quality of life and functionality in patients with chronic post-operative (neuropathic) pain following total knee arthroplasty. The rate of adverse events is low.

Objectives

The data demonstrates the effectiveness (providing pain relief, improved life quality, reduced drug usage), reliability and safety of DRGS in patients suffering from chronic postsurgical neuropathic pain after TEP.

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370. INS19-0259

DO PATIENTS WITH SPINAL CORD STIMULATOR FOR TREATMENT OF CHRONIC PAIN SYNDROME DEMONSTRATE NEUROPLASTICITY: RETROSPECTIVE REVIEW

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Introduction: The phenomenon of neuroplasticity suggested that brain has ability to reorganize & functionally remodel itself following neural injury. This phenomenon has not been studied in patients with spinal cord stimulator (SCS) for management of chronic pain. As SCS is lifelong therapy, a valuable opportunity exists to examine the long term usage and parameters overtime to review if there is any evidence that could suggest that neuroplasticity phenomenon is occurring with in spinal cord as seen in brain in this group of patients. We propose to examine the long term SCS usage and implant (IPG) parameter data for all active patients with SCS in our institution and pose a question about role of neuroplasticity in this group of patients.

Materials/Methods: We reviewed 238 current active spinal cord stimulator patients implanted over last three decades for chronic pain syndrome. We collected data on SCS usage, as recorded by the IPG, and amplitude change over 10 years period, at regular interval of 1 month, 6 months, 1 year, 5 years and 10 years.

Results: The data showed that 57% of patients either reduced or went unchanged in their usage of SCS as per IPG data. Only 14% increased the usage over the same time. In the remaining 29%, the IPG did not collect data. Amplitude data showed that 36% of patients decreased or went unchanged whereas 53% of patients increased their amplitude setting over of time.

Discussion: The data collected on IPG usage would appear to suggest that majority of patients with implanted SCS for chronic pain are decreasing the amount of IPG usage time over the years. We hypothesize that there may be neuroplasticity phenomenon in this cohort of patients causing decreased usage. The analysis of amplitude showed that 53% of patients increased the amplitude and 36% either decreased or remained unchanged. These amplitude changes could be skewed due to change in electrode configuration.

Conclusions: Our retrospective review demonstrated that 57% of patients with implanted SCS for chronic pain demonstrated decreased or unchanged usage of IPG over time. However, increases in amplitude use could be due to more complex electrode configurations.

Objectives

1. Is there neuroplasticity phenomenon?
2. Is there progressive tolerance?
3. Causes for variable IPG usage?

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Spine - Pain

371. INS19-0262

OPIOID DOSE REDUCTION AFTER SPINAL CORD STIMULATION

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Table 1. Patients Completely Weaning Off Opioids

Pre-SCS	Completely Wean Off	Move to Lower Group	Stay in Same Group
No Use	N/A	N/A	71.1%
≤ 20 MME	34.2%	34.2%	46.9%
20-50 MME	12.7%	36.0%	43.3%
50-90 MME	6.7%	39.0%	38.1%
> 90 MME	5.1%	29.5%	70.5%
Overall	17.0%	34.2%	54.1%

Table 2. Multivariate Regression of Completely Weaning Off Opioids

Preoperative Opioid Usage	Opioid Use Reduction OR (95% CI)	*p-value*
No Use	Not included	.
50-90 MME	1.34 (0.97, 1.85)	.077
20-50 MME	2.50 (1.93, 3.24)	*<.001
≤ 20 MME	4.85 (3.76, 6.26)	*<.001
> 90 MME	reference	.
Patient Factor	**Opioid Use Reduction OR (95% CI)**	***p-value***
Long-term use of opioids	0.26 (0.21, 0.30)	*<.001
Usage of other pain medications	0.75 (0.65, 0.87)	*<.001
Polypharmacy	0.84 (0.71, 1.00)	*.0498
Obesity	0.75 (0.60, 0.94)	*.014

Introduction: Opioid usage in the US has become an epidemic, with fatal overdoses growing, numbering 33,091 in 2015[1], and the total economic burden estimated at $78.5 billion in 2013[2]. Therapies like neuromodulation for refractory chronic pain may reduce the economic costs and abuse potential of opioids. We examined the impact of spinal cord stimulation (SCS) on opioid dose reduction and weaning.

Materials/Methods: The Truven MarketScan® database was retrospectively queried for patients who underwent SCS implantation between 2010-2015, and subsequent change in opioid usage was calculated. Opioid usage before and after SCS were classified into dose groups based on CDC guidelines[3]. Multivariate logistic regression assessed associations between patient factors and completely weaning opioids post-SCS.

Results: Among 8,479 adult patients, 60.4% of patients using opioids saw reduced daily morphine milligram equivalents (MME) after SCS, with a median daily MME reduction of 58% in those patients. Median percentage reduction in usage of selected opioids was: oxycodone (-30%), methadone (-40%), hydrocodone (-50%), transdermal fentanyl (-50%), hydromorphone (-100%), tramadol (-100%). Additionally, 17% of all chronic pain patients weaned their opioids entirely. The proportion of patients completely weaning increased with decreasing pre-SCS dose, ranging from 5.1% in the >90 MME group to 34.2% in the ≤20 MME group. 71.1% of patients remained in the No Use group post-SCS. Using >90 daily MME as a reference group and controlling for >30 Elixhauser comorbidities and other confounders, patients in the 50-90 MME (OR=1.34, 95% CI [0.97, 1.85], p=0.077), 20-50 MME (OR=2.50, 95% CI [1.93, 3.24], p<0.001), and ≤20 MME (OR=4.85, 95% CI [3.76, 6.26], p<0.001) were more likely to wean off opioids. Factors significantly associated with decreased odds of weaning include long-term opioid use, other pain medication use, polypharmacy, and obesity (Table 2).

Discussion: We have characterized the largest and most updated US cohort of patients who underwent SCS and identified the impact of SCS and other patient factors on opiate dose reduction.

Conclusions: SCS can reduce daily MME and is an effective non-opiate solution for chronic pain. 60.4% of patients taking opioids decreased their daily MME with SCS and 17% weaned off entirely. Oxycodone and methadone may be more difficult to wean, while hydromorphone and tramadol may be easier. Patients on lower preoperative doses have significantly higher odds of weaning off opioids.

Objectives

-Quantify post-SCS daily opioid reduction

-Investigate likelihood of weaning opioids entirely after SCS

-Identify patient factors associated with weaning opioids

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372. INS19-0385

MODELLING THE EFFECTS OF POSTURE IN SPINAL CORD STIMULATION

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Introduction: In spinal cord stimulation, patients' sensitivity to stimulation varies with their posture. When using traditional open-loop spinal cord stimulation (SCS) systems, this results in a continuous variation of neural recruitment as the patient moves about, with consequent side effects.

It has been hypothesised that this is due to the spinal cord moving about within the cerebrospinal fluid (CSF). This changes the coupling between the epidural electrode array and the target fibres in the dorsal columns. Closed-loop SCS aims to compensate for this effect, measuring the evoked compound action potential (ECAP) and adjusting the stimulus in real time.

This work examines the cord movement hypothesis and the effect of closed-loop by developing a computational model of SCS.

Materials/Methods: The model extends previous work in the field to be able to simulate ECAP waveforms. A geometric component calculates the coupling between the epidural electrodes and the dorsal columns. A neural component then simulates the dorsal column nerve fibres, calculating the ECAPs resulting from a stimulus.

Results: In any cord position, the activation plot shows no response below threshold and a linear growth region above threshold. As the cord-electrode distance is increased, the threshold increases and the slope of the linear region decreases.

Recruitment curves are calculated for open-loop (constant-current) and closed-loop (constant-ECAP) stimulation as cord position is varied.

Discussion: The activation plots mimic those seen in patients, with the variation in threshold and slope resembling that seen as patients change postures. Patient activation plots are limited by uncomfortable side effects, so no saturation effects are observed in humans.

The model predicts that open-loop stimulation will result in significant variation in recruitment, including a complete loss of stimulation in some positions. Closed-loop results in improved constancy of recruitment, and eliminates drop-out.

Conclusions: A model of spinal cord ECAP generation is demonstrated to reproduce features seen in patients. Postural changes observed in patients correspond to cord movement in the model. Closed-loop stimulation outperforms open-loop stimulation in maintaining constant recruitment.

Objectives

ECAP generation can be simulated using coupled models.

Cord movement can cause postural sensitivity changes in SCS.

Closed-loop stimulation compensates for these changes in sensitivity.

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Spine - Pain

373. INS19-0089

SPINAL CORD STIMULATION FOR FAILED BACK SURGERY SYNDROME: BENEFITS IN PAIN PERCEPTION, ABILITY FUNCTION AND HEALTH-RELATED QUALITY OF LIFE IN CLINICAL PRACTICE SETTING

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Introduction: FBSS represents one main cause of chronic neuropathic or mixed pain, functional disability and reduced HRQoL. SCS can be a value for money option to treat patients refractory to conventional medical management (CMM). We estimated from real-world data: 1) amount of reduced levels of HRQoL of target patients compared to general population, 2) relationship between pain intensity, functional disability, and overall HRQoL, 3) improvement of patients' health from SCS intervention,

Materials/Methods: Before SCS and every 6 months for 2 years after SCS a battery of questionnaires/tests were completed: EQ-5D and SF-36 for HRQoL, NRS to measure pain intensity, ODI to measure functional disability. We conducted multilevel regression analyses to investigate association of HRQoL with NRS and ODI indexes, to compare EQ-5D data with those of general population adjusted for age, sex and education, and statistical tests to compare changes of HRQoL, NRS and ODI estimates at baseline with those measured during follow-up.

Results: Eighty patients participated. HRQoL was significantly worse in patients than in corresponding general population. Pain, functional disability and HRQoL significantly related each other during follow-up. Significant improvements ($p < 0.001$) in pain intensity, functional capability and HRQoL were reached after 6 months from SCS and generally remained stable during follow-up. Specific instruments provided detailed information on disability and pain, while generic instruments assessed overall HRQoL and allowed comparison with general population's one.

Discussion: At enrolment patients had serious impairment in terms of pain perception, functional disability and related aspects, and HRQoL at a whole, which was significantly lower than HRQoL assessed in corresponding general population. During follow-up, pain and functional disability measured with condition-specific instruments NRS and ODI, respectively, significantly related with HRQoL assessed with EQ-5D and SF-36. After only 6 months from SCS intervention, an improvement of health was found in every domain of every instrument used, which was generally statistically significant

Conclusions: SCS + CMM treatment reaches statistically significant and clinically relevant improvement in pain perception, functional disability and HRQoL in patients with FBSS refractory to CMM. Appropriate selection of instruments for use in clinical practice is crucial for routine assessment of health perception in patients, aimed to guide decisions for optimal treatment.

Objectives

SCS efficacy in neuropathic pain, Appropriate decisions on FBSS treatment, Health instruments for use in routine clinical practice

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374. INS19-0083

POSTERIOR LUMBAR/SACRAL NERVE ROOT STIMULATION FOR TREATMENT OF CHRONIC FOOT AND/OR ANKLE PAIN

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Introduction: Chronic focal pain relief has been reported using Dorsal Root Ganglion (DRG) stimulation.[1] However, a high incidence of adverse events associated with this technique has been documented.[2-4] Effective treatment of groin and pelvic pain using stimulation with leads over the L1 dorsal nerve root has recently been reported.[5] We therefore evaluated outcomes of proximal dorsal somatic nerve root stimulation as an alternative method for chronic foot/ankle pain. We chose to evaluate in a case series the clinical outcomes of a surgical implantation technique as an alternative method of targeted dorsal nerve root stimulation to treat chronic foot and/or ankle pain.

Materials/Methods: This is a single-center, case-series evaluating patients with chronic foot/ankle pain diagnosed with Complex Regional Pain Syndrome or Diabetic/non-Diabetic peripheral neuropathy (N=9) as part of an ongoing retrospective chart review evaluation of SCS outcomes for chronic pain (Clinicaltrials.gov identifier: NCT01550575). Patients were implanted with a neurostimulator capable of anatomically-guided (3D) neural targeting (3DNT, Precision Spectra, Boston Scientific). Using a previously described technique, leads were placed antegrade through the sacral hiatus within a range of L5-S1.[6]

Results: A 6.3-point reduction in NRS ($p<0.0001$) was reported at mean last follow-up duration=315.6 days. Fifty-five percent (5/9) of patients reported 91-100% improvement in their pain and 44% (4/9) reported no pain (NRS=0) at last follow up. Additionally, >75% (7/9) of patients reported NRS≤1, 56% preferred standard rate and 44% preferred higher rate stimulation. Additional data to be presented.

Discussion: DRG stimulation may be associated with additional risks in addition to a more complex procedure. This small case-series demonstrates that neurostimulation within the L5-S1 range using 3DNT is a viable option to treat focal foot/ankle pain.

Conclusions: DRG stimulation may be associated with additional risks in addition to a more complex procedure. This small case-series demonstrates that neurostimulation within the L5-S1 range using 3DNT is a viable option to treat focal foot/ankle pain.

Objectives

To report demographic, programming preference, and pain relief data in a real-world patient case-series using a surgical implantation technique as an alternative method of targeted dorsal nerve root stimulation to treat chronic foot and/or ankle pain.

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375. INS19-0084

EARLY CLINICAL EXPERIENCE WITH A NEW SPINAL CORD STIMULATION LEAD FOR MULTI-SITE PAIN

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Introduction: Advancements in Spinal Cord Stimulation (SCS) lead designs are thought to help facilitate an improved patient experience and outcomes with SCS and in combination with new neural targeting technologies may help to better treat patients with multi-site pain. In this study, we examined the early clinical experience using a newly available lead with a longer span covering over 3 vertebral levels and minimal spacing between electrodes (versus other traditional linear designs) used as part of an SCS system for treating chronic pain. Here we evaluate the early clinical experience using a newly available lead with a longer span covering over 3 vertebral levels and minimal spacing between electrodes (versus other traditional linear designs) used as part of an SCS system for treating chronic pain.

Materials/Methods: This is an observational clinical study based on retrospective chart review as part of an ongoing evaluation of real-world SCS outcomes for chronic pain (Clinicaltrials.gov identifier: NCT01550575). Patients were implanted with at least one 16-electrode lead, designed with a span length of 67 mm, and electrode spacing of 1 mm (Infinion CX, Boston Scientific). Data assessments consist of the following: pain locations and outcomes, including pain scores, at follow up.

Results: Initial results from 29 patients so far have demonstrated a 5.9-point reduction in NRS ($p<0.0001$) from baseline to a mean last follow-up duration of 45 days ($n = 29$). Mean NRS at baseline, trial, and last post-implant follow-up were 8.6, 2.4, and 2.7 respectively for 29 patients. Over 96% (24/25) of patients reported greater than 50% improvement in their pain at last follow up post-implant and 52% (15/29) of patients reported NRS≤2. Additional updated data will be presented.

Discussion: New lead designs offering greater adaptability may be important in reducing treatment failures and enhancing more personalized SCS treatment approaches. A 16-electrode lead with minimal contact spacing and longer vertebral span capable of covering over 3 levels represents another potential tool in the drive to help better SCS patient outcomes.

Conclusions: A 16-electrode lead with minimal contact spacing and longer vertebral span capable of covering over 3 levels represents another potential tool in the drive to help better SCS patient outcomes.

Objectives

To report demographic, programming parameters, and pain relief data in patients using a lead with a longer span covering over 3 vertebral levels and minimal spacing between electrodes (versus other traditional linear designs) used as part of an SCS system for treating chronic pain.

References

NA

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376. INS19-0134

ANATOMICALLY PLACED LEADS PROVIDE SUPERIOR PAIN RELIEF WHEN USING A NOVEL, PULSED SPINAL CORD STIMULATION PATTERN: RESULTS FROM A PROSPECTIVE, MULTI-CENTER STUDY

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Introduction: Epidural lead location in traditional, low-frequency tonic spinal cord stimulation (SCS) is an important factor of treatment success. Presumably, by targeting the correct underlying dorsal column fibers, one can modulate the appropriate upstream and downstream neurons to produce analgesia. More recent therapeutic approaches utilizing higher frequencies and bursting stimulation patterns are incorporating anatomically based lead placements. We tested this technique with a novel, pulsed stimulation pattern in the treatment of low back pain (LBP).

Materials/Methods: A prospective, randomized, multi-center clinical study was undertaken to test if a novel stimulation pattern utilizing pulsed pattern elements can evoke superior LBP and leg pain relief. Local ethics committee approval for all experimental procedures were obtained and all subjects provided written consent. Subjects met all inclusion criteria including presenting with low back and/or leg pain. During an SCS trial, subjects were randomized to either a physiologically placed SCS lead position utilizing traditional paresthesia coverage, or anatomically placed leads (T8-10 levels). Subjects were allowed to test both low-frequency tonic as well as the new stimulation pattern for up to 14 days. Pain scores were obtained prior to stimulation and during each experimental time period.

Results: In total, n=48 subjects were included in the study. Subjects with anatomically based lead positioning showed a much greater trial success rate (^{3}50% pain relief) when compared to subjects in the physiologically placed group (70% versus 30%). Overall, mean reductions in LBP in the pulsed pattern group was 77% compared to 52% in the tonic SCS group. Leg pain relief was also greater with pulsed stimulation (71% versus 51%). Anatomical localization of programmed cathodes was clustered around the T9 vertebra body.

Discussion: Findings from this study utilizing a novel, pulsed stimulation pattern are consistent with prior reports of, 1) larger pain relief in LBP when utilizing stimulation frequencies ^{3}500 Hz, and, 2) ability to epidurally position leads around the T8-10 spinal level to effectively deliver SCS therapy for low back pain. We found that the anatomic location where cathodal stimulation produced the best results clusters around the T9 vertebral body. This spot likely is aligned with important dorsal neural structures that, when appropriate stimulation patterning is applied, produces superior LBP relief. Further research is needed, and is underway, to verify that the results reported here are sustained over longer time periods.

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377. INS19-0314

SPINAL CORD STIMULATION FOR INTRACTABLE PAIN: EARLY RESULTS OF A PROSPECTIVE, MULTI-CENTER, REAL-WORLD CLINICAL OUTCOMES STUDY SHOW REDUCED INCIDENCE OF LEAD MIGRATION AND FRACTURE

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Introduction: Spinal cord stimulation (SCS) systems have been used for more than 30 years to safely and effectively treat chronic pain. The most frequent complications associated with SCS therapy include lead migration or fracture and loss of therapy effectiveness. The purpose of this study is to obtain real-world data on a new SCS system designed to address the most frequent SCS therapy complications.

Materials/Methods: This prospective, multi-center, single-arm study in the USA and Europe will enroll up to 120 subjects who complete a stimulation trial and agree to permanent implant with the Algovita® SCS System (Nuvectra, Inc., Plano, TX). Each subject will be followed for 24 months for safety and effectiveness including pain, adverse events, and quality of life.

Results: To date, 52 patients have undergone permanent SCS implant, with mean follow-up of 6.3 months. Mean age was 58.7 $\pm$ 14.7 years and 50% (26/52) were female. Median time since diagnosis was 5.5 years, and the most common primary diagnosis was failed back surgery syndrome (46%, 24/52). Safety outcomes included 2 (4%) lead migrations and 0 (0%) lead fractures. Among 9 AEs in 8 (16%) patients, 3 resulted in SCS explant. One death at 155 days was unrelated to the device or procedure.

Discussion: The most frequent complications of SCS include lead migration and fracture. In this ongoing study, early rates of SCS lead migration (4%) and fracture (0%) are considerably less than those observed in the literature; the review by Eldabe (2016) cites migration of 15.5% and fracture of 6.4% across over 4,000 patients.

Conclusions: Early data in this real-world SCS study indicate lower rates of lead migration and fracture, confirming overall clinical experience with over 3,000 permanent implants performed over 3 years; fracture and migration rates in those cases were 0.44% and 0.46%, respectively. This suggests that the *a priori* design approach to minimize lead fracture and migration by using a coil-in-coil design and a more elastic lead body has been successful.

Objectives

Demonstrate ways to improve SCS therapy for intractable pain.

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378. INS19-0076

PAIN RELIEF AND OPIOID REDUCTION SEEN WITH DORSAL ROOT GANGLION STIMULATION

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Introduction: Dorsal Root Ganglion Stimulation (DRGS) is an advance of neuromodulation for pain. DRGS has been demonstrated to provide superior pain relief and improvement in quality of life when compared to conventional tonic stimulation[1]. Since the release in the United States there have not been any additional prospective study examining DRGS in a real-world application. This study is a prospective review of sixty-three consecutive cases of DRGS examining pain relief and opioid use in a university pain clinic for neuropathic pain.

Materials/Methods: Sixty-three consecutive patients who had neuropathic pain not responsive to conservative medical therapy, regional neural blockade or suboptimal response to conventional tonic spinal cord stimulation (SCS) were consented for study. A smaller select group of patients (n=5) who had conventional tonic SCS implanted 2 years or more and who had diminishing relief were also included.

Clinical outcomes included pain relief recorded via a 11-point Numeric Rating Scale (NRS), Percentage Global Impression of Change (PGIC), daily opioid use in mg Morphine Equivalents (MME) prior to DRGS and following DRGS. Disability was evaluated using the Oswestry Disability Index (ODI). Adverse events were also collected. Patients were generally followed post implant with office visits of 2 weeks, 6 weeks, 3, 6, 9, 12 and 18 months. Patients were instructed to begin weaning their preoperative opioid after the 6-week visit if they had not already begun to do so on their own.

Results: Baseline NRS pain scores were 8 (6 to 9) and baseline ODI scores were at 33% (28% to 37%). At longest follow-up NRS pain scores were 4 (2 to 7), median difference -2 (95% CI of the difference -5 to -1, P<0.001) and ODI was 23% (15% to 30%), median difference -10 (95% CI of the difference -3 to -16, P<0.001). Prior to implantation daily opioid consumption was 40 (5 to 60) MME and at the longest follow-up was 7.5 (0 to 30) MME, median difference -32.5 MME (95% CI of the difference -11 MME to -60 MME, *P*<0.001). 5 patients (7.4%) required revision of lead placements and 2 patients (3%) had their DRG system explanted.

Discussion: This is the first single-center study which demonstrates a decrease in opioid use following DRG implantation.

Conclusions: Opioid use decreases following dorsal root ganglion stimulation

Objectives

Dorsal root ganglion stimulations may be a preferable option to treat neuropathic pain.

Opioid use decreased after dorsal root ganglion stimulation.

Dorsal root ganglion stimulation improves function

References

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Poster Presentations - May 27 - May 30
Spine - Pain

379. INS19-0269

NEUROMODULATION IN PELVIC PAIN TREATMENT

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Introduction: Pelvic pain is a group of the different conditions. Among pain syndromes, approximately 25% of the patients have refractory pelvic pain syndromes which consider one of the most difficult diseases to be diagnosed and cured. The methods of neuromodulation can be used in refractory pain, but a frequency of occurrence of these methods is very low.

Materials/Methods: In our case series were included 32 patients with refractory pelvic pain. In 16 patients were implanted sacral lead on one side of the sacral root, in 5 patients were implanted sacral lead on both side of the sacral root, in 5 patients were implanted spinal cord stimulation lead, in 3 patients were implanted spinal cord stimulation lead and sacral lead and in 3 patients were implanted sacral and pudendal nerve leads. We evaluate pain intensively with visual analog scale (VAS) and Brief Pain Inventory before test period, after the test period, after implantation of the pulse generator and in follow-up.

Results: Test stimulation was successful in 26 patients. Of the 26 patients with the implant 24 had a decrease in the severity of the worst pain compared to baseline. Mediana VAS before the operation was 9 points and 3 points in follow-up (p<0,05). Average mean of physical activity scale before the operation was 14.03 points and 3, 125 points in a follow-up (p<0,05). In our case series not found a significant difference between pain duration and efficacy of neuromodulation therapy.

Discussion: Neuromodulation treatment is a very important method for pelvic patients but in real time we needed new trials.

Conclusions: Neuromodulation therapy is an effective and safe method to manage pelvic pain.

Objectives

different methods for treatment pelvic pain

reasons inefficacy

new modality

References

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Poster Presentations - May 27 - May 30
Spine - Pain

380. INS19-0080

SUCCESSFUL USE OF HIGH-FREQUENCY SPINAL CORD STIMULATION (HF-SCS) IN CRPS (COMPLEX REGIONAL PAIN SYNDROME): A CASE REPORT

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Introduction: CPRS is a painful, disabling multifactorial disorder involving the musculoskeletal and neurological system, which usually occurs after a trauma. The diagnosis is primarily clinical and invasive treatments should only be used in carefully evaluated cases. In observational studies, SCS has reduced the pain in CRPS. This case report describes the dramatic improvement in pain and functional conditions in a young lady (36 YO) treated with HF-SCS.

Materials/Methods: Patient with local dorsal-lumbar spine pain, drug-resistant since 2009, was diagnosed with a severe discopathy related with myelopathy (T11-L1) in 2012 and underwent dorsal and lumbar arthrodesis and mechanical stabilization. She reported relapse of pain symptoms in 2014 and severe functional deficit (Failed Back Surgery Syndrome-like), even after the mechanical stabilization tools removal.

After a new mechanical stabilization procedure, she showed no change in pain (VAS score 9). Moreover, patient condition aggravated by episodes of local allodynia in the epigastric region and anterior ribs and abdominal pain with functional impairment (Oswestry Disability Questionnaire score 36) and sympathetic symptoms of the whole right leg.

Physical and occupational therapies, drugs, epidural injection and nerve blocks failed to alleviate symptoms.

Patient was assessed as suitable for HF-SCS and trialed in October 2018: an 8-poles lead was positioned midline in the epidural space with upper end at T3.

Therapy parameters were set as per standard protocol.

Results: After 15 days, VAS score dropped from 9 to 2 and ODQ from 36 to 20, with complete suspension of pain-related treatments with no rebound effects. With the trial device removal, all baseline symptoms relapse and the patient had to go back to pain treatment. Permanent implant will be performed in November 2018.

Discussion: This case describes a substantial improvement of symptoms in a CRPS-patient treated with HF-SCS.

Conclusions: In patients with refractory pain related to CRPS, HF-SCS could present an effective alternative to ablative sympathectomy to improve pain and quality of life.

Objectives

To explore the opportunity and efficacy of HF-SCS in CPRS with a strong sympathetic component, triggered by anterior surgery approach.

To monitor and analyze patient outcome for 12 months.

References

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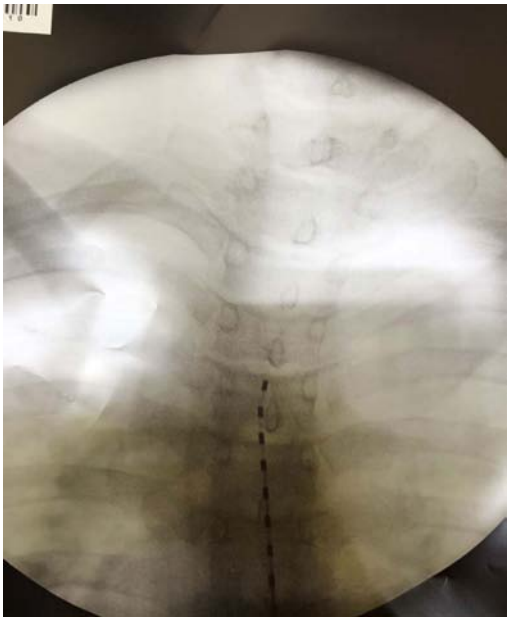

Poster Presentations - May 27 - May 30
Spine - Pain

381. INS19-0158

REAL WORLD EXPERIENCE USING AN INNOVATIVE SCS-DEVICE WHICH PROVIDES INDIVIDUALIZED TREATMENT CUSTOMIZATION

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Introduction: The spinal cord stimulation (SCS) therapy is an evolving field. Nowadays we can customize simultaneously stimulation waveforms and field shapes. The scope of this work is to provide real world experience using a new system in treating chronic pain patients.

Materials/Methods: Seven consecutive patients were treated with SCS and implanted with a new neurostimulator (IPG) (Precision Spectra WaveWriter™, Boston Scientific). We collected baseline characteristics and reviewed the procedure information. The pain intensity was evaluated with the visual analogue scale (VAS).

Results: The mean age of the patients (3 males, 4 females) was 56.2 years. Four patients had failed back surgery syndrome (FBSS), one lumbar stenosis, one pelvic ring fracture and one post-herniorraphy pain. Four patients reported back and leg pain, one only leg pain, one groin pain and one sacroiliac joint and atypical leg pain. The baseline VAS was 8.4, at the end of the trial 3.5 and after one month 2. Five patients had a SCS-system and 2 had a hybrid-system (SCS and PNFS). Four patients received a lead with 16 contacts. The tip of the lead was at T8 (44.4%), T9 (33.4%), and T10 (22.2%). The mean duration of the trial was 59 minutes. The mean number of the programs tested was 4. Four patients preferred a polytherapy (tonic and 1kHz or tonic and Burst) and 3 a monotherapy (Burst or 1kHz). We had one lead migration.

Discussion: It was possible to achieve a considerable pain relief even in patients where the coverage was not optimal. These results could be attributed to the combination therapy (layering more than one therapy at the same time), the subperception algorithms (Contour™) over multiple vertebral levels, and the waveform automation (automatic rotation through waveforms). Of note, the patients could enter real-time therapy ratings into their remote control which helped us identify which therapy provides the most relief with the lowest energy usage.

Conclusions: The goal of any advances in SCS-field should be to simplify personalization, achieve better outcomes and deliver the most effective therapy with the lowest energy usage.

Objectives

To critically examine the first outcomes using a new SCS system.

References

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Poster Presentations - May 27 - May 30
Spine - Pain

382. INS19-0179

IDENTIFICATION OF THE RESERVOIR ACCESS PORT OF INTRATHECAL PUMPS BY TEMPLATE VERSUS ULTRASOUND GUIDANCE: A PILOT STUDY

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Introduction: Targeted drug delivery is a common method to manage chronic pain and spasticity. Drugs are delivered by an implanted pump into the intrathecal space through a catheter. Drug refill is the most common performed maintenance procedure. Identification of the reservoir access port (RAP) can be challenging for many reasons (excessive subcutaneous tissue, scar formation, depth of the pump, pump tilt or mobility). Multiple punctures increase the risks of infection, pain and discomfort for patients. Accidental injections outside the reservoir can lead to life threatening complications. RAP is usually identified by palpation and using commercially available template. Ultrasound guidance or fluoroscopy have been showed to be useful in difficult cases(1). Ultrasound is preferred over fluoroscopy because of easiness of use and non-radiating method. The purpose of the study was to identify factors affecting the accuracy of template versus ultrasound guidance method.

Materials/Methods: Included patients had an intrathecal pump (Synchromed II Medtronic®) subcutaneously implanted in the abdominal wall. Collected data included age, gender, height, weight, abdominal circumference and depth of the pump as measured by ultrasound. The RAP was localized using the dedicated template and by ultrasound guidance. The two points were marked and the distance measured. The silicone septum of the RAP measuring 7 mm in diameter, every distance of more than 7 mm with a successful puncture of the ultrasound guidance point was considered as a failure of the template method. Correlation between the distance and each demographic and anatomical characteristic was computed using Spearman and Pearson coefficients.

Results: 35 patients were enrolled and a total of 67 refill procedures were assessed. There was no significant correlation between distance and age, height, weight, BMI or abdominal perimeter. The only significant correlation was found with depth of the pump (Pearson rho = 0.389, IQR: 0.033 – 0.657, p=0.034; Spearman rho = 0.725, IQR: 0.494 – 0.861, p <0.001).

Discussion: The results suggest that ultrasound guidance is more precise than template identification only when the pump is deeply implanted. Demographics or abdominal perimeter are not correlated with a better performance of the ultrasound guidance over template technique for identification of the RAP.

Conclusions: In conclusion, our results suggest that the only advantage of ultrasound guidance for identification of the RAP is for deep implanted pumps.

Objectives

Know the different indications for intrathecal pumps
Know the different methods for pump refills
Discuss the advantages of ultrasound guidance

References

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Poster Presentations - May 27 - May 30
Spine - Pain

383. INS19-0227

BURST CERVICAL SPINAL CORD STIMULATION (SCS) TO TARGET DISTANT ANATOMIC AREAS IN DIFFICULT TO TREAT UNCONVENTIONAL PAIN SYNDROMES : A CASE SERIES

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Introduction: Both small animal and human studies have shown that electrical stimulation of high cervical area (C2) can target low back pain and even broader areas of spinal pain. Peripheral C2 stimulation has further shown to target whole body neuropathic pain conditions such as fibromyalgia. Here, we evaluate the efficacy of Burst stimulation in the high cervical spine and its ability to modulate multiple different target areas.

Materials/Methods: Four patients from a single center who were eligible for cervical SCS were implanted with a device capable of delivering Burst stimulation. Patients' pain, disability, mood and sleep were assessed pre- and post-operatively (range: 6 weeks to 6 months). Patients were diagnosed with multiple painful neuropathic indications, including severe fibromyalgia (whole body neuropathic pain) (3 out of 4 patients), cervical neuritis (2 out of 4 patients), occipital neuralgia (2 out of 4 patients), atypical facial neuralgia (1 patient), and failed back surgery syndrome (1 patient with extensive scoliosis surgery). Only 2 patients were on small doses of weak opioids (tramadol and Tylenol -codeine) Tonic mapping did not cover the painful areas in all patients but BURST stimulation provided substantive pain relief in those areas.

Results: All four female patients were implanted just beyond the C2 level. (High cervical zone) Average age was 50.3 years (33 - 66 years) and the average BMI was 28 (20 - 41). Baseline Visual analog scale (VAS) was 9 cm (8 - 10 cm) and improved to 2.8 cm (0 - 4 cm) at follow up. All patients reported at least a 50% improvement in their sleep, disability and mood post-operatively. All patients on opioids reported reduction of analesics by 50%.

Discussion: One possible explanation for this phenomenon could be due to Burst stimulation modulating the medial pain pathway, recruiting dorsal column fibers not captured by traditional tonic stimulation.

Conclusions: These results show that high cervical SCS using Burst stimulation therapy can be effective in treating multiple distant target areas such as neck, face upper extremity pain, low back pain and even whole-body neuropathic pain. Patients with extensive hardware and a compromised epidural space in thoracic and lumbar areas can be targeted at the high cervical area rather than relying on escalating doses of analgesics.

Objectives

neuromodulation for fibromyalgia

neuromodulation for facial pain

alternative strategies for fibromyalgia

References

C2 subcutaneous stimulation for failed back surgery syndrome: a case report

C2 Nerve Field Stimulation for the Treatment of Fibromyalgia: Prospective, Double-blind, Randomized, Controlled Cross-over Study

Poster Presentations - May 27 - May 30
Spine - Pain

384. INS19-0246

TREATING SYMPTOMATIC ADJACENT SEGMENT DISEASE AFTER LUMBAR SPINE FUSION WITH INTERSPINOUS PROCESS SPACER - A MULTICENTER RETROSPECTIVE ANALYSIS OF CASES AND OUTCOMES

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Introduction: Patients with lumbar spine fusion commonly present during followups with a presentation consistent with adjacent segment disease, leading to mild to moderate stenosis above the level of existing fusion. This is due to the restriction of motion at the original fusion site and the resulting motion stress which is transferred to nearby spinal segments. Extending the surgical fusion or treating the FBSS presentation may lead to more chronic pain. One possible approach to avoid perpetuating the spinal deterioration and to treat the symptomatic adjacent segment is to use interspinous process spacers which have been shown to increase stability in extension while simultaneously reducing rigidity in flexion due to that adjacent segment.

Materials/Methods: The medical records of 13 patients who received the Superion Interspinous spacer were reviewed and summarized. Each patient had previous spinal fusion surgery and subsequent adjacent segment disease. Patient reported outcomes such as procedure satisfaction, self-reported pain, changes in medications, and changes in functionality were assessed.

Results: Of the 13 reviewed surgical cases, 6 were women and the average age was 79 (66-97). All patients carried a diagnosis of neurogenic claudication and lumbar spinal stenosis. 9 of the 13 patients had prior treatment to alleviate pain including physical therapy and electrical stimulator implants. 11 of the 13 patients had significant medical history including diabetes, arterial and cardiac stents, and fibromyalgia. The average pain score prior to the procedure was 8.5/10 (5-10). Following the procedure, the average pain score was 3/10 (0-9). Average satisfaction with the procedure was 3/4 (0-4). All subjects taking pain medication reported reduced use following the procedure.

Discussion: Patients receiving the Superion Interspinous spacer as treatment for adjacent segment disease reported high levels of satisfaction with the procedure, reduced pain in the affected area, reduced usage of pain medications and improvements in mobility and functionality. Taken together, the minimally invasive interspinous spacer is a valuable tool in spinal surgical treatment to increase stability of the affected region while limiting rigidity often associated with spinal fusion. Ultimately, the use of the spacer should reduce the need for future treatment of adjacent segment disease.

Conclusions: Interspinous spacer is a reasonable treatment option for patients with FBSS with symptomatic adjacent segment disease.

Objectives

Treating FBSS presentations

Supplementing SCS for FBSS with other interventions for complete relief

Superion as a salvage if SCS not working for claudication

References

Superion Interspinous Spacer Treatment of Moderate Spinal Stenosis: 4-Year Results

Poster Presentations - May 27 - May 30
Spine - Pain

385. INS19-0128

IMPLANTER'S INTEGRATED INFORMATION (I3) SYSTEM: AN AID FOR SPINAL CORD STIMULATION PROCEDURES

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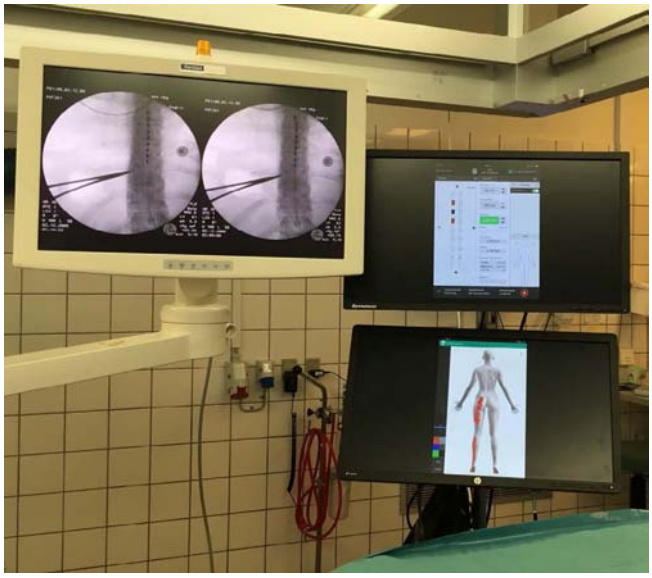
Introduction: In spinal cord stimulation (SCS), the electrical stimulation of the spinal cord with an implanted lead evokes a tingling peripheral sensation known as paresthesias. Newer stimulation paradigms allow paresthesia-free treatment, but during the implantation of the lead, paresthesias must cover the painful area to achieve optimal treatment effect. The localization of the evoked paresthesias can be difficult to accurately describe for the patient, and furthermore depends on a complex and only partially predictable set of parameters that includes the anatomical localization and the programming of the electrical field.

We aimed to optimize SCS implantation procedures by devising a way to aid the patient in making useful descriptions of the evoked paresthesias, then to visually convey the full set of information – anatomical position of the lead, programming parameters, and evoked paresthesias – directly to the implanting physician.

Materials/Methods: To aid the patient in making accurate descriptions of the evoked paresthesia, we employed an app dedicated to creating pain drawings on a tablet.

We used Chromecast and Apple TV to project the information from the pain drawing tablet and the programming device to two monitors placed in the implanter's field of vision, right next to the fluoroscopy monitor.

Results: The three monitors combined provide a direct visual representation of the dynamic dataset used during SCS implantation: Position, Programming, and Paresthesias, essentially creating the equivalent of the dashboard of a car.



Discussion: A spinal cord stimulation procedure is an intricate process where complex information from several sources must be communicated and combined.

Our aim was to create a low-cost, simple solution to alleviate the communication challenges inherent to SCS surgery.

Conclusions: We present an Implanter's Integrated Information (I3) system; a simple, inexpensive solution for gathering, integrating, and conveying the complex set of information necessary for a successful SCS procedure.

Objectives

1) To ease SCS implantation procedures

2) To demonstrate how existing technology can be employed in a clinical setting

3) To point out obstacles to a successful SCS implantation procedure

References

Meier K, Knudsen ALH, Boudreau SA, Sørensen JCH: *Implanter's Integrated Information (I3) System: An Aid for Spinal Cord Stimulation Procedures*. Neuromodulation 2018 Oct 16 (Epub ahead of print).

Poster Presentations - May 27 - May 30
Spine - Pain

386. INS19-0085

EVALUATION OF CRPS PATIENTS USING AN SCS SYSTEM WITH MULTIPLE WAVEFORM AND STIMULATION FREQUENCY OPTIONS

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Introduction: Complex Regional Pain Syndrome (CRPS) can be successfully treated with Spinal Cord Stimulation (SCS), but some patients experience loss of treatment effectiveness over time. A recent study demonstrated that strikingly different frequencies and waveforms were preferred by individual patients with CRPS.[1] To further verify and expand upon this work, we assessed clinically diagnosed CRPS patients implanted with a newer generation SCS system that provides for multiple waveform and stimulation frequency options.

Materials/Methods: All eligible patients of this real-world case-series were assessed by retrospective chart review as part of an ongoing evaluation of SCS outcomes for chronic pain (Clinicaltrials.gov identifier: NCT01550575). All analyzed patients were diagnosed with CRPS and implanted with a multiple waveform SCS system (Precision Spectra, Boston Scientific). Assessments of (or related to) pain relief over time are actively being conducted as captured from retrospective chart review. Additionally, documentation of particular waveforms and/or stimulation frequencies utilized during the duration of treatment will be presented.

Results: Mean NRS at baseline and last follow-up (mean duration: 389 days) were 7.6 and 3.7, respectively (Δ=3.9, $p< 0.0001$) for 35 patients. 81% of patients (17/21) reported greater than 50% improvement at their last follow-up and 38% (8/21) reported 91-100% pain relief at last follow-up.

Discussion: The ability to provide various options within a single SCS device is thought to be helpful in avoiding loss of efficacy due to adaptation or other modes of disease plasticity over time. This study therefore seeks to add to the overall compendium of data investigating SCS-implanted patients with CRPS who have access to multiple options that enable individually selected use of various waveforms and/or stimulation frequencies.

Conclusions: This study intends to add to the overall compendium of data investigating SCS-implanted patients with CRPS who have access to multiple options that enable individually selected use of various waveforms and/or stimulation frequencies.

Objectives

To report demographic, programming parameters, and pain relief data (NRS scores, Percent Pain Relief) in SCS-implanted patients with CRPS who have access to multiple options that enable individually selected use of various waveforms and/or stimulation frequencies.

References

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Poster Presentations - May 27 - May 30
Spine - Pain

387. INS19-0192

A NOVEL SUB-PERCEPTION THERAPY ENABLING CLINICALLY SIGNIFICANT SCS PAIN RELIEF

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Introduction: Sub-perception Spinal Cord Stimulation (SCS) is an option for patients using SCS to treat chronic pain who prefer not to feel paresthesias. However, the use of this modality is typically associated with longer wash-in times and can take 1-2 days to achieve analgesia, sometimes requiring lengthy programming sessions to determine the optimal neural target. Achieving a more rapid onset sub-perception pain relief represents an unmet patient need. We now report discovery of a novel sub-perception therapy that seemingly delivers pain relief equal to, or in some cases better than currently available methods of SCS, and with a reduced wash-in time as compared to traditional sub-perception approaches.

Materials/Methods: This is a multicenter, observational study of permanently-implanted patients (up to N=50) assessed as part of an ongoing review of SCS outcomes for chronic pain (Clinicaltrials.gov identifier: NCT01550575). Patients were implanted with a neurostimulator (Spectra WaveWriter, Boston Scientific) capable of providing a novel sub-perception SCS algorithm. Pain relief scores (NRS) and functional mobility assessments were collected at baseline and following titration of frequency, pulse-width, and amplitude (neural dose) at a follow-up visit. Patient charging burden was calculated based on stimulation parameters.

Results: Data analysis is ongoing and finalized results will be presented.

Discussion: Utilizing a novel sub-perception paradigm with reduced wash-in time may be helpful for delivering improved patient outcomes and overall quality of life experience by arriving at optimal parameters sooner.

Conclusions: This study reports use of a novel sub-perception SCS therapy that allows for clinically significant pain relief with reduced wash-in time. Further studies are needed to confirm the preliminary findings described in this report.

Objectives

1. To assess SCS pain relief in real-world patients using a novel sub-perception therapy.
2. To assess functional mobility in real-world patients using a novel sub-perception therapy.
3. To assess patient charge burden using a novel sub-perception therapy.

References

NA

Poster Presentations - May 27 - May 30
Spine - Pain

388. INS19-0416

IMPROVEMENT OF SURGICAL INTERVENTION AND SPINAL CORD LEAD PLACEMENT THROUGH AWAKE SURGERY COMBINED WITH HYPNOSIS

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Introduction: Hypnosis is used since 1995 to improve surgery and to decrease the quantities of analgesics and anaesthetics. Awake surgery is increasingly used during neurosurgery with promising results. We report 5 cases of awake surgery using hypnosis to improve the positioning of the spinal cord leads and to decrease the quantities of sedatives used during surgery.

Materials/Methods: The patients were aged 25-55 years and presented with refractory failed back surgery syndrome patients, presenting with significant and drug-resistant pain. All patients met the hypnotherapist just before the surgery. The technique used was conversational hypnosis with guided imagery. The patients were subjected to a prick with a sharp pencil and were shown that if they interacted with the hand of the hypnotherapist, the pain decreased. The leads were implanted using a Minimal Access Spinal Technology under a TCIVA protocol. During the surgery, each patient was asked to interact with the hypnotherapist using their favourite sports, hobbies and different journeys they had made.

Results: This technique helped to position the surgical lead with a patient actively participating in the tests performed. The quantity of analgesics-anaesthetics was lower and the interaction with the patient was a great experience during the whole surgery.

Discussion: NA

Conclusions: Hypnosis should be more often associated with invasive, awake spinal surgery. For the reported cases, it improved the positioning of the leads and allowed a greater interaction between the surgical team, the anaesthetists and the patient, the latter being thus encouraged and proud of having performed in such a helpful way.

Objectives
NA

References
NA

Poster Presentations - May 27 - May 30
Spine - Pain

389. INS19-0241

STAND-ALONE INTERSPINOUS SPACER TREATMENT OF LUMBAR SPINAL STENOSIS IN A HIGHLY COMORBID PATIENT POPULATION

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Introduction: Patients with lumbar spinal stenosis (LSS) and multiple comorbidities despite needing surgery for symptomatic relief may pose surgical and anesthetic challenges making surgery a high risk. One possible option is the use of interspinous process spacers to indirectly decompress and provide symptomatic relief while imparting less trauma to a patient. This minimally invasive treatment option is well proven and may be especially appropriate for highly comorbid patients that have not responded to prior conservative care or interventions for function limiting claudication.

Materials/Methods: The medical records of 46 patients with LSS who received the Superion Interspinous spacer at either one or two levels were reviewed and summarized. Each patient had multiple comorbid conditions and a history of failed conservative treatment for LSS. Patient reported outcomes such as procedure satisfaction, self-reported pain (10-point VAS scale), changes in medications, and changes in functionality were assessed.

Results: Of the 46 reviewed surgical cases (24 single-level and 22 two-level), 18 were women and the average age of the population was 68.44 (range: 38-97). The average overall VAS pain score prior to the procedure was 8.6/10, VAS leg pain score 7.8/10 and VAS back pain score 8.5/10. Following the procedure, the average overall VAS pain score was 2.7/10, VAS leg pain 1.9/10 and VAS back pain 2.4/10. Average patient satisfaction with the procedure was 3.4/4 (range: 0-4). All but two patients reported significant improvements in walking and standing abilities after the procedure. All patients had a diagnosis of neurogenic claudication and LSS, failed prior treatments to alleviate pain such as physical therapy, analgesic medications, steroid injections or SCS. Past medical histories included conditions like diabetes, cardiac conditions, stroke, COPD, cancer, depression, OA/RA or fibromyalgia.

Discussion: Comorbid patients receiving the interspinous spacer as treatment for lumbar spinal stenosis with neurogenic claudication reported high levels of satisfaction with the procedure, reduced pain, and overall improvements in mobility and functionality. These comorbid patients require additional consideration when selecting appropriate treatment pathways, with a focus on alternative surgical and non-pharmacological treatments options being particularly relevant.

Conclusions: Degenerative LSS is common in the aging population. Some of these patients may pose a high risk for invasive surgery which may be denied as a result. Debilitating claudication may then be treated using an interspinous spacer

Objectives
1. Learn Minimally invasive options for LSS
2. Learn Non opioid strategies for LSS
3. Discuss functional improvement in LSS

References
Superion Interspinous Spacer Treatment of Moderate Spinal Stenosis:4-Year ***Results***: World Neurosurg. 2017

Poster Presentations - May 27 - May 30
Spine - Pain

390. INS19-0331

HIGH DOSE OPIOID USE ASSOCIATES WITH FAILURE OF SPINAL CORD STIMULATION IN 211 PATIENTS WITH FAILED BACK SURGERY SYNDROME

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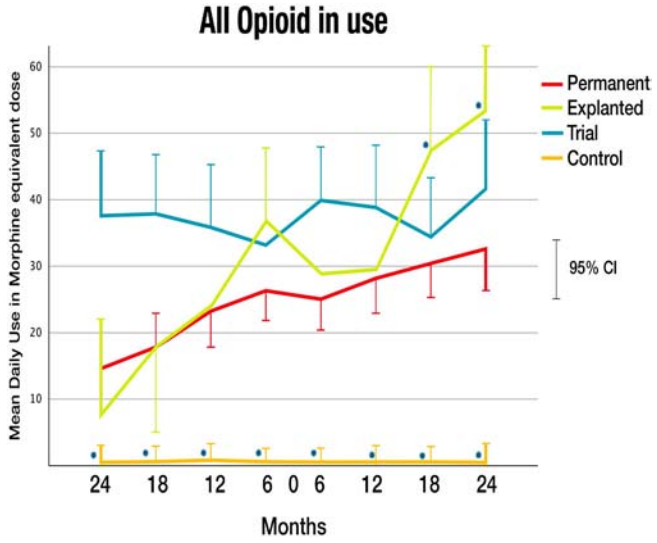
Introduction: Failed back surgery syndrome (FBSS) is a challenging condition that lacks a curative treatment. Opioids are often started before trialing spinal cord stimulation (SCS), which has proven to be an efficacious treatment in selected patients[1]. Opioid overuse is an increasing problem in modernized world[2]. We present a retrospective analysis of opioid usage among FBSS patients treated with SCS in a single institution[3].

Materials/Methods: Study group consists of all 211 patients who underwent SCS trial with a surgical lead between January 1, 1997 and March 31, 2014. For each patient, 3 controls were randomly selected by the Population Register Center of Finland, matched by age, sex, and birthplace.

All purchases of prescribed opioids between January 1, 1995, and March 31, 2016, and their daily defined doses (DDD) were retrieved from the nationwide registry, maintained by the Social Insurance Institution of Finland, including all refundable purchases of medications.

Patients were divided into three groups: SCS trial only, SCS implanted and in use throughout the follow up, and SCS implanted but explanted during the follow up. We analyzed the differences in opioid use between these groups during a period starting two years before SCS and ending two years after SCS implantation.

Results: Based on a one-week trial, permanent SCS was implanted in 164 (78%) patients. Of them, 112 (68%) were opioid users, as compared with 38 (70%) of patients with SCS trial only and 14 (2%) of controls. During the 2 years follow up period 23 (14%) SCS devices were permanently explanted, of which 19 (12%) due to inadequate pain relief. Opioid use was discontinued in 24 (21%) patients with permanent SCS but only 2 (9%) patients with explanted SCS and 4 (9%) patients with SCS trial only.



Opioid dose escalated in all SCS groups during the follow up, but not in controls (Figure 1).

Discussion: SCS patients with underlying FBSS use opioids more often and in higher doses than their matched controls.

Conclusions: Higher-dose opioid use associates with failure in SCS trial. With continuous SCS therapy, opioid dosage stabilizes, and opioids are discontinued more often.

Objectives

1) the prevalence of opioid use among SCS patients as compared to their matched controls,

2) amount of opioids used and

3) the effect of SCS on opioid use in a long-term follow up.

References

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Poster Presentations - May 27 - May 30
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391. INS19-0090

WHISPER RCT: AN UPDATED POST-HOC EVALUATION OF SUB-PERCEPTION SCS AT ≤1.2 KHZ IN PREVIOUSLY-IMPLANTED SUBJECTS

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Introduction: Results from a recent randomized controlled trial provided Level 1 evidence that equivalent pain relief using a range of frequencies from 1 kHz to 10 kHz spinal cord stimulation (SCS) with appropriate neural dosing was achieved (1). Furthermore, it was reported that 1 kHz SCS required significantly less charge than higher frequencies. The WHISPER randomized controlled trial (RCT) evaluates safety and clinical effectiveness of sub-perception Spinal Cord Stimulation (SCS) at ≤1.2 kHz in a cohort of subjects previously implanted with a SCS System for treatment of chronic, neuropathic pain.

Materials/Methods: WHISPER is a prospective, multicenter RCT with a crossover design sponsored by Boston Scientific (ClinicalTrials.gov: NCT02314000). Subjects previously implanted with SCS and a baseline overall pain score ≥6 (with SCS off) at study start were enrolled. Eligible subjects were randomized to either receive sub-perception or supra-perception for a period of 90 days and then crossed over to receive vice versa. At the completion of crossover, outcomes related to overall pain, satisfaction and preference were collected

Results: The study met its primary endpoint, based on overall pain responder rate (≥ 50% improvement from Baseline) with no increase in medications, in a pre-specified cohort of 70 randomized subjects (interim analysis) who had been previously implanted for about 4 years and with a mean disability score (Oswestry Disability Index) of 69.4. The study met its secondary endpoints. For those subjects using sub-perception SCS, significant pain relief was sustained ($p < 0.001$) at 1 year. Additionally, improvement in disability and treatment satisfaction was noted. Post-hoc analysis demonstrated that multiple options provide superior outcomes when subjects could choose the most effective option.

Discussion: The WHISPER study demonstrates that sub-perception SCS at ≤1.2 kHz is safe and effective. Waveform options provided superior outcomes when subjects could choose the most effective therapy.

Conclusions: Using sub-perception SCS, significant improvement in pain relief was sustained up to 12 months. The outcomes of the WHISPER RCT suggest that providing multiple options to patients with chronic pain has the potential to extend SCS therapy and may in turn, reduce the need for explantation.

Objectives

The WHISPER randomized controlled trial (RCT) evaluates safety and clinical effectiveness (pain relief, satisfaction, and preference) of sub-perception Spinal Cord Stimulation (SCS) at ≤1.2 kHz in a cohort of subjects previously implanted with a SCS System

References

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Poster Presentations - May 27 - May 30
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392. INS19-0093

VERITAS: PROSPECTIVE, MULTICENTER STUDY OF A NEW SCS SYSTEM CAPABLE OF MULTIPLE NEUROSTIMULATION MODALITIES

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Introduction: Technological developments can address unmet patient needs. Given the highly dynamic nature of chronic pain, a Spinal Cord Stimulation (SCS) device engineered to provide multiple neurostimulation options can enable treatment of chronic pain according to the specific, individual needs of each patient. Chronic pain patients, when given a choice, often do utilize a variety of SCS waveforms suggesting that more personalized application of neurostimulation may be a more desired and/or effective approach for managing chronic pain (1,2). We present initial results from prospectively-collected data using a system allowing for personalized SCS-based treatment of chronic pain via patient-specific utilization of combination therapy (simultaneous or sequential) and/or waveform automation.

Materials/Methods: VERITAS (ClinicalTrials.gov: NCT03251937) is a prospective, multicenter, open-label study evaluating the value of an SCS system capable of multiple modalities in obtaining significant pain relief in chronic pain patients (Precision Spectra WaveWriter, Boston Scientific). Subjects with a positive trial will receive a permanent implant and are followed up to 2 years. Assessments collected will include NRS, quality of life, ODI, and other endpoints. Key inclusion criteria include eligible candidates for SCS with no back surgery in the 6 months prior to screening. Subjects with significant cognitive impairment that may confound study results are excluded.

Results: Real-world data utilizing the same SCS System demonstrated, in a cohort of 312 subjects, a statistically significant improvement in overall targeted pain scores (NRS) at last follow up (7.3 -> 2.1, mean 106 days). This improvement was also noted at 3 and 12 months follow-up ($p < 0.0001$). This report will provide details of the study design and preliminary outcomes using the same system in prospective study where data was collected by sites.

Discussion: Results from this prospective, clinical study of an SCS system that allows for personalized based treatment for chronic pain will inform regarding patient utilization and outcomes associated with combination therapy (simultaneous or sequential) and/or waveform automation.

Conclusions: This study aims to share experience regarding the use of newly introduced SCS system that can provide multiple neurostimulation modalities. This is particularly relevant in patients who prefer multiple available options to manage their chronic pain.

Objectives

The objectives of this investigation are to collect the following clinical assessments in patients using a newly introduced SCS system capable of delivering multiple neurostimulation modalities: NRS, quality of life, ODI, and other endpoints.

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Spine - Pain

393. INS19-0082

OUTCOMES USING AN SCS DEVICE CAPABLE OF DELIVERING COMBINATION THERAPY (SIMULTANEOUS OR SEQUENTIAL) AND ADVANCED WAVEFORMS/FIELD SHAPES

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Introduction: Developing "all in one" spinal cord stimulation (SCS) systems with capability for multiple types of neurostimulation paradigms will likely empower patients to identify the best treatment approach suitable for their own needs. As these SCS systems continue to come "online", it will be important to track and evaluate how patients use these devices and their associated clinical outcomes. In this report, we provide observed real-world outcomes in patients who used an SCS system designed to combine multiple waveform availability, both sequentially and simultaneously, with an algorithm designed to enable highly manipulatable control of stimulation field shape.

Materials/Methods: This is a consecutive, multi-center case-series of patients based on retrospective chart review as part of an ongoing real-world evaluation of SCS outcomes for chronic pain (Clinicaltrials.gov identifier: NCT01550575). Patients were treated with a newly designed SCS system (Precision Spectra WaveWriter, Boston Scientific) capable of combination therapy (either sequential or simultaneous), multiple waveforms and advanced field shapes, and waveform automation for the treatment of low back and/or leg pain. Data collection includes: 1) Baseline characteristics: demographics, medical history; pain diagnosis 2) procedural information: lead configuration, programming parameters; and 3) pre- and post-implant numerical rating scale pain intensities (0-10 NRS).

Results: To date, 217 patients have been analyzed. A statistically significant improvement in overall targeted pain scores (NRS) at last follow-up was reported (Baseline NRS: 7.5; at last follow-up [96.6 $\pm$ 80.9 days] NRS: 2.4; $p < 0.0001$). Thirty-nine percent of all patients indicated >80% pain relief at their last follow-up. Twenty-two percent (48 of 217) of all patients reported being pain free (NRS = 0) at last follow-up. Updated data will be presented.

Discussion: Given the overall diversity of etiologies and experiences associated with chronic pain, the SCS-implanted patient population may particularly benefit from devices with considerable adaptability providing for individualized treatment customization. This study provides initial clinical experience regarding use of an SCS system capable of offering combination therapy and waveform automation.

Conclusions: These results provide support for the postulate that an SCS system designed to provide combination therapy, multiple waveform options, and enhanced anatomical targeting capabilities, allows for highly effective pain relief outcomes in a patient-specific manner within the real-world clinical setting.

Objectives

To report demographic, programming parameters, and pain relief data (NRS scores, Percent Pain Relief) in real-world patients using an SCS system designed to provide combination therapy, multiple waveform options, and enhanced anatomical targeting capabilities.

References

NA

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Spine - Pain

394. INS19-0150

CERVICAL SPINAL CORD STIMULATION FOR NEUROPATHIC PAIN AFTER BRACHIAL PLEXUS INJURY: THREE CASES

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Introduction: Brachial plexus injury usually occurs because of traumatic reasons especially industrial and motor vehicle accidents. After deafferentation in the upper limb, patients complain about trophic changes and neuropathic pain in cosalgia form. Pain is characterized by burning, shocking like sensation and usually resistant to conservative treatments

Spinal cord stimulation is electrical neuromodulation method that used for chronic intractable pain. In this case report we are going to present three cases that applied spinal cord stimulation due to brachial plexus injury.

Materials/Methods: Patients who diagnosed brachial plexus injury by electromyography, magnetic resonance imaging and clinical findings recruited in this study. They had neuropathic pain (DN4 score≥4). Patients undergone cervical spinal cord stimulation by using 8 contact electrodes (Medtronic) with c-arm fluoroscopy guidance. Effectivity of spinal cord stimulation was assessed with visual analog scale, decrease of pain in percentage and decrease of medication use.

Results: Spinal cord stimulation applied to three patients. Demographic parameters of patients are shown in table 1. Significantly improvement in VAS scores and decrease of medication usage were observed in all patients. Changes in clinical parameters after spinal cord stimulation are shown in Table 2.

Discussion: Neuropathic pain is common problem after brachial plexus injury. In the literature there is one case report that showed improvement in neuropathic pain after cervical spinal cord stimulation of brachial plexus injury patients. Similar with that study our patients' vas scores decreased after spinal cord stimulation.

Conclusions: In our experience spinal cord stimulation is effective treatment option in chronic intractable neuropathic pain after brachial plexus injury.

Objectives

Importance of cervical spinal cord stimulation in neuropathic pain after brachial plexus injury patients.

Effects of cervical spinal cord stimulation on medication usage.

Interventions and drugs which are used for neuropathic pain management in brachial plexus injury patients

References

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Table 1: Demographic Properties							
Patient Number	Age/Gender	Pain Localisation	Etiology	Duration after trauma	Interventions before spinal cord stimulation	Duration after spinal cord stimulation	Trial period duration
1	36/Male	Pain starting from neck and spreads to hand. Most severe in hands	Motorcycle accident	5 Years	-	18 Months	5 weeks
2	21/Female	Pain starting from neck and spreads to hand. Most severe in hands	Falling from high	7 Years	Stellate ganglion pulsed radiofrequency	9 Months	4 weeks
3	62/Male	Pain starting from elbow and spreads to hand. Most severe in 2nd and 3rd Fingers	Motorcycle accident	17 Years	Stellate ganglion blockade	2 Months	1 Week

Table 2: Spinal Cord Stimulation Effectiveness					
Patient Number	VAS before SCS	VAS after SCS	Decrease of pain (%)	Medication before SCS	Medication after SCS
1	9	3	60	Gabapentine 3200 mg/day Fentanyl patch 225 mcg/hours	
2	8	2	75	Pregabaline 150 mg/ day Amitrptilline 10 mg /day	Amitrptilline 10 mg /day
3	9	3	70	Gabapentine 1800 mg/day Amitryptilline 10 mg/day	Gabapentine 1800 mg/day Amitryptilline 10 mg/day
VAS: Visual anaog scale, SCS: Spinal Cord Stimulation					

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395. INS19-0330

RETROSPECTIVE MULTICENTER STUDY USING DORSAL ROOT GANGLION STIMULATION FOR POSTHERPETIC NEURALGIA: SPANISH AND ITALIAN RESULTS

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Introduction: Postherpetic neuralgia (PHN) is a painful complication of shingles, caused by the chickenpox (herpes zoster) virus. PHN affects nerve fibres and skin, causing burning pain and allodynia that could persist more than 3 months after the rash and blisters of shingles have healed. These patients have a reduced quality of life (QoL), physical functioning, and psychological well-being. Currently, there is no therapy for PHN.

Materials/Methods: Patients were implanted with a quadripolar lead placed over the dorsal aspect of the DRG using a minimally invasive epidural approach. The following assessments were evaluated at 3 time points, i.e. before DRG stimulation, and 6 and 12 months after: Pain scores: pain intensity and continuity of pain (rated on a 6-point ordinal scale), allodynia (3-point ordinal scale), attention to pain (5-point ordinal scale), and the intensity of continuity pain and pain crisis (10-point continuity scale). • QoL scores: personal care, activity, sleep, social life and work (rated on a 6- point ordinal scale) and mood (5-point ordinal scale). Satisfaction with the therapy (rated on a 5-point ordinal scale), and patients were asked if they would recommend the therapy or not.

Results: A total of 22 patients was enrolled at 3 sites in Spain and Italy. The mean follow-up period was 13.39 months (range: 3.47-39.27) (Table 1). After DRG stimulation, patients considered their pain as less intense, measured by their pain intensity score on a 6-point ordinal scale (1=no painkillers needed; 6=painkillers do not relieve pain, therefore not taken). Six months after DRG stimulation, 60% of the patients reported a pain intensity score of 1-3, whereas all patients (100%) reported a score of 4-6 before the therapy (see Figure 1).

Discussion: DRG stimulation has shown to be an effective therapeutic option for different localised neuropathic pain syndromes.1-3 Different neuromodulation techniques have shown to have mixed results in the treatment of PHN.4–7 As to the treatment of PHN with neurostimulation, research has been limited and an extensive body of evidence is lacking to provide better guidelines.

Conclusions: This multicentre, retrospective study shows promising results for the use of DRG stimulation in PHN patients in terms of their level of pain and quality of life. Further study is recommended and ongoing.

Objectives

Outcomes of this study showed that the intensity of allodynia and pain in general reacted positive on DRG stimulation

References

Deer T. Et al The Neuromodulation Appropriateness Consensus Committee on Best Practices for Dorsal Root Ganglion Stimulation. Neuromodulation 2018

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396. INS19-0332

PRELIMINARY DATA FOR DRG STIMULATION IN SEVERAL CONDITIONS: OBSERVATIONAL STUDY

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Introduction: The stimulation of the dorsal root ganglion is shown as an obvious advance in the therapy of neuropathic pain conditions difficult to control, especially when it is located in areas of difficult coverage for the stimulation of posterior cords such as feet, hands, inguinal area, limbs amputated and in various circumstances of visceral pain at the thoracic, abdominal or pelvic level.

Materials/Methods: From February 2014 to May 2018, 126 patients were implanted with 116 effective test periods, and a high effectiveness in the control of analgesia and other symptoms of neuropathic pain as well as a significant improvement in the quality of life with an important satisfaction of the patients. The demographic data, indication by the base pathology and effectiveness in the analgesia, as well as the anatomical levels of implant are shown in Table I.

Results: Of the total number of implanted patients, the average number of electrodes placed was 1.86 per patient, with a mobilization rate of 12.4% and a rupture rate of 24.6%. In 6 cases it was necessary to replace the generator due to exhaustion and in another 6 it was necessary to remove the generator and/or the electrodes due to pocket infection. The electrical and programming parameters are shown in Table II.

Discussion: The therapy by means of the stimulation of the dorsal root ganglion is shown as a significant advance in the chronic pain therapy of difficult control with important advantages in terms of effectiveness in certain pathologies that require precise anatomical localization of the stimulation. Likewise, the stimulation of the DRG provides alternatives to a cord stimulation of the posterior cord, which was previously ineffective. On the other hand, the need to explore new indications such as visceral pain due to the possible autonomic involvement of ganglionic stimulation give it a promising future in this regard.

Conclusions: Probably in view of the data are necessary improvements in the design of electrodes and the type of generator (rechargeable) as well as various forms of stimulation would be required as an alternative to the traditional tonic stimulation that is the only one currently designed for this device.

Objectives

Retrospective analysis indexed

References

Deer T. Et al. The Neuromodulation Appropriateness Consensus Committee on Best Practices for Dorsal Root Ganglion Stimulation. Neuromodulation 2018

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397. INS19-0392

STIMULATION OF GANGLION OF THE DORSAL ROOT FOR THE TREATMENT OF VISCERAL PAIN

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Introduction: The application of medullary electrical stimulation for the treatment of visceral pain is a controversial therapeutic procedure in regard to pain control conveyed by the sympathetic system. So far, the application of spinal neurostimulation of posterior cords for various visceral pain conditions has been made specific to refractory angina, chronic pancreatitis and other forms of abdominal pain (1). The appearance of the new concept of stimulation of the dorsal root ganglion where a functional and anatomical connection with the autonomic control pathways is established (2) has made assessing the dorsal root ganglion stimulation as a possible effective therapy for visceral pain.

Materials/Methods: We present 6 cases of patients affected by different types of visceral pain (2 chronic pancreatitis, 2 ischemic heart disease 1 achalasia and 1 nutcracker esophagus) that after an effective test of pain relief by selective metameric blockade of the dorsal root ganglion was implanted bilateral at various thoracic levels, first in the trial phase and then definitively.

Results: The reduction of pain and improvement in the quality of life score (Table 1) in all cases was significant, and only in the case of the nutcracker esophagus had to proceed to the expansion of the number of electrodes implanted to expand the area of coverage.

Discussion: Although the number of cases is still scarce, the quality of pain relief using this type of stimulation in the cases of visceral pain described, promises this indication of neurostimulation for the future in the treatment of visceral pain of different etiologies.

Conclusions: Although the number of cases is still scarce, the quality of pain relief using this type of stimulation in the cases of visceral pain described, promises this indication of neurostimulation for the future in the treatment of visceral pain of different etiologies.

Objectives

visceral pain and drg stimulation

References

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Poster Presentations - May 27 - May 30
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398. INS19-0325

SINGLE-CENTER 3-YEAR ANALYSIS OF NEUROSTIMULATION EXPLANTS

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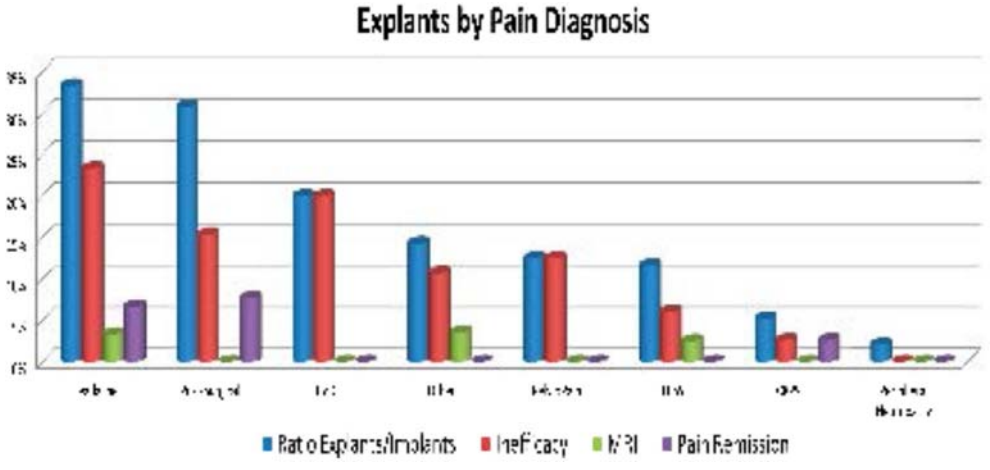
Introduction: Neurostimulation explants are rather common and arise from different causes, the most frequent probably is loss of efficacy. Other reasons for explantation are clinical complications, need for MRI, malfunctions, and pain remission.

Materials/Methods: A special form was designed to record explants, including gender, age, BMI, medical history, psychologic issues, pain characteristics; Neurostimulation system, plus data related to infection when applicable.

Results: Of a total population of 368 patients with SCS implants when the survey was initiated, 46 systems were explanted in the last 36 months. Remarkable findings were:

- Most common reasons for explantation are loss of efficacy (n=26, 56.5%), MRI (n=7, 15.2%), infection (n=6, 13.0%) and Pain Remission (n=4, 8.7%)
- FBSS is the most common indication for neurostimulation (53.54% of all implants) and is well correlated with its explantation rate (50.0%), despite the fact that "need for MRI" was relatively relevant in this group (5/23, 21.7%).
- The lowest explantation rates were scored by Peripheral Neuropathies (1/27, 3.7%) and CRPS (2/14, 14.3%).
- The highest explantation rate was found in headache (10/30, 33.3%), but it also scored the highest ratio of pain explants due to pain remission (2/10, 20%).
- The other two cases of pain remission which allowed system explantation was 1 CRPS and 1 post-surgical pain.



- Explants due to loss of efficacy seem to be more common in women (which represent 67% of explants vs only 58% of implants), and in patients younger than 40 years old (35% of explants vs only 14% of implants) vs. patients older than 50 (13% vs. 23%) and 60 (13% vs. 24%).

- No conclusions could be reached from the 6 cases of infection.

Discussion: Loss of efficacy and need for MRI were the most common reasons for SCS explant. New systems capable of producing different stimulation types and/or conditionally compatible with MRI imaging, will possibly help to improve explantation rates.

Conclusions: Aware that the series is too short so far, we will continue to use and share this tool as routine in our Unit to try to understand and improve explantation rates in the future.

Objectives

- Reasons for explant in neurostimulation
- Loss of response to neurostimulation
- Managing unsatisfied neurostimulation patients

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Spine - Pain

399. INS19-0068

THE EPWORTH HEALTHCARE NEUROMODULATION REGISTRY: 16-MONTHS OF DATA COLLECTION

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Introduction: The Epworth Neuromodulation registry was developed following recent low trial-to-permanent conversion rates of 41%[1] and long-term stimulation failure. Data collection commenced for spinal cord stimulation (SCS) procedures in July 2017 including past medical history, pain history, diagnoses, procedural details and standardised patient-reported outcome measures including visual analogue scale, brief pain inventory, patient global impression of change and pain self-efficacy questionnaire. A clinical registries utility is the ability to gain insight into real-world care and current practice[2,3]. This study aims to provide a descriptive summary of the performance of this registry 16-months on since data collection commenced.

Materials/Methods: All patients that underwent trial/stage 1 procedures or both the trial/stage 1 and permanent/stage 2 procedures were included in this descriptive summary. Total number of trial/stage 1, permanent/stage 2 and revision procedures were reported. Gender ratios, age breakdown, insurance status and clinical diagnoses were also reported.

Results: Eighty-nine patients were entered into the registry following trial/stage 1 procedures between July 2017 and October 2018. Of these, 59 were private patients, 21 WorkCover, 5 DVA and 4 TAC. Three patients were aged between 0-29 years, 9 between 30-39 years, 15 between 40-49 years, 14 between 50-59 years, 19 between 60-69 years, 24 between 70-79 years and 5 over 80 years. There have been 22 diagnoses of failed back surgery syndrome, 21 of low back pain, 15 of a history of spinal surgery, 9 of lower limb radiculopathy, 4 of pelvic pain, 12 of peripheral neuropathy, 5 of neck pain, 6 of failed neck surgery syndrome and 6 of headaches. Of these 89 patients, fifty-six (63% trial-to-permanent conversion rate) underwent permanent/stage 2 procedures (25 males and 31 females). Thirty-five of these have reached the six-month post permanent/stage 2 procedure milestone, while eleven have achieved the twelve-month milestone. Three patients have returned for revision procedures.

Discussion: As data collection continues, this registry will provide additional insight for clinicians into predictors of SCS success, long-term outcomes and complication monitoring.

Conclusions: This registry has the potential to set a benchmark for quality data collection following SCS procedures with the ultimate goal to contribute to improving overall trial-to-permanent conversion rates and long-term outcomes.

Objectives

- Data collection is from a wide range of clinical diagnoses and patient demographics
- Current trial-to-permanent conversion rate is greater than previous reports
- Data collection will continue to inform future clinical practice

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400. INS19-0069

THE EPWORTH HEALTHCARE NEUROMODULATION REGISTRY: COMPARING PATIENT-REPORTED OUTCOMES IN PATIENTS RECEIVING TEMPORARY LEAD TRIALS VERSUS PERMANENT LEAD TRIALS

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Introduction: The Epworth Neuromodulation Registry commenced data collection following spinal cord stimulation (SCS) procedures in July 2017. While clinical registries gain insight into current clinical practice and inform future practice, reports of low trial-to-permanent conversion rates[1] highlight the importance of investigating different procedural techniques. Given SCS success is largely dependent upon correct lead positioning and recent reporting on failed-trial rates and complications comparing temporary lead trials to permanent lead trials[2], this study aims to utilise registry data to compare patient-reported outcomes following temporary lead trials versus permanent lead trials.

Materials/Methods: Patient data was extracted from the registry that met the following criteria. Diagnoses of low back pain, failed back surgery syndrome or history of spinal surgeries. Patient-reported outcome measures at baseline, during trial period and post permanent implant. Patient-reported outcomes included visual analogue scale (VAS) and brief pain industry (BPI). Patient data were divided into two groups; temporary or permanent lead trials.

Results: Eight patients were included, five temporary lead trials and three permanent lead trials. The average number of days between trial and permanent implant was 65.8±13.65 for the temporary lead group and 6.33±1.15 for the permanent lead group. For the temporary lead group, VAS scores were 6.40±2.07 at baseline, 3.80±1.10 during trial period and 2.60±1.52 at 21 days post permanent implant while BPI scores were 64.91%±22.91% at baseline, 39.00%±21.69% during trial period and 30.91%±10.81% post permanent implant. For the permanent lead group, VAS score were 6.00±1.41 at baseline, 4.00±2.65 during trial period and 4.00±2.00 at 23 days post permanent implant while BPI scores were 58.28%±22.78% at baseline, 40.91%±32.88% during trial period and 44.85%±26.80% post permanent implant.

Discussion: These results suggest both temporary and permanent lead trials improve VAS and BPI scores post permanent implant. While both techniques improved patient-reported outcomes, the magnitude appeared greater following temporary lead trials versus permanent lead trials, consistent with previous reports2. Given low samples sizes however, these preliminary conclusions must be made with caution.

Conclusions: As data collection continues and sample sizes increase, this registry will provide unique insight into the long-term outcomes of these two lead trial techniques.

Objectives

- This registry identified two lead trial techniques
- Despite low sample sizes, these results show improvements in VAS and BPI scores for temporary and permanent lead trials
- Continued data collection and increased sample sizes, will allow this registry to provide ongoing comparisons between both lead trial techniques

References

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2. Simopoulos et al. Neuromodulation 2018;21:508-512.

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401. INS19-0333

CASE STUDY: REFRACTORY ANGINA PECTORIS PATIENT TREATED WITH DORSAL ROOT GANGLION STIMULATION

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Introduction: Refractory angina pectoris pain has been successfully managed with SCS since 1990's, and has proven to be a cost-effective treatment for RAP. Although a single epidural lead placed at T3 level is usually enough to cover the painful area, some patients may need more stable and specific stimulation patterns.

Materials and Methods: Patient suffering from highly debilitating non-manageable microvascular ischemic cardiopathy (multiple daily angina episodes triggered by mild exercise). She received the implant of a SCS system, which significantly decreased number and severity of angina episodes. Nevertheless, right side coverage was difficult from the beginning, requiring high levels of energy. The system was finally replaced by a bilateral T3 DRG stimulation system.

Results: Full coverage was achieved with low levels of energy in both sides. Patient refers stable and specific stimulation covering her anginous pain entirely, refers controlled pain. These results remain 10 months after implantation.

Discussion: DRG stimulation's ability to produce very stable and precisely targeted paresthesias may serve for some RAP patients whose long-term management with conventional SCS is difficult.

Conclusions: RAP as potential indication for DRG stimulation

***Objectives*:** RAP as potential indication for DRG stimulation.

***References*:** de Jongste MJ, et al. Efficacy of spinal cord stimulation as adjuvant therapy for intractable angina pectoris: a prospective, randomized clinical study.

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402. INS19-0334

DORSAL ROOT GANGLION STIMULATION (DRGS). LONG-TERM EXPERIENCE WITH 100 PATIENTS.

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Introduction: DRGs has been thoroughly used in the past few years in the treatment of several so-called focal chronic pain syndromes [1] and has demonstrated superiority over the traditional tonic SCS in patients with CRPS [2]. Here we present our experience with our first 100 patients implanted with permanent DRG systems.

Materials/Methods: All patients implanted with DRG systems in our hospital from 2014 to 2018 have been included in this review. We present an analysis of the therapy's performance depending on each patient's diagnosis and painful area.

Results: 108 patients received the implant of DRG leads between March 2014 and October 2018. 55 patients passed a stimulation trial phase and 53 received straight permanent system. There were 7 negative tests, and one patient had its system explanted 3 months after implantation. A total of 100 implants for 21 different pain pathologies in 9 areas are analyzed.

Discussion: Permanent electric stimulation of the DRG is a valid long-term therapy for neuropathic focal pain syndromes and may render optimum results in pathologies/anatomical areas hard to reach with traditional SCS, such as anterior/posterior chest regions, distal upper and lower extremities, groin and knee. With regard to more extended regions, DRG may yield positive results but dorsal column stimulation should still be considered the best choice.

Conclusions: After 100 patients treated with DRG stimulation, this therapy is well established in our Unit as best choice for several syndromes.

Objectives

Indications & targets for DRG stimulation.

References

1: doi: 10.1111/ner.12685
2. doi: 10.1097/j.pain.0000000000000814

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403. INS19-0255

DEVELOPMENT OF A MR COMPATIBLE MECHANICAL STIMULI FOR FMRI ASSESSMENT OF PAIN

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Introduction: fMRI studies on pain perception have been limited by use of thermal stimuli due to the lack of a reliable, reproducible mechanical stimuli that is MR compatible. We have developed a mechanical device that is MR compatible, applies a measurable amount of pressure and includes a base and finger support to limit the impact of patient variability on results (Fig 1). Here we validate its use in control and chronic pain patients.

Materials/Methods: Healthy controls (n=11, mean age 39 (range 22-57), 5 men/6 women) and patients with chronic pain (n=4, mean age 65 (range 61-71) underwent testing with our device. The level of pressure where discomfort occurred was documented on repeated trials.

Results: In healthy controls, discomfort was induced with a mean pressure of 17.3$\pm$0.04 psi with a variance of 0.06. Pressure scores remained consistent for three repeat trials at various time points in a single day ($p=0.82$, using a repeated measures ANOVA). In chronic pain patients, the mean pressure was to discomfort was 16.5$\pm$0.15with a variance of 0.07. The amount of pressure to induce pain was significantly less in chronic pain patients ($p<0.001$). There was a small but significant correlation between pressure scores and pain levels on numeric rating scale score in control patients ($p=0.03$, $R2=0.23$).

Discussion: The reproducibility of pressures necessary to induce pain over three trials in the healthy control group help to demonstrate the validity of this novel stimulation device and its viability as a tool in future fMRI pain studies

Conclusions: Future studies will be implemented to validate our mechanical pressure device in a larger sample of chronic pain patients.

Objectives

To validate the use of a novel mechanical pain stimuli in control and chronic pain patients.

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404. INS19-0351

EFFECTS OF 10 KHZ HIGH FREQUENCY STIMULATION ON SPATIO-SEPCTRAL NEURAL PATTERNS IN CHRONIC PAIN

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Introduction: The success of spinal cord stimulation (SCS) for refractory chronic pain conditions is well documented[1]. Yet, treatment remains suboptimal for significant subsets of patients with little to no control over their pain[1]. Even though increased benefit has been shown with novel waveforms such as 10 kHz high frequency stimulation (HFS), only one study has examined the SCS and EEG to date[2], and the effect of SCS on neural patterns in chronic pain is still unclear. Therefore, we explored the spatio-spectral dynamics of SCS at the cortical level in chronic pain.

Materials/Methods: We recorded 16-channel resting state EEG from 3 chronic pain patients (68±7.5yo), who were diagnosed with Failed Back Surgery Syndrome, during stimulation OFF (baseline) and stimulation ON at 10kHz. Following preprocessing of EEG signals, power spectral density estimates were computed, and the spectral features were extracted from motor (MI) and somatosensory cortex (SI). The primary and secondary outcome measures were collected before and 4±2.6mo after SCS surgery. Finally, the trends between the objective measures and the multi-dimensional pain scales were evaluated.

Results: The spectral power distribution of baseline EEG and HFS showed clear peaks at theta (4-7Hz) and alpha (8-12Hz) bands. When the alpha-to-theta peak power ratio between OFF and ON states were investigated, two subjects (P2, P3) showed increased power ratio (≥2dB) indicating faster rhythms in MI and SI under pain relief while one subject (P1) showed less amount of positive change in SI. Total power in beta band (13-21Hz) was lower in P2-3 under HFS while P1 did not present visible changes. Assessment of pain scores indicated negative linear trends with relative alpha and beta power while positive linear trends with power ratio in SI.

Discussion: These preliminary results provide initial evidence for alterations in brain electric activity in response to 10 kHz HFS in the short term. As previously indicated in chronic pain subjects compared to healthy controls[3], our findings also showed decrease power in theta and beta bands and faster alpha rhythms in MI-SI regions in response to HFS (pain relief).

Conclusions: Our preliminary results might show an underlying pathophysiology and its responses to 10 kHz HFS in chronic pain patients.

Objectives

1) Investigate EEG dynamics under 10 kHz HFS in chronic pain conditions

2) Characterize spatio-spectral features as objective measures in pain

3) Evaluate interactions between objective and subjective pain measures

References

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[2] De Ridder et al., 2013. *World Neurosurg*.
[3] Sarnthein et al., 2006. *Brain*

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405. INS19-0209

HIGH FREQUENCY SPINAL CORD STIMULATION EFFECTIVE TREATMENT FOR DRUG-INDUCED PERIPHERAL POLYNEUROPATHY

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Introduction: The treatment of refractory chronic pain with epidural spinal cord stimulation has become one of the hallmarks of neuromodulation. The types of pain etiologies treated using spinal cord stimulation have grown immensely. The use of spinal cord stimulation for peripheral neuropathy is well cited in the literature. [1,4,5,6] Many drugs can cause particularly painful mono and polyneuropathies, particularly, chemotherapeutic agents such as platinum agents, vinca alkaloids, and taxanes. [9] Less commonly, long term therapy with antibiotics such as linezolid can cause painful peripheral neuropathies.[2,3,7,8]

Materials/Methods: We present a case of a 72 year old male treated with long-term Linezolid for a lower extremity mycobacterium chelonae who developed subsequent polyneuropathy of the lower extremities.

Results: A 72 year old male presented with a 2 years of painful, bilateral lower extremity neuropathies. Three years prior, the patient was treated with an 8 month course of Linezolid for leg ulcers caused by mycobacterium chelonae. The linezolid therapy was terminated due to interval development of peripheral polyneuropathy. His neuropathy was described as bilateral, lower extremity painful parasthesias that radiated to his feet. EMG/NCS demonstrated bilateral sensorimotor polyneuropathy of the lower extremities. He was trialed on both, gabapentin and pregabalin, which did not offer any relief. On physical examination, the patient had multiple scars on his lower extremities and hypesthesia of his distal lower extremities in a non-dermatomal distribution. The rest of the physical examination was unremarkable.

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A trial of high-frequency, paresthesia free stimulation gave greater than 50% reduction in pain. The patient desired the least invasive procedure possible so two 1x8 percutaneous leads were staggered over T8-T10 and connected to an internal programmable generator. Post-operatively patient had excellent coverage of pain and continues to use his therapy daily.

Discussion: Treatment of drug-induced peripheral polyneuropathies is difficult. Often first line medications do not offer significant benefit. High-frequency, paresthesia free spinal cord stimulation offered significant improvement in pain. Spinal cord stimulation has been shown to improve neuropathic pain. We believe more studies are needed to expand its indications to include drug-induced peripheral polyneuropathies.

Conclusions: Spinal cord stimulators are an excellent treatment for multiple types of peripheral neuropathies that are refractory to conservative measures. This includes uncommon drug-induced peripheral neuropathies such as those caused by linezolid.

Objectives

1. Describe drug-induced peripheral polyneuropathies.
2. Review common treatment options for drug-induced peripheral polyneuropathies.
3. Provide an example to support the use of high-frequency, paresthesia free spinal cord stimulation use in drug-induced peripheral polyneuropathies.

References

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406. INS19-0212

REVIEW OF CAUSES OF POST-OPERATIVE WEAKNESS AFTER SPINAL CORD STIMULATION PADDLE PLACEMENT AND CASE REPORT OF HEMOSTATIC AGENT CAUSING SPINAL CORD COMPRESSION

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Introduction: Post-operative weakness due to mass effect is an uncommon, and possibly, underreported complication associated with small thoracic laminectomies for spinal cord stimulator placement.[2] The vast majority of these cases are associated with epidural hematomas. Hemostatic agents, such as gelatin matrices, have also been reported to cause epidural compression after spine surgery.[1]

Materials/Methods: We present a case of a patient with von Willebrand's disease who developed post-operative weakness in a relatively delayed fashion caused by a hemostatic agent.

Results: A 67 year old female with Von Willebrand's Disease presented with chronic pain in back and bilateral lower extremities. It was felt spinal cord stimulation could offer her significant benefit. Given her bleeding disorder, a staged paddle trial was performed. The surgical bed was noted to be very dry upon closure and a cellulose hemostatic agent was left in the epidural space to help prevent any further epidural bleeding. Just under 36 hours from surgery the patient developed severe weakness (2/5) in her right lower extremity. Imaging was concerning for fluid collection causing spinal cord compression. The patient was taken for emergent decompression. Intraoperatively a gelatinous mass was discovered where previous hemostatic agent had been left. The mass was removed and the paddle and cord were noted to resume a more normal anatomical position. Fluoroscopy verified the paddle was at the desire location. Post-operatively the patient did very well and underwent permanent generator placement a week later without complication.

Discussion: Thoracic laminectomies for spinal cord stimulation paddle placement have similar risks and causes of post-operative weakness. The most common culprit is epidural hematoma2; however, hemostatic agents may also expand with time causing cord compression. This risk must be considered when performing paddle placement.

Conclusions: Placement of hemostatic agents with expansile properties in the thoracic spine should be done with caution. These agents may potentially cause epidural spinal cord compression in the setting of spinal cord stimulator placement.

Objectives

1. Review common causes of post-operative weakness after paddle placement.
2. Provide an example of hemostatic agent causing spinal cord compression.
3. Review workup of post-operative weakness after paddle placement.

References

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407. INS19-0215

ASYMMETRIC RESPONSE TO HIGH-FREQUENCY 10KHZ SPINAL CORD STIMULATION AND DISCUSSION OF POTENTIAL MECHANISMS

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Introduction: High-frequency 10kHz spinal cord stimulation (SCS) has been shown to improve chronic pain in patients with failed back surgical syndrome without production of paresthesias. Rationalized by extensive, long-term outcome data and lack of correlation of sensory stimulation mapping data to distributions of pain, anatomic placement of electrodes in midline over T9-10 interspace is recommended by the manufacturer. Typical responses include paresthesia-free bilateral reduction in pain.

Materials/Methods: We present a patient with asymmetric response to 10kHzSCS.

Results: A 52 year-old male with loss of therapy from a long-standing SCS system underwent a percutaneous trial for salvage first at T7-11 with high density stimulation (80 microseconds, 1000 Hz) with <40% improvement in left lower extremity pain only. The trial leads were repositioned to span the T9-10 interspace and 10kHzSCS was trialed for an additional 3 days with 60% relief in pain. He underwent removal of previous SCS device and implantation of epidural paddle over T9-11 (Figure1). 6 weeks postoperatively, the patient reported 60% improvement in left leg pain and 20% improvement in back and right leg pain. Stimulation mapping over the majority of the lead created paresthesias in left leg, thigh, or chest. The inferior 2 contacts on the paddle's right side provided paresthesias in the right shin and ankle. A 10kHzSCS program over these contacts was provided. After 4 months, left leg VAS had decreased from 8 to 2 and on the right from 8 to 5. Back VAS decreased to 4 bilaterally, and the patient was overall very satisfied with his device, able to reduce pain medication doses by 50%, and go fishing for first time in years.

Discussion: This is the first reported instance of asymmetric response to 10kHzSCS therapy. Prior investigations into lack of correlation between lead position and 10kHzSCS outcomes were performed with percutaneous leads in non-SCS salvage patients; the biophysical and geometrical differences in this patient may have contributed to the asymmetric response.

Conclusions: Anatomical midline placement of epidural SCS may not correlate with physiologic midline and may result in asymmetrical response to stimulation. While this has been a foundational premise for paresthesia-based SCS, there may be some sensitivity to electrode mediolaterality in 10kHzSCS. Further exploration using sensory mapping data may provide further insights into mechanisms of 10kHzSCS.

Objectives

1. Review proposed mechanisms of action of 10kHz SCS.
2. Present case of unilateral response.
3. Discuss anatomic versus physiologic midline and its role in SCS.

References

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408. INS19-0378

SPINAL CORD STIMULATION FAILURES: UNDERLYING MECHANISMS AND CLINICAL OUTCOMES

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Introduction: Despite a successful trial before implant of a spinal cord stimulation (SCS) device, long-term treatment failures characterized by device explants still occur in ~25% of SCS cases. Some underlying mechanisms of action (MOA) for SCS are well understood and may offer insight into the long-term failure rate.

Materials/Methods: Review literature for the causes and rates of SCS failure, accepted MOA for SCS, possible explanations for therapy failure, and potential solutions.

Results: The MOA for SCS in humans proposes an inhibitory effect of dorsal column (DC) stimulation on neuropathic pain. However, patient

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physiology and physical activity may result in significant variation in DC activation leading to recruitment of A-fiber nociceptors. If Aβ nociceptor input increases spinal cord excitability through sensitization, then the pain inhibition afforded by SCS may be overcome. Evoked compound action potential (ECAP) recordings can now be made in humans using new neuromonitoring platform technology, which measures the magnitude of spinal cord activation with each electrical stimulus delivered (ie, ECAP amplitude), thereby facilitating closed-loop SCS. Although the ECAP amplitude cannot be predicted from reported stimulus intensity, it should be possible to correlate ECAP amplitude and pain relief. Initial clinical findings and ECAP recordings with fixed-output SCS in humans suggest that long-term failure is likely due to intolerance to stimulation over time. Data from animal models suggests that there may be a correlation between the magnitude of spinal cord activation and the duration and degree of pain relief. Consequently, a treatment window (ie, therapeutic window) may be available for improving efficacy of SCS-induced analgesia by maintaining Aβ fiber activation and avoiding overstimulation that leads to intolerance.

Discussion: Literature suggests researchers have had little success in improving responder rates in SCS for 3 reasons: [1] few randomized, controlled trials characterize responders; [2] assessment of the effectiveness of SCS has been limited to subjective outcomes (eg, Visual Analogue Scales); [3] measuring neural response to SCS has not been technologically feasible until recently.

Conclusions: A novel closed-loop SCS device records ECAPs from the spinal cord, a measure of the number of activated Aβ fibers. The establishment of the relationship between DC activation and therapeutic outcome will provide an objective basis for monitoring outcomes over time.

Objectives

1. Identify rates and causes for SCS long-term failure
2. Explain underlying mechanisms for loss of efficacy, and describe the difference between SCS tolerance and intolerance
3. Understand the difference between closed-loop and open-loop SCS and its effect on long-term outcomes

References

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409. INS19-0146

A PILOT STUDY TO SEE THE EFFECTIVENESS OF HIGH DOSE SPINAL CORD STIMULATION FOR INTRACTABLE LUMBAR RADICULOPATHY ON VIRGIN-BACKS – UK SINGLE CENTRE INTERIM DATA

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Introduction: Spinal Cord Stimulation (SCS) is traditionally used for patients with neuropathic pain following failed back surgery. However, SCS is increasingly being used in patients with intractable neuropathic pain who have not undergone previous spinal surgery[1]. Nevertheless, data in the use of paraesthesia-free stimulation in this population is limited. Therefore, the primary aim of this study is to investigate the clinical response following SCS implant and High Dose (HD) programming in this group. The secondary objectives are to investigate the effect on quality of life and adverse events.

Materials/Methods: This is an open label, single-centre pilot study. Patients with intractable neuropathic pain (n=20) due to undergo SCS (Medtronic RestoreSensor™®) as part of their standard treatment are being recruited. Pain scores (Numerical Rating Scale, NRS) and quality of life outcomes will be collected pre-implant and at 4-weeks, 12-weeks and 12-months postoperatively.

Results: At present, 13 patients have completed baseline questionnaires. Twelve patients have completed 4-week follow-up and 11 have completed 12-week follow-up questionnaires. Six patients have completed 12-month follow-up. At baseline, the mean NRS score for lower back pain and leg pain were 7.64±1.29 and 6.15±2.10 respectively. At 4-weeks post-implant, the average reduction in lower back pain is 5.30±3.02 (−67.76% vs. baseline) and 3.04±2.54 (-52.89% vs. baseline) for leg pain. At 12-months post-implant (n=6), the average reduction in lower back pain is 4.06±4.07 (−49.53% vs. baseline) and 4.06±2.66 (-57.77% vs. baseline) for leg pain.

Furthermore, a reduction in ODI scores of an average 20.33±24.35 (31.65% vs. baseline) is seen at 4-weeks follow-up and 20.17±26.05 (34.74% vs. baseline) at 12-months. Up-to-date interim results will be presented at INS.

We have had 3 adverse events including two falls prior to 3-month follow-up and 1 charging issue resulting in sub-optimal therapy until IPG surgical revision.

Discussion: This study is over half-way through recruitment. So far the results indicate that patients in this population sustain around 50% pain relief at 12-month post-implant.

Conclusions: Currently, the interim data of this study demonstrates High Dose SCS may be an effective therapy to reduce lower back and leg pain in patients who have not previously undergone spinal surgery.

Objectives

Investigate the clinical response following HD SCS in patients with lumbar radiculopathy who have not undergone any spinal surgery.

Investigate the effect of HD frequency parameters on the improvement of quality of life.

Report adverse events following SCS.

References

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Spine - Pain

410. INS19-0300

TREATMENT OF CHRONIC BACK AND LEG PAIN (CBLP) PATIENTS WITH A NOVEL MINIATURE WIRELESS SPINAL CORD STIMULATION SYSTEM

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Introduction: Spinal cord stimulation (SCS) is an evidence-based therapy for chronic back and leg pain (CBLP). Most current SCS systems depend on an implantable pulse generator (IPG) to pace epidural leads. The objective of this study was to investigate the efficacy and safety of a novel miniaturized multi-contact SCS device in selected patients with CBLP.

Materials/Methods: A total of 30 patients (15 males and 15 females, 31-90 years) with medically intractable CBLP were selected according to recommended clinical criteria. They underwent implantation of one epidural SCS device with the tip at T8. Responders had > 50% reduction in back and leg pain visual analog score (VAS). After a 4 week trial, a second device was placed parallel to the first one and staggered at T9.

Results: After a trial with the single SCS device, 28 patients (93,4 %) responded with reduction of 50-90% of baseline. At 3 months, 29 patients (96,7 %) reported a greater amount of pain relief than with the single device, and 25 patients (83,5 %) were able to significantly reduce or stop oral analgesics. One patient reported insufficient pain relief (< 50 % of baseline) with both devices. There were no procedure-related complications, no hardware failures, no infections and no undesirable side effects. At 12 months follow-up, VAS scores did not change significantly, indicating stable long-term pain relief. One patient (3,3 %) was explanted because of lacking efficacy of the devices.

Discussion: The trial period with the novel SCS device could be extended to any desired length because the risk of infection was mitigated. The use of two multicontact SCS devices allowed for the transmission of the highest possible density of electromagnetic energy to the dorsal column, resulting in successful treatment of back pain in addition to improvement of leg pain. The use of multiple implants increased the overall pain reduction and improved the long-term results, making them stable over the course of at least 12 months.

Conclusions: In our hands, this novel miniaturized IPG-free SCS device is effective, safe, convenient to the patient, simple to place, and promises to substantially impact the management of medically intractable chronic pain conditions. The device simplifies the process of evaluation of trial effectiveness. The subcutaneous implantation of an IPG of considerable size is avoided. The simplified implant procedure and the excellent safety profile of the new device may offer health cost savings.

Objectives

Spinal cord stimulation for chronic back and leg pain

References

None

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411. INS19-0044

CERVICAL STIMULATION WITH PADDLE LEAD: HOW TO MANAGE?

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Introduction: Spinal cord stimulation is now a treatment of pain in refractory failed back surgery syndrome. Upper limb pain comprises a significant proportion of neuropathic pain patients, but is often difficult to target specifically and consistently with paresthesias.

Materials/Methods: 30 patients (aged 27-88, mean value 50.2) with chronic cervical and /or upper limb pain were evaluated, with VAS Score, Medication quantification Scale (MQS), the patient satisfaction, before and after stimulation. Stimulation was proposed after failure of multidisciplinary management

Electrode stimulation was implanted under general anaesthesia and a test of 7 days was performed at home. The battery was implanted only if VAS score decreased than more 50%. Mean Follow up was 37 months (range 4 to 96 months).

Results: 28 patients were implanted with good VAS score decreased from 8.6 in preoperative conditions to 2.6 in postop conditions. 63% of patients estimated than they were very satisfy of the surgery and they could propose that to other patients. The MQS decreased from 25 in preop to 11 at the last follow up. We have 2 infections and 2migration of électrodes.

Discussion: This surgery was well tolerated, safe. The results of the literature are comparable with our series. Tonic stimulation is well tolerated but other waveforms can provide a significant benefit to the patient by decreasing the paresthesia

Conclusions: Cervical stimulation is safe for patients and can treat upper limb pain as well as neck pain. Multiwaves stimulation can avoid some side-effects.

Objectives

Cervical stimulation is safe
Good results with paddle lead
Multiwaves can be useful

References

Deer T, Slavin KV, Amirdelfan K, North RB, Burton AW, Yearwood TL, Tavel E, Staats P, Falowski S, Pope J, Justiz R, Fabi AY, Taghva A, Paicius R, Houden T, Wilson D. Success Using Neuromodulation With BURST (SUNBURST) Study: Results From a Prospective, Randomized Controlled Trial Using a Novel Burst Waveform. Neuromodulation. 2018 Jan;21 (1):56-66. 29 ; Thomson SJ, Tavakkolizadeh M, Love-Jones S, Patel NK, Gu JW, Bains A, Doan Q, Moffitt M. Effects of Rate on Analgesia in Kilohertz Frequency Spinal Cord Stimulation: Results of the PROCO Randomized Controlled Trial. Neuromodulation. 2018 Jan;21(1):67-76.

Poster Presentations - May 27 - May 30
Spine - Pain

412. INS19-0104

THE DORSAL ROOT GANGLION (DRG) IS A TARGET FOR STIMULATION IN CHRONIC PAIN SYNDROMES A SINGLE CENTER EXPERIENCE WITH STIMULATION OF THE DRG IS PRESENTED

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Introduction: Chronic neuropathic pain syndromes may develop after trauma, injury or surgery at or in the region of peripheral nerves. In many cases a causative treatment is not possible and patients are treated conservative, pharmacological and in multimodal settings. In cases of peripheral nerve lesions and refractory pain the dorsal root ganglion plays a significant role for pain transmission and since 2012, it is a target for invasive neuromodulation implants. The clinical experience of dorsal root ganglion stimulation (DRGS) and a patient cohort of a single centre are presented.

Materials/Methods: Refractory chronic neuropathic pain syndromes of the upper, lower extremities or the trunk were diagnosed in 47 patients (23 female, 24 male; age: 23-89 years). Chronic pain developed after peripheral nerve injury of the extremities, intercostal nerves, inguinal nerves etc. The quadripolar leads were implanted at multiple spinal levels from C5- down to S1-DRG. A test trial for 7 days was conducted. In case of pain reduction of > 30% and concomitant withdrawal of analgesics the indication for the permanent stimulation device was given.

Results: In all patients at least two leads were positioned at the targeted DRG´s using fluoroscopic guidance. Usually, implantation was performed in local anaesthesia and with intraoperative paraesthesia testing. In two patients with neuropathic pain of the upper and lower extremities, two leads each were implanted at the cervical and lumbar levels. Significant pain reduction was achieved in 45/47 (96%) patients. In all positive responders a reduction of analgesics was initiated. In the follow-up course from 3 months up to 6.5 years a total number of 40 procedures were noted in the patient sample. These include battery replacements (n=18) but also revision procedures because of lead dislocations and breakage of the leads or extensions. In two patients the devices were explanted due to ineffectiveness after 2 and 5 years.

Discussion: In comparison to spinal cord stimulation certain advantages like lower amplitudes, less motion dependant effects and a more consistent stimulation were observed.

Conclusions: DRGS is a safe and effective procedure to treat neuropathic pain syndromes in well described areas of the extremities or the trunk.

Objectives

Favourite indications seem to be neuropathic pain syndromes after peripheral nerve lesions like complex regional pain syndromes, post-herniorraphy-pain, post-thoracotomy-pain, knee pain after surgery etc.

Complication management in the follow-up course is recommended.

This specific procedure should be performed in experienced centres for functional neurostimulation and invasive neurosurgical pain therapies.

References

T. Deer et al: Pain. 2017 Apr;158(4):669-681.

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413. INS19-0223

ARE PAIN SCORES AN APPROPRIATE MEASURE OF TRIAL SUCCESS AND LONG-TERM EFFICACY, IN CHRONIC PAIN PATIENTS TREATED WITH SPINAL CORD STIMULATION?

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Introduction: Spinal Cord Stimulation (SCS) is recommended by the National Institute of Health and Care Excellence (NICE) guidelines for the management of patients suffering from chronic neuropathic pain. The guidelines suggest patients should complete a trial period prior to full implantation. A majority of literature appears to have measured trial success by a given reduction in Visual Analogue Scale (VAS) or numerical rating scale (NRS) pain score over 1-2 weeks (often quoted at ≥50% reduction). The literature also appears to measure the long-term efficacy of SCS using VAS/NRS pain scores, suggesting that SCS is effective only when pain scores reduce significantly (≥50%).

Materials/Methods: Retrospective data from patients been to theatres between September 2015 and December 2016 was collected. Pain and Quality of Life (QoL) scores pre- and post- implantation were collected using paper files and electronic records. Each clinic letter with qualitative data was documented. This data was collated and analysed using STATA.

Results: Pain and QoL scores for n=185 participants were analysed. The age range was 18-92, there were 92 males and 93 females. Trial failure rate was 14.1%, the most common reason being insufficient pain relief. Of the n=142 fully implanted participants only 26% had a ≥50% reduction in 'average pain' VAS scores, however there was statistically significant reduction in 'average' and 'worst' VAS pain scores ($p<0.0001$) shown in figure one. Furthermore, there was a significant increase in EQ5D QoL scores ($p<0.0001$).

Discussion: Literature suggests that unidimensional scoring systems, such as VAS/NRS pain scores, are not an effective tool for assessing chronic pain. This was reflected in LTHT, where cross-referencing clinic letters with patient reported VAS pain scores demonstrated a discrepancy between verbally reported benefit and VAS score. Furthermore, QoL scores reflect restoration of function and hence could be superior in assessing efficacy of SCS.

Conclusions: The improvement in both VAS pain and EQ5D QoL scores in LTHT allows for reliable conclusions to be made about the efficacy of SCS. We conclude that multidimensional measures should be analysed in future research to reflect clinical practice; where function, pain and QoL will all influence progression to full implant and demonstrate success of treatment. Reduction in opioids and anti-neuropathic drugs are also a key indicator of success. Furthermore, development of guidance with regards to trial success may be necessary to ensure patients do not fail trial based purely on VAS/NRS pain scores.

Objectives

to access and improve quality measures in our institute

References

https://www.nice.org.uk/guidance/ta159/chapter/2-Clinical-need-and-practice

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414. INS19-0229

INCIDENCE OF PAIN AT IMPLANTABLE PULSE GENERATOR (IPG) SITE FOLLOWING SPINAL CORD STIMULATOR (SCS) SURGERY – A RETROSPECTIVE CASE SERIES

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Introduction: Spinal Cord Stimulation (SCS) has been increasingly utilised in the treatment of chronic pain. While a growing body of literature continues to establish SCS as an effective treatment for chronic pain, commonly arising complications clearly hinder the positive outcomes for patients. Complication rates of SCS implantation are often reported at around 35-40%. Pain at the Implantable Pulse Generator (IPG) site is not commonly reported.

Materials/Methods: This was a retrospective cross-sectional service evaluation, with data collected from patients who received SCS implants at a tertiary centre between September 2015 to December 2016. Data was collected from hospital electronic records and paper files. Themes including IPG site pain, infection and hardware failure were coded and analysed using Microsoft Excel and STATA.

Results: A cohort of n=185 participants were trialled with SCS, of these n=161 were fully implanted and data analysed for complication rates. The age range was 18-92, there were 92 males and 93 females. 40 (24.84%) out of the 161 patients complained of IPG site pain. 19 out of the 40 patients reporting pain went on to have a revision to reposition the device. This gives 11.8% for IPG site revision surgery.

Abdomen 4/4 (17.4%)
Buttock 6/16 (21.4%)
Chest wall 6/19 (6.8%)

Discussion: This study found that IPG site pain was a common problem with SCS implantation, with nearly 1 in 4 individuals reporting pain. 50% of those reporting pain needed IPG site revision. Even when not requiring revision, this complication will influence patient satisfaction and hence success of SCS

When analysing IPG location sites, it was found that the number of participants with pain at implant in the buttock was disproportionately high when compared with the implant locations of the total cohort. Abdomen was rarely used due to the complexity of turning the patient to a lateral position and the need for extension. Some of the IPG site pain at the chest wall was due to under garment related in female patients. We classified the devices based on primary cell vs rechargeable and within rechargeable, whether it was small or large cell. (Table 2)

Conclusions: IPG site pain is a common problem which needs exploring. There could be some advances in IPG less systems in the future.

Objectives

IPG site pain evaluation

References

1. 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

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415. INS19-0226

A RETROSPECTIVE EVALUATION ON THE EFFICACY AND COMPLICATIONS OF THE USE OF SCS IN TREATING CHRONIC PAIN PATIENTS AT LEEDS TEACHING HOSPITALS TRUST (LTHT)

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Introduction: Spinal Cord Stimulation (SCS) has been increasingly utilised in the treatment of chronic pain since 1967. Currently around 34,000 patients are implanted annually, with approximately 130 of these being within LTHT. There has been a flurry of publications on recent RCT's in SCS. This is a real-world data of the use of SCS in a teaching hospital.

Materials/Methods: This was a retrospective cross-sectional evaluation, with data collected from patients who received SCS implant surgery between September 2015 to December 2016. Some of these patients on the list for revision from the past are also included. Data collected on Pain, Quality of Life (QoL) scores pre- and post- implantation, complications and revisions from paper files and hospital electronic records.

Results: A total of n=207 participants were eligible for this study with varied indications. Due to high levels of missing data and complex cases only n=185 went forward for analysis. The age range was 18-92, there were 92 males and 93 females. The majority of patients in this study population were suffering with FBSS and CRPS. BurstDR, DRG and HF10 are the common modalities of treatment used in this period. There was a statistically significant ($p<0.0001$) reduction in 'average pain' and 'worst pain' visual analogue scale (VAS) scores (26.89 and 24.5% respectively). EQ5D QoL scores increased by >0.22 ($p<0.0001$). Lead migration and failure secondary to fractures formed the major reason for revisions (table 1). Implantable Pulse Generator (IPG) site pain was reported by nearly 25% of the patients with 11.8% undergoing revision (Table 2) to the IPG site.

Discussion: We found a trial failure rate of 14.1% compared to 12% described in the literature (1,2). This was taken mainly from recent randomised controlled trials than a real-world data. We know this varies widely in the literature. Our explant rate was also less than described in the literature. Total explant rate in our cohort was 14.9% compared to therapy related explant of 18.8%

Conclusions: Our current retrospective data (Figure 1) has shown that we are achieving good outcomes for patients with reduced complications than what has been published in the literature. This data is still being collected retrospectively and we will have a much bigger data of unto 500 patients by May 2019.

Objectives

Service development and audit

References

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

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416. INS19-0380

EVOKED COMPOUND ACTION POTENTIAL RECORDING TO FURTHER UNDERSTAND EFFECT OF TITRATING MEDICATION WITH SPINAL CORD STIMULATION

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Introduction: Evoked compound action potential (ECAP) recording during spinal cord stimulation (SCS), as a measure of neural recruitment (of Aβ mechanoreceptor fibers) and correlation of ECAP amplitude with paresthesia coverage, has been reported (*Pain*. 2012;153:593-601). ECAP recording, with a new SCS system, can measure patients' therapeutic window (TW) for SCS (*Neuromodulation*. 2018;21:38-47). Moreover, maintaining ECAP amplitude within the TW could lead to more effective therapy and fewer side effects (*Proc IEEE*. 2008;96:1108-19; *Neurosurg*. 1997;40:990-9). This case study presents data collected from a patient undergoing SCS for chronic pain and reducing medication dose over several weeks.

Materials/Methods: Data collection occurred during set medication adjustments (Table). Neurophysiological data collection included ECAPs for the full range of the TW (threshold, comfort, and maximum [level that patient tolerates for 1 minute]), strength-duration curves (to estimate chronaxie and rheobase), and ECAP conduction velocities.

Results: As gabapentin and oxycontin dose decreased, so did the size of the TW. ECAP amplitudes at the patient's comfort and maximum level decreased without gabapentin and decreased further without oxycontin. The current amplitude required was independent of ECAP amplitude as medication dose was decreased. Therefore, while neural recruitment was correlated with medication dose, the amount of current required to elicit a response was not. No observable correlation existed between conduction velocity or chronaxie and rheobase with changes in medication dose.

Discussion: The data from this case study correlate with previous work showing that preferred ECAP amplitude decreased with pregabalin dose reduction (Brooker et al. Presented at INS 2017). Once off medication, ECAP amplitude may need to be maintained within a smaller TW. Furthermore, medications may increase a patient's tolerance to stimulation; therefore, artificially increasing the size of their TW and/or the amount of neural recruitment needed to maintain pain relief.

Conclusions: Lack of correlation between current amplitude and medication dose suggests that a measure of neural recruitment (eg, ECAP) is required to monitor and understand these effects. ECAP amplitude may be used to titrate and optimize dosing of anticonvulsants and opioids. An SCS system with closed-loop control, which continuously measures ECAP amplitude, better maintains neural recruitment within a patient's TW compared to a fixed-output system, potentially leading to sustained long-term outcomes. Further research is required and currently ongoing.

Objectives

1. Opioid dose appears to affect neural recruitment.
2. Opioid dose appears to affect the size of the therapeutic window (correlates with medication dose).
3. ECAP measurement is required to understand the effect of medication on neural recruitment.

Table: The Medication Dose Status, Including Baseline, and Dates Data Were Collected

Date	Medication status Baseline = Gabapentin 600 mg/day Oxycontin 30 mg 1x/day	Neurophysiology Collection
27 Feb 2018 (3 Month visit)	Gabapentin **600 mg**/day Oxycontin **30 mg** 1x/day	27 Feb
28 Feb – 09 Mar 2018	**Off** Gabapentin Oxycontin **30 mg** 1x/day	02 Mar 09 Mar
10 Mar – 16 Mar	Gabapentin **600 mg**/day Oxycontin **30 mg** 1x/day	16 Mar
17 Mar – 28 Mar	**Off** Gabapentin Oxycontin **30 mg** 1x/day	28 Mar
29 Mar – 04 Apr	**Off** Gabapentin Oxycontin **20 mg** (10 mg 2x/day)	04 Apr
05 Apr – 11 Apr	**Off** Gabapentin Oxycontin **10 mg** 1x/day	Not captured
12 Apr – present	**Off** Gabapentin **Off** Oxycontin	20 Apr

Note: there were no other changes to medication over this time period. All data were collected with the patient sitting, at rest.

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417. INS19-0373

PROSPECTIVE, RANDOMIZED STUDY COMPARING CONVENTIONAL, BURST AND HIGH FREQUENCY SPINAL CORD STIMULATION IN REFRACTORY FAILED BACK SURGERY SYNDROME PATIENTS AFTER A 32-CONTACT SURGICAL LEAD IMPLANTATION

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Introduction: Many studies have demonstrated the efficacy and economic value of conventional Spinal Cord Stimulation (SCS) for chronic neuropathic pain, and randomized controlled trials (RCTs) have shown SCS to be a clinically effective adjunct to medical management. Two new paraesthesia free stimulation waveforms based on traditional SCS technology have appeared to further optimize the outcome for specific painful conditions (Burst stimulation and High-frequency stimulation). Several studies have demonstrated the potential interest of these 2 new waveforms to treat FBSS patients compared to traditional SCS. It seems important to conduct RCT in crossover, thanks to the new SCS Stimulator, to compare the effects of these 3 different SCS modalities in Failed Back Surgery Syndrome (FBSS) patients and to determine which concept is the most effective in terms of pain reduction and energy consumption.

Materials/Methods: MULTIWAVE is a monocenter, prospective, double bind randomized study between BURST and HF groups. Twenty eight refractory FBSS patients considered for SCS lead implantation, according to "French health authority" recommendations should be included. Subjects who meet all of the inclusion criteria and none of the exclusion criteria will undergo an SCS screening test with a CoverEdge 32-contact surgical lead™ and, if successful (global pain VAS score decrease ≥ 50%), will receive a Precision Spectra SCS System™ implant. The primary objective is to compare the efficacy of TONIC, BURST and HF Stimulation in refractory FBSS patients after a 32-contact surgical lead implantation.

Results: Preliminary results are expected to be published in 2020.

Discussion: NA

Conclusions: Trial recruitment starts since January 2017.

Objectives

NA

References

NA

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418. INS19-0275

SPINAL CORD STIMULATION AT 10 KHZ FOR TREATMENT OF ELHERS DANLOS SYNDROME

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Introduction: Chronic Widespread Pain (CWP) including fibromyalgia affects 10-15% of all world populations with a female prevalence about double that observed in males (1). Here, we describe a group of Elhers Danlos Syndrome (EDS) patients who developed severe widespread nociplastic pain at an early age, and their subsequent experience with high frequency spinal cord stimulation (HF-SCS) at 10 kHz, for treatment of their chronic pain symptoms. Widespread pain is an unconventional target for neurostimulation therapy, primarily because of the technical challenge of obtaining parasthesia coverage of large pain areas required for traditional SCS efficacy. HF-SCS at 10 kHz provides good diffuse analgesic effects in the trunk and limbs without the requirement for parasthesias and likely has mechanisms different from other stimulation modalities (2).

Materials/Methods: Ten EDS patients (9 females) with CWP intractable to conservative modalities including CBT pain management (for an average of 11.1 ± 9.0 years) were selected for combined cervical and thoracic HF-SCS. Leads were placed over the C2/T2 or C2/T9 vertebral levels, or three electrode leads placed over the C2/T2/T9 vertebral levels. Patients were followed up an average of 2.6 ± 2.0 years post permanent implant. Patient outcomes were recorded and presented as mean ± standard deviation

Results: A statistically significant pain reduction post-IPG implant was observed (baseline: 7.4±0.9 numerical rating scale (NRS) vs. follow-up: 3.4±1.1 NRS, $p \leq 0.05$). Percentage pain relief ranged between 63.0±19.9%, 69.3±18.4% and 68.6±17.7% for head and neck pain, upper back pain and lower back pain, respectively. Nine patients had typically trialled a variety of analgesics and anti-neuropathic pain medications over a long period of time. Following HF-SCS, 4 of the 9 patients ceased strong opioid medication, whilst 2 patients halved their use. Further improvements in quality of life were observed with 5 out of the 9 work eligible patients returning to work or study following HF-SCS.

Discussion: Having leads staggered across the cervical and thoracic spine requires optimized programming. The improved return to work outcomes and opiate reductions suggest that cost effectiveness as well as clinical effectiveness may be achieved with this treatment approach.

Conclusions: HF-SCS provides long term widespread pain relief in this difficult to treat EDS patient group.

Objectives

To consider the use of HF-SCS as an option for chronic widespread pain conditions.

References

1. Mansfield KE, Pain. 2016; 157(1):55-64.
2. Kapural L. Neurosurgery. 2016; 79(5):667-677.

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419. INS19-0233

SPINAL CORD STIMULATION IN PATIENTS WITH FAILED BACK SURGERY SYNDROME IN TESTING PHASE. STUDY PROTOCOL

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Introduction: Traditionally, pain relief through spinal cord stimulation has been associated with the appearance of paresthesia in the affected area. Several parameters are set to maximize the overexposure zone, such as frequency, and pulse width. Although this technique has improved pain in many patients, paresthesia itself can be uncomfortable. Traditionally, the occurrence of paresthesias has been considered to be a predictor of success in pain elimination, while the non-occurrence of paresthesias would indicate failure. So far, few studies have reported pain relief below the threshold of onset of paresthesia.

Materials/Methods: Randomized single blinded crossover clinical trial, with an estimated enrollment of 24 patients with failed back surgery syndrome. Two epidural thoracic leads will be placed, and they will be randomizedly programmed in tonic or in EVOLVE stimulation. They will change their stimulation to the one they didn't receive in the beginning.

Results: We will compare visual analogue score (VAS) between the 2 kinds of stimulation at the end of test phase as our first outcome. Second outcomes will be the number of patients in each group that diminished the VAS score in more than 50%, the disability, measured with the Oswestry scale, and the number of adverse effects in each group.

Discussion: The new modes of stimulation, paresthesia-free, have been a good alternative to conventional tonic stimulation. The parameters such as frequency and pulse width are the ones that determine the kind of paresthesia free stimulation. Burst, high frequency, high density are some of the names of the different waveforms that have recently appeared.

Conclusions: It is necessary to perform high quality research to assess if these new kinds of stimulation can be a better alternative to tonic stimulation.

Objectives

Performing trials in spinal cord stimulation.

EVOLVE protocol could reduce VAS score more than tonic stimulation in phase test.

Both kinds of stimulation should have the same rate of complications.

References

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Spine - Pain

420. INS19-0099

A PROSPECTIVE, MULTI-SITE, CLINICAL TRIAL OF THE HIGH-FREQUENCY SPINAL CORD STIMULATION AT 10 KHZ (HF-SCS) SYSTEM IN THE TREATMENT OF CHRONIC PELVIC PAIN

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Introduction: Chronic pelvic pain (CPP) is known to disproportionately affect women and have multiple causes such as traumatic injury and post-surgical changes. Standard-of-care treatments often fail to resolve the pain, leaving CPP patients with long term disabilities. High-frequency SCS (HF-SCS) at 10 kHz has been previously shown to provide long-term relief for chronic low back and leg pain patients[1,2].

Materials/Methods: In this multicenter, prospective study, subjects clinically diagnosed with chronic pelvic pain of ≥5 cm (on a 0-10 cm visual analog scale [VAS]) refractory to conservative therapy for ≥3 months were enrolled following IRB approval. Significant spinal stenosis, epidural scarring or symptoms of myelopathy and other progressive neurological diseases were causes for exclusion. Subjects were implanted with two epidural leads spanning appropriate vertebral bodies as determined by the location of pain and were implanted with a Senza system (Nevro Corp., Redwood City, CA) if they had successful trial stimulation (≥50% pain relief). Safety and effectiveness endpoints were captured up to 12 months post-implant. Interim 3-month results are presented as mean ± 95% CI in the permanent implant population.

Table 1. Domain scores for short form McGill Pain Questionnaire (SF-MPQ-2)

	Total Score	Continuous Pain	Intermittent Pain	Neuropathic Pain	Affective Descriptors
Baseline	4.20±0.94	5.75±0.98	4.66±1.26	2.28±0.88	4.08±1.33
3 Months	1.69±1.00	2.28±1.38	1.50±1.02	1.33±0.84	1.63±1.07

Table 2: Three-item pain and sleep questionnaire

	Trouble falling asleep due to pain	Awakened from sleep (night)	Awakened from sleep (morning)
Baseline	6.86±1.45	7.11±1.43	7.64±1.17
3 Months	1.44±0.95	2.38±1.66	2.58±1.82

Results: Twenty-four subjects were enrolled in the study of whom 3 failed screening. Twenty-one subjects underwent trial stimulation and 15 had successful trial (71.4% trial success rate) and received a permanent implant. Baseline pain scores of 7.8±0.6 cm (n=15) improved to 2.1±0.7 cm (n=14), 3.8±1.7 cm (n=12), 2.5±1.5 cm (n=12) at the end of trial, 1- and 3-month follow-ups, respectively. Pain disability index of 43.9±4.9 (n=15) improved to 20.5±10.2 (n=11) at 3-month follow-up. Significant improvements were also reported in all domains of McGill Pain Questionnaire including affective scores (Table 1) and 3-item pain and sleep questionnaire (Table 2).

Discussion: The results from this study are line with previously reported findings from studies in back and leg pain patients 1,2.

Conclusions: Interim study results show HF-SCS 10 kHz could potentially provide clinically meaningful pain relief to the patients with CPP, a condition that is traditionally difficult to treat.

Objectives

The objective of this study is to assess effectiveness of the HF-SCS at 10 kHz in the treatment of chronic intractable pelvic pain.

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421. INS19-0431

INTRACTABLE NEUROPATHIC PAIN POST CAUDA EQUINA SYNDROME, SCOPE FOR NEUROMODULATION

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Introduction: Neuropathic pain involving perineal, perianal and allodynic vulval pain is a significantly debilitating complication of cauda equina syndrome (CES). Our review aims to evaluate the outcome of spinal cord stimulator (SCS) in these patients and discuss optimisation of approach to maximise responder rate.

Materials/Methods: Retrospective analysis of patients who underwent SCS implants between 2005- 2018 with sub group analysis of patients with perineal and/or vulval allodynic pain following CES.

Parameters including patient demographics, dermatomal distribution of pain, the level of SCS implanted, type of electrode and stimulation current used, overall pain reduction, any complications of surgery and duration of follow up were studied.

Results: 256 patients had SCS implant in this period. Out of these,12 patients had SCS inserted for neuropathic pain related to CES or perineal pain with similar topographic distribution. 10 out of 12 patients developed these symptoms post cauda equina surgery, 1 patient after bilateral herniorraphy and 1 patient had pudendal neuralgia.

8 patients were on paraesthesia producing stimulation. On traditional setting, the pulse width ranged from 120-480, rate was 60 and amplitude used were from 1.2 to 4.7volts. Two patients were on non-paraesthesia producing settings.

An analysis of the active contact electrodes suggested a responsive segment of spinal cord between T9/T10 and T10/T11 intervertebral disc on the midline with conus located not below L1/L2 disc.

There was 100% initial responder rate with 8 patients (75%) having more than 50% overall pain reduction over a follow up period ranging from 4 months to 114 months (average 52 months). 3 patients returned to work.

2 patients developed migrainous headache treated with pharmaceuticals. 1 patient had SCS removed to facilitate MRI investigation.

Discussion: There are studies reporting mixed success in treating Neuropathic pain following CES using various peripheral nerve stimulation. However, there are no studies relating to SCS in neuropathic pelvic pain, perineal, perianal pain following cauda equina surgery. The nerve fibres serving lower sacral dermatomes are very central and deep in the spinal cord and capturing these in thoracic spinal cord required conscious field morphing to have a deeper effect and therapeutic benefit. We discuss our programming parameters and strategies to maintain prolonged therapy benefit.

Conclusions: Our study shows that SCS may be of beneficial effect in patients with cauda equine neuropathic pain and may be considered in these group as well.

Objectives

To determine and describe the scope, techniques used for SCS in intractable neuropathic pain following cauda equina syndrome.

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422. INS19-0417

DORSAL ROOT GANGLION STIMULATION UNDER REAL LIFE CONDITIONS – A SINGLE-CENTER CASE SERIES OF 115 PATIENTS

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Introduction: Dorsal root ganglion stimulation has established its role in chronic pain states of different origin. The bulk of data on DRG stimulation originates from small case series and clinical trials. We report a consecutive series of 115 patients treated in the clinical routine to provide unfiltered data of DRG stimulation results and complications.

Materials/Methods: Between January 2014 and February 2018 115 patients were implanted with DRG electrode in a single neuromodulation unit. In most patients, trialing was performed and considered successful if an at least 50% pain reduction could be achieved. Data on this patients was prospectively collected during in- and out-patient follow-ups. Beside response to stimulation measured by pain reduction, trial-to-implant ratio and explantation rates were recorded.

Results: Of 115 patients implanted with leads, 104 were implanted with a permanent system resulting in a trail-to-implant percentage of 90.4 percent. The mean pain levels at baseline were 8.6 cm VAS (range 6.0-10.0). Stimulation with the permanent system resulted in a decrease in pain levels to a mean of 4.1 (range 0 – 10), mean time to first follow-up was 1.9 month (2nd f/u @ 9.5 month VAS 5.1, 3rd f/u @ 18.9 month VAS 4.2, 4th f/u 23.6 month VAS 5.3). 23 patients had their devices removed due to inefficacy (19.8%). Parametric testing for statistical differences resulted in highly significant reduction of pain levels between baseline VAS and all consecutive follow-ups.

Discussion: This data provides an overview of DRG stimulation results from a mixture of indications and includes patients from the introduction of this therapy in the market, this might influence observed outcomes negatively. Additionally, only patients with insufficient or mediocre stimulations efficacy might have shown up for out-patient follow-up as patients were not actively followed. This might additionally negatively influence follow-up data and has to be kept in mind when interpreting the results.

Conclusions: DRG stimulation resulted in a statistically significant and stable treatment response. Explantation numbers are higher than anticipated. High level of evidence clinical trials looking into distinct indications have to be performed.

Objectives
indications for dorsal root ganglion stimulation
expected outcomes in dorsal ganglion root stimulation
complications of dorsal root ganglion stimulation

References
none

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423. INS19-0418

SYNERGETIC EFFICACY OF SIMULTANEOUS DRG- AND TRADITIONAL SPINAL CORD STIMULATION

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Introduction: Dorsal root ganglion stimulation has established its role in chronic pain states of different origin and is commonly used as an alternative treatment to traditional spinal cord stimulation. Due to its approach, DRG stimulation is preferable used in pain conditions affecting a small area or a distinct nerve root. Traditional spinal cord stimulation can be used to treat larger areas as the back in FBSS. In selected patients, a combination of both techniques might be useful. Little is known about the feasibility, possible technical difficulties in program and efficacy of this combined approach.

Materials/Methods: We report a series of 5 patients treated with DRG stimulation and traditional spinal cord stimulation. Four patients suffered from a FBSS syndrome with severe chronic mixed lumbar pain and chronic neuropathic radicular pain, one patient suffered from CRPS. In all but one patient SCS was implanted first and complemented with a DRG in the course (4-90 month between implantation). In all but one patient, DRG and SCS systems came from the same manufacturer.

Results: In all patients, an additional stimulation system was implanted as the previous stimulation, despite reprogramming and revision surgery where considered promising, failed to reach the area of pain. In all but the CRPS patient, DRG stimulation was implanted to reach pain in the groin and/or leg whereas SCS stimulation was used to cover the lumbar pain in these FBSS patients. During programming only one system at a time was activated. No adverse events and no technical difficulties were observed during surgery and programming. All but one patient had a consistent and satisfying therapeutic effect with both systems activated.

Discussion: The combination of dorsal root ganglion and traditional spinal cord stimulation is surgically and technical feasible. In selected patients the combination of both methods offers an option to amend pain states not sufficiently treatable with one method alone. This introduction of IPGs combining DRG and SCS stimulation paradigms might increase acceptance of this option.

Conclusions: With the widespread use of neuromodulation the frequency of patients having more than one stimulation device will increase. Traditional spinal cord stimulation and dorsal root ganglion stimulation is an exceptional useful combination in selected patients.

Objectives
indications for spinal cord stimulation
indications for dorsal root ganglion stimulation
technical and programming aspects of combined application

References
none

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424. INS19-0195

COMPRESSION OF THORACIC SPINAL CORD WITH DECREASED CEREBROSPINAL FLUID SPACE FOLLOWING IMPLANTATION OF PADDLE LEAD SPINAL CORD STIMULATION AT T9: 3-DIMENSIONAL MYELOGRAPHIC COMPUTED TOMOGRAPHY STUDY

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Introduction: Although significant reduction in T9 spinal canal and inclination of paddle lead in posterior epidural space following SCS with paddle leads were reported, the degree of compression of intraspinal neural structures was not determined. We investigated the extent of spinal cord compression and CSF space following paddle lead implantation using three-dimensional myelographic CT scans.

Materials/Methods: Preoperative and postoperative three-dimensional myelographic CT scans were performed in 15 patients with implanted paddle leads at T9 (3-column, n=3; 5-column, n=12) for refractory back and leg pain. Four axial levels between each row of the electrodes were selected and the cross-sectional areas of thecal sac and spinal cord, the width of anterior and posterior CSF space, and contact angle of the lead within T9 spinal canal were measured with 12-month pain relief assessment.

Results: The cross-sectional areas of thecal sac and spinal cord under each contact of paddle leads decreased significantly by 23.89 $\pm$ 11.48% and 9.45 $\pm$ 4.80% ($p < 0.05$), respectively. No difference in the degree of reduction in area between each level of contact. The width of posterior CSF space decreased by 38.65 $\pm$ 20.97% and that of anterior CSF space showed a greater reduction by 59.09 $\pm$ 18.39% ($p < 0.05$). No significant correlation was evident between the contact angle of paddle lead and percentage (%) reduction in cross-sectional areas of the thecal sac and spinal cord and those of the width of anterior and posterior CSF spaces ($p >$ 0.05). Mean pain relief of 45.49 $\pm$ 13.73% at 12-month follow-up. significant correlation with percentage reduction in the area of the spinal cord was found.

Discussion: More significant compression of underlying, intradural neural structures including the spinal cord was found. Close approximation of paddle lead to the dorsal column due to significant compression of intradural neural structures may be related to successful clinical outcomes and also pose safety concerns.

Conclusions: Significant reduction in the cross-sectional area of spinal cord and anterior CSF space as well as thecal sac and posterior CSF space resulted in deformation of the spinal cord under paddle leads at T9 within 7 postoperative days. Close approximation to the dorsal column and the mass effect of paddle leads may be determine the clinical outcome of paddle lead SCS and also raise safety concerns.

Objectives

To further elucidate the extent of CSF space reduction around the spinal cord and compression of neural structures following paddle lead implantation at T9,

References

World Neurosurgery 2018:118:e323-e334

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425. INS19-0198

MULTIMODAL, INTRAOPERATIVE MONITORING DURING PADDLE LEAD PLACEMENT FOR CERVICOTHORACIC SPINAL CORD STIMULATION

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Introduction: We investigated the efficacy of combined somatosensory evoked potential (SSEP) and electromyography (EMG) monitoring during paddle lead placement through cervicothoracic laminectomy under general anesthesia in a retrospective review of data from 25 patients.

Materials/Methods: Muscle MEP recordings and SSEP monitoring were used for surveillance of the spinal cord. Collision testing of SSEPs and threshold amplitudes of compound muscle action potentials (CMAP) in the bilateral upper and lower extremities evoked by electrode contacts of the paddle lead were checked to determine the laterality of lead in mediolateral direction.

Results: A significant decrease in amplitudes of muscle MEPs in spite of stable SSEPs occurred in two patients: one patient with retrograde C1-C2 insertion and another patient with anterograde C4/5 insertion. Repositioning of leads based on significantly asymmetrical collision testing of SSEPs and thresholds of CMAPs in bilateral extremities was needed in 6 and 8 patients, respectively. In 22 patients, paresthesia coverage of the painful area was consistently located in the painful side, either unilaterally or bilaterally. There was no episode of revision for suboptimal lead placement.

Discussion: We could perform paddle lead SCS in the cervicothoracic spine safely and accurately under general anesthesia with neurophysiologic SSEP and muscle MEP monitoring. Combined SSEP and MEP monitoring could provide information about the safety and neurophysiologic guidance related to laterality of paddle lead placement.

Future studies are needed to determine whether intraoperative neurophysiologic guidance can improve the outcome of pain control after SCS.

Conclusions: Intraoperative neurophysiological guidance using SSEP and muscle MEP was useful for safe and accurate placement of paddle leads for cervicothoracic SCS.

Objectives

Insertion of epidural paddle leads in the cervicothoracic spine has an inherent risk of neurologic compromise.

References

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426. INS19-0278

SPINAL CORD STIMULATION AT 10 KHZ FOR CHRONIC INTRACTABLE PAIN: A PROSPECTIVE CASE SERIES IN A REAL-WORLD COMMUNITY PRACTICE

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Introduction: Intractable pain has traditionally been treated with conventional spinal cord stimulation (SCS) using conventional paresthesia-based SCS [1]; however, paresthesia-independent SCS using a frequency of 10 kHz (HF-SCS) has been used, especially following the publication of a randomized clinical trial demonstrating safety and effectiveness in both back and leg pain populations[2,3]. Efficacy in the real world is often debated, thus, we present patients undergoing HF-SCS for various chronic pain conditions in a typical non-affiliated, provincial community-based multidisciplinary private pain practice setting, working in an inter-disciplinary manner.

Materials/Methods: Over 6-years, 64 patients underwent a HF-SCS trial, with those reporting a successful trial phase (≥50% pain relief) implanted with a permanent system (Nevro Corp., Redwood City, CA). Patient outcomes were collected prospectively and consecutively with a mean follow up range of 6-48 months. Results are presented as mean ± standard deviation, with data collection ongoing.

Results: Of the 64 patients, 56 (87.55%) reported a successful HF-SCS trial and proceeded to a permanent implant. Patients reported a reduction in their overall pain conditions from baseline at the follow up audit visit (Table 1). Improvement in psychological and disabilities were observed. Medication use was reduced, and on occasions ceased, and substantial enhancement of occupational participation observed. Two battery revisions were required and 2 system explants occurred due to failure of sufficient pain relief or other patient issues. No long-term complication were noted.

Discussion: From this community setting, which included compensable workcover patients, predominantly successful outcomes were reported which are encouragingly similar to those published (3). Efficacy in non-neuropathic conditions adds weight to the evidence that neuromodulation is modifying central sensitisation, or nociplastic factors and not by the commonly held view of neuropathic pain factors per se.

Conclusions: This data demonstrates that HF-SCS is a reliable and effective therapy for a wide-range variety of intrusive pain conditions. Improving pain relief of itself contributes to improved physical, psychological and occupational function.

Objectives

1. To appraise the clinical effectiveness and safety of HF-SCS in a common private generalist multidisciplinary pain setting
2. To consider HF-SCS in a variety of medical conditions
3. To appraise HF-SCS over a 6-year period

References

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Cohort	Disease duration (yrs)	Age (yrs)	Duration of Therapy (Follow (mth)	Baseline Pain Score (Numerical Rating Score [NRS])	Follow up Pain Score (NRS)	Reported pain relief
Failed Back Surgery Syndrome (FBSS) (n=31)	11.2 ±9.1	58.0 ±14.6	29.3 ±17.6	7.3 ± 1.5	3.8 ± 1.7	64.1 ± 20.3
Non-Specific Refractory Back Pain (NSRBP) (n=18)	11.7 ±10.7	54 ±14.9	17 ±15.1	6.2 ± 2.7	2.8 ± 1.1	61.6 ± 29.1
Peripheral Neuropathy (n=6)	5.0 ± 4.2	44.4 ± 15.5	10.8 ± 5.0	6.0 [a]	4.3 ± 3.2	80.0 ± 14.4
Chronic Daily Headaches (n=4)	10.4 ± 9.9	36.5 ± 10.4	22.5 ± 12.1	6.8 ± 1.9	4.0 ± 1.7	72.5 ± 15.0
Chronic Regional Pain Syndrome (CRPS) (n=2)	2.4 ± 1.6	27.5 ± 0.7	37.5 ± 23.3	4.0 [b]	2.0[b]	75.0 ±7.1
Miscellaneous (n=3)	12.3 ± 12.4	63.0 ±21.2	3.0[b]	6.2 ± 2.7	2.8 ± 1.1	95[b]

[a] All patients reported same baseline score. [b] At time of data collection, data available for 1 patient, additional data will be available for INS

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427. INS19-0363

LONGITUDINAL DATA FROM THE TARGETED DRUG DELIVERY (TDD) PRODUCT SURVEILLANCE REGISTRY: MRI RISK MITIGATION

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Introduction: Magnetic resonance imaging (MRI) is an increasingly frequent diagnostic tool for a wide range of disorders. MRI for patients with implanted medical devices presents varied risks and impacts to device function based on device type. Patients registered in the Product Surveillance Registry (PSR) and implanted with a Medtronic Targeted Drug Delivery Device are monitored for motor stalls and adverse events relating to an MRI procedure. Understanding and mitigating patient risk and device impact associated with the use of a specific implanted pump is discussed.

Materials/Methods: The Product Surveillance Registry was established by Medtronic as a prospective, long-term, multi-center (US, Western Europe and Latin America) registry in 2003 to monitor infusion system performance. Data are collected on product-performance following IRB/EC approval at respective sites; patients providing informed consent are enrolled at initial system implant or pump replacement. Patients are followed prospectively for events related to the device, procedure, and therapy. Investigators provide event descriptions, patient symptoms, and patient outcomes.

Results: A total of 8,444 patients with implanted pumps were followed in the registry as of October 31, 2018. MRI occurrences and frequency of MRI-related motor stall (temporary and permanent) will be presented, along with associated adverse events, treatment, and patient outcome.

Discussion: Motor stall, especially prolonged or permanent, is the key risk associated with MRI in patients with implanted peristaltic pumps. Motor stall can result in the return of underlying symptoms and possible underdose/withdrawal, but can also be identified with pump interrogation and review of programmer logs. Prolonged post-MRI motor stalls in peristaltic pumps are infrequent, but if the patient has return of symptoms or signs of withdrawal following MRI exposure, action to assure pump function is required.

Conclusions: Understanding the risks associated with MRI exposure and adverse events aid in the identification of events and mitigation of immediate and delayed consequences. Peristaltic pump motor stall in the presence of the magnetic field during MRI mitigates risk of overdose during MRI, but necessitates verification of pump function post-MRI.

Objectives

Positive identification of the manufacturer, make and model of implanted medical devices prior to MRI and proper risk mitigation is critical to patient safety. Data presented from this registry and discussion of necessary pre- and post-MRI actions specific to implanted peristaltic pumps will aid in understanding proper risk mitigation and reduction in patient risk.

References

None

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428. INS19-0368

TARGETED DRUG DELIVERY AND CATHETER TIP LOCATION: IS THERE A DIFFERENCE IN ADVERSE EVENTS?

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Introduction: Trends in targeted drug delivery have moved toward lower dosages with catheter tip location placements throughout the Intrathecal space. Little data has been presented documenting safety with catheter position.

Materials/Methods: Data from 826 participants in the Product Performance Registry from a single center were examined regarding catheter tip location and serious adverse advents (SAE) recorded from 4/2010-6/2018 (2950 patient treatment days).

Table 3.

Catheter tip	number
C1-4	123
C5-T2	222
T3-T6	409
T7-T10	72
T11 –S1	0

Results: 104 Associated SAEs not including unrelated deaths in 83 of 826 patients. SAEs were divided into drug related, procedure related and device related categories.

Drug related SAEs N=56. 26 adverse drug reactions 10 drug withdrawal syndromes (1 catheter leak, 3 motor stalls) 10 overdose 1 respiratory distress 1 respiratory failure 2 non-medical device related severe pain 4 mental status changes 2 non-medical device related severe pain

Procedure related N=31. 2 cranial bleeds: 1cerebral hemorrhage 1subdural hematoma 8 CSF leaks with 2 persistent headaches 1 general physical health deterioration 13 implant site infections 6 meningitis 1 procedural pain

Device related N=10. Catheter dislodgement with hypoaesthesia 9 pain from device malfunction: 3 motor stalls, 2 catheter kink, 3 dislodgements, 1 pump inversion 1 paresthesia

Discussion: Little long term data has been reported with catheters placed in the thoracic and cervical levels. In this data set, 10% of the patients experienced a SAE and more often was drug related. Patients in this cohort had cancer related, chronic non cancer related pain and spasticity. Further data analysis will delineate the treatment type and whether a subtype of patient is more likely to experience a SAE. Catheter tip position and delineation of SAE per catheter level will also need to be looked at more closely.

Conclusions: A large cohort of high level catheter tip locations has been examined with a 10% adverse event reporting.

Objectives

Provide long term safety data on intrathecal catheters by catheter tip placement.

References

None

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429. INS19-0371

MOTOR STALLS WITH AN IMPLANTABLE PAIN PUMP

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Introduction: We evaluated motor stalls in 1667 pumps implanted between 4/2003 and 7/2018.

Materials/Methods: Product Surveillance Registry (PSR) [1] data were evaluated for motor stall secondary to MRI, stall without a trigger, time of stall vs. expected battery life, clinical presentation, return product analysis (RPA), and pump medications.

Results: 37 patients had confirmed motor stalls not associated with MRI; 10 had multiple stalls. 32/37 experienced terminal motor stall without recovery. 18/37 had motor stall confirmed by RPA. 4/37 were confirmed as overinfusion, but these patients experienced no overdose symptoms. RPA identified no motor stall for 1/37, and no analysis occurred for 14/37. 8/38 stalls resulted in a serious adverse event (hospitalization, no deaths).

35/37 stalls occurred in pumps with at least one lipophilic medication *and* at least one other medication. 20/37 had hydromorphone + bupivacaine, 6/37 had bupivacaine + fentanyl, 6/37 had hydromorphone + one other non-lipophilic medication. 3/37 had bupivacaine + 1 non-lipophilic medication, 2/37 had no lipophilic medication but had compounded baclofen or clonidine/morphine. Medication concentration ranges were bupivacaine 10-40mg/ml, hydromorphone 50mcg-30mg/ml, and fentanyl 200-800mcg/ml. Medication recommendations have been published.[2]

27/37 stalls occurred between 5 and 30 months on the elective replacement indicator, with the most stalls at 13-24 mos (13) and 25-36 mos (11). Secondary to MRI, one stall occurred in 4 patients, and 2 stalls in 2 patients. Other device-related events (e.g., catheter kink) did not correlate with more stalls. Frequency or duration of stalls did not predict terminal stalls, which were associated with gear shaft decreased lubrication, wear/corrosion, and electrical shorting. Overinfusion was confirmed in 4 RPAs but pumps were replaced because of motor stall, as device malfunction was the priority.

Discussion: Stalls can result in the return of symptoms and possible underdose/withdrawal. Lipophilic medications are associated with the most motor stalls. Motor stall frequency and duration do not correlate with terminal stalls, nor do prolonged post-MRI stalls, which are infrequent.

Conclusions: Providers should examine logs, compare expected and interrogated volumes at refill, and take a thorough history to detect possible pump malfunction when using off-label medications. Pump replacement should be considered after 30 months with off-label medications.

Objectives

Identify likely contributors to pump motor stall

Demonstrate knowledge of pump mechanics and limitations

Name medications that may contribute to decreased product performance

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430. INS19-0272

SPINAL CORD STIMULATION AT 10 KHZ FOR CHRONIC INTRACTABLE LEG PAIN: A PROSPECTIVE, MULTICENTRE AUSTRALIAN STUDY

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Introduction: Intractable leg pain has traditionally been treated with conventional spinal cord stimulation (SCS) using conventional paresthesia-based SCS [1]; however, there is limited long-term data, especially on changes to quality of life and functional improvements. Recent studies, including a randomized clinical trial (RCT) investigating SCS using a frequency of 10 kHz, have shown that this paresthesia-independent therapy is effective and safe in a population with both back and leg pain[2,3]. Here we present interim results from an Australian multi-center, prospective, clinical study, documenting the performance of paresthesia-independent high frequency SCS (HF-SCS) at 10 kHz for the treatment of chronic leg pain.

Materials/Methods: Subjects with chronic, leg pain of ≥5 cm (on a 0-10 cm visual analog scale [VAS]) were enrolled after human research ethics committee approval was obtained (ISRCTN:11720855). Each subject was implanted with two epidural leads spanning T8-T10 vertebral bodies. Subjects with successful trial stimulation (≥50% pain relief) were implanted with a HF-SCS system (Nevro Corp., Redwood City, CA) and included in the evaluation of the primary safety and effectiveness endpoints (≥50% pain relief) at 3 months post-implant. Results are presented as mean $\pm$ standard deviation.

Results: Of the twenty-eight subjects enrolled in the study thus far, and undergone a HF-SCS trial, 22 (78.5%) reported a successful outcome and proceeded to receive a permanent implant. Fourteen patients had progressed to their 3 month post-implant visit at the time of data collection, with 10 subjects (71.4%) meeting the effectiveness endpoint. Subjects reported a reduction in their leg pain from baseline at the 3-month follow up visit (7.3 $\pm$ 1.4 vs. 2.4 $\pm$ 2.2). Disability, as measured by Oswestry disability index score, decreased from 24.0 $\pm$ 5.3 at baseline to 12.1 $\pm$ 7.3 at 3 months post-implant. No neurological deficits were reported. None of the subjects reported experiencing paresthesia from HF-SCS. Enrolment and data collection is ongoing, with all implanted subjects being followed up to 12 months post-implant.

Discussion: This early data from a commercially managed study population, encouragingly reports similar outcomes to those published (3).

Conclusions: Early results from the study demonstrate that HF-SCS is a promising therapy option for intractable chronic leg pain, improving both pain and function outcomes at levels consistent with the prior RCT.

Objectives

To observe the outcomes from a commercially managed, standard of care study.

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431. INS19-0026

HUMAN DORSAL ROOT GANGLION STIMULATION REDUCES SYMPATHETIC OUTFLOW AND BLOOD PRESSURE

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Introduction: **Background:** We demonstrated previously that deep brain stimulation (DBS) can modulate peripheral sympathetic nerve activity and hemodynamic parameters in humans. The ability to modulate such parameters peripherally, by stimulating the Dorsal Root Ganglion (DRG), an accepted treatment for chronic pain, is attractive because of the lower risk. The DRG contains sympathetic neurones in addition to C-fibres that mediate pain. We hypothesised that DRG stimulation would reduce sympathetic nerve activity, based on previous studies showing that decreasing peripheral sympathetic activity reduces the excitability of DRG neurones. In addition, we hypothesised that DRG stimulation would alter hemodynamic variables.

Materials/Methods: We directly recorded Muscle Sympathetic Nerve Activity (MSNA) during *ON* and *OFF* stimulation of the DRG whilst evaluating pain and measuring haemodynamic (blood pressure and heart rate) parameters. The order of stimulation was randomised and the stimulation parameters double-blinded. The stimulation amplitude was at a level just below paraesthesiae induction. Chronic Blood Pressure (BP) was measured at baseline and at 6 months.

Results: 16 subjects were recruited and we obtained nerve recordings in 14. DRG stimulation significantly reduced the firing frequency of sympathetic nerves, with greater reductions evident when stimulation was left-sided. MSNA burst frequency was reduced by 13.3% (n=14, $p<0.0001$). The decrease in sympathetic nerve traffic occurred independently of reduction in pain scores. Both acute- and chronic BP measurements demonstrated that left-sided DRG stimulation significantly reduced BP but not right-sided stimulation, despite stimulation on both sides leading to significant pain relief at 6 months. Heart rate remained unchanged between stimulation phases.

Conclusion

DRG stimulation lowers sympathetic nerve activity, at least partly independent to its effect on pain. This leads to acute and chronic BP phenotypic changes that are largely due to left-sided stimulation. This raises the potential of DRG stimulation being used to treat de novo autonomic disorders such as hypertension or heart failure.

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432. INS19-0143

NON-LINEAR BURST SPINAL CORD STIMULATION RE-CAPTURED PAIN RELIEF AFTER 100+ MONTHS OF TONIC STIMULATION.

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Introduction: The efficacy of tonic spinal cord stimulation (SCS) seems to decrease over time. There are several studies that show superior efficacy of non-linear burst spinal cord stimulation when compared to tonic SCS. Here, we evaluated 8 patients with non-linear burst SCS who were reporting insufficient pain relief for at least 100 months with tonic SCS.

Materials/Methods: 8 patients (5 females and 3 males) were receiving tonic SCS for at least 100 months (average = 133±27.5 months). Average age of these 8 patients was 64.5±12.9 years. Four patients received tonic SCS for failed back surgery syndrome (FBSS), 3 for peripheral neuropathy and one for complex regional pain syndrome (CRPS). Three patients reported pain in their lower back, two in their upper extremities and three in their lower extremities. The average pain score using the Visual Analog Scale (VAS) with tonic SCS was 71.3±24mm. All patients switched to non-linear burst SCS.

Results: All patients achieved superior pain relief after switching to non-linear burst SCS. VAS score, on average, was reduced to 26.3±23mm immediately and 33.1±22mm after 3 months. Immediate post-op pain reduction was 66%, and 53% after 3 months. Patients with peripheral neuropathy had the most pain reduction with 83% immediately. Among pain area, low extremity pain showed the highest pain reduction with 77% immediately.

Discussion: Non-linear burst SCS is expected to be effective even in patients who have been treated with SCS therapy for a long period. Non-linear burst SCS is thought to have a different mechanism of action from tonic SCS.

Conclusions: Non-linear burst SCS re-captured pain relief in patients who were receiving long-term tonic SCS. Although preliminary, these results imply that non-linear burst SCS could be provided as a rescue option for tonic non-responders.

Objectives

Chronic pain is refractory.

SCS is effective for refractory neuropathic pain.

Non-linear burst SCS is more effective than tonic SCS.

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433. INS19-0202

DRG STIMULATION PREVENTS THE DEVELOPMENT OF POST-AMPUTATION PAIN: TWO CASES

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Introduction: Dorsal root ganglion (DRG) stimulation is an accepted neuromodulation therapy with excellent treatment results (1). Recently, we have seen two patients with noteworthy clinical trajectories.

Materials/Methods: Case report retrospective chart review.

Results: Two male patients were referred independently to our clinic for significant pain following multiple surgeries to repair foot injuries. Unilateral DRG stimulation reduced neuropathic pain from 8 to 1. In addition, both patients reported elimination of allodynia and reduction of pain medications. However, functional limitations continued due to ongoing mechanical pain and instability in the affected limb. Both patients elected to have below-knee amputations. DRG stimulation was continued before and after the amputations. Neither patient developed stump pain or phantom limb pain, and prosthesis fitting was not painful. Both patients increased their physical activity and were satisfied with their outcomes.

After 12 months, DRG stimulation cessation was trialled:·

- Patient 1 (work-related injury; treated at L4-5): Intense stump and phantom limb pain emerged within 24 hours. DRG stimulation was resumed at a lower amplitude, to good effect·

- Patient 2 (traumatic military injury; treated at L5-S1): No pain, aside from occasional bursts when exercising with his prosthesis, has been experienced in the four months since DRG stimulation cessation. An explant is planned.

Discussion: DRG stimulation normalises the neural hyperactivity that develops in primary sensory neurons following an injury (2); this may explain the pre-amputation experience of both patients with DRG stimulation. In addition, DRG stimulation was employed before and after elective amputations; although up to 95% of amputees develop post-amputation pain (3), neither of these patients did. When stimulation was turned off, Patient 1 experienced severe post-amputation pain for the first time: DRG stimulation may have continued to effectively filter out pain signals from the periphery (2). Patient 2, on the other hand, persisted pain-free after cessation of DRG stimulation, suggesting that it may have prevented the biochemical neural changes that could otherwise cause neuropathic pain following amputation (4).

Conclusions: In addition to effectively relieving already-established neuropathic pain, DRG stimulation may also have prophylactic utility to prevent the development of stump and phantom limb pain.

Objectives

DRG stimulation in foot/ankle pain.

Discussion of DRG stimulation in prophylactic post-amputation pain prevention.

Mechanisms for neuromodulation's pain relief.

References

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434. INS19-0384

AUTOMATED, ROUTINE MONITORING OF NEUROPHYSIOLOGICAL PARAMETERS IN SPINAL CORD STIMULATION

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Introduction: Current spinal cord stimulation (SCS) systems provide no information to clinicians about the state of the spinal cord nerves being stimulated. A new SCS system can record evoked compound action potentials (ECAPs) to measure neurophysiological parameters of the stimulated nerves.

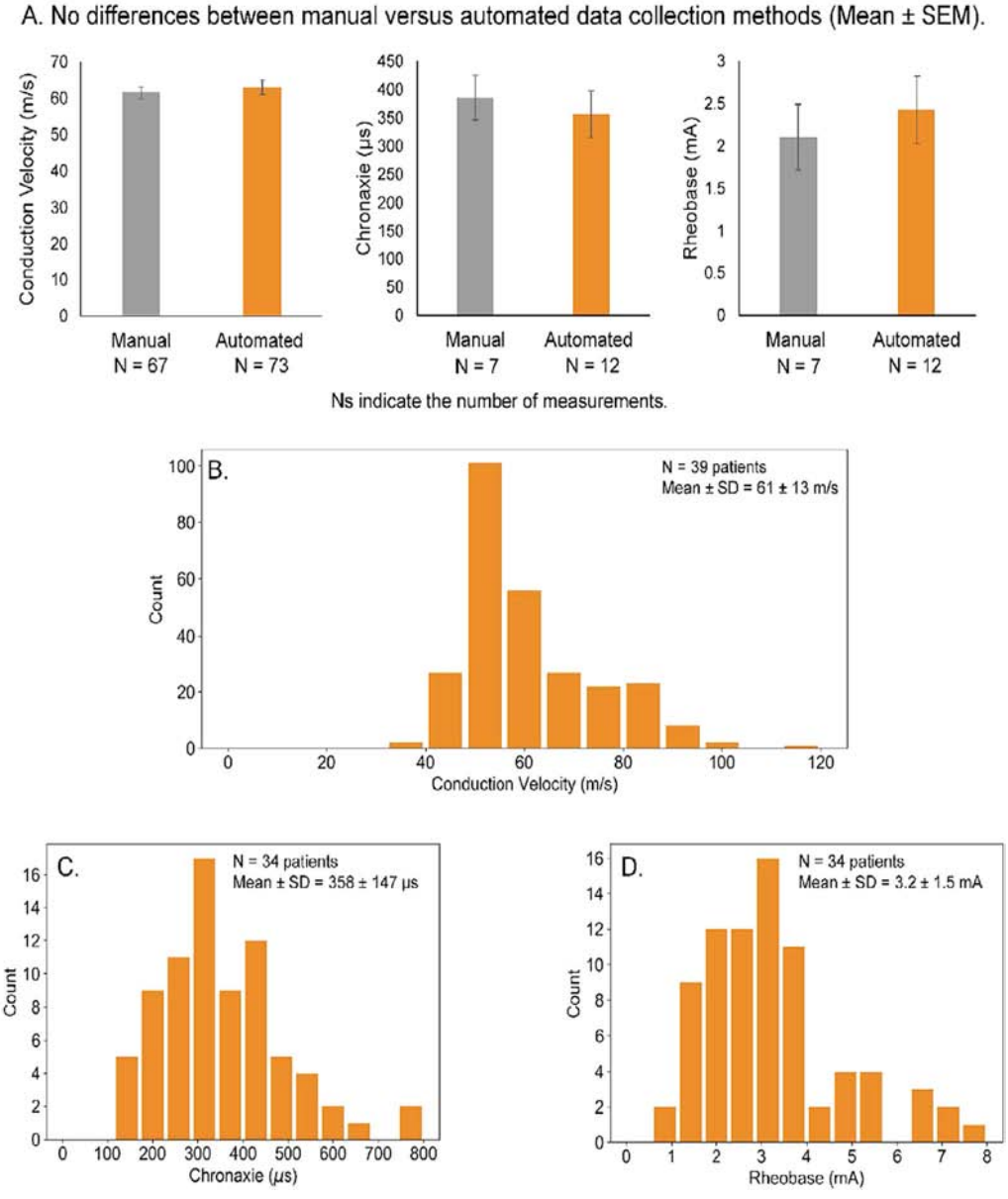
Materials/Methods: Conduction velocity (CV), chronaxie, and rheobase were measured in chronic pain subjects implanted with a closed-loop SCS system as part of the Avalon study (*Neuromodulation*. 2018;21:38-47).

Results: Automated data collection methods were validated against manual methods to ensure that there were no differences between methods (Figure 1A). At the time of submission, 269 CV measurements were obtained in 39 patients, with a mean of 61±13m/s (Figure 1B). Mean chronaxie was 358±147μs and rheobase was 3.2±1.5mA from 78 strength-duration curves measured in 34 patients (Figure 1C, 1D). Automated CV measurement involved setting the stimulation to a comfortable level and automatically scanning the measurement electrode along the lead, detecting ECAP peaks. Automated strength-duration curve measurement involved automatically varying current at different pulse widths and using ECAPs to determine the threshold for activation. The CV was within the reported range of 16-100m/s for Aβ sensory fibers. Chronaxie and rheobase were comparable to previous studies (*Pain Physician*. 2010;13:321-35).

Discussion: Routinely collected, objective neurophysiology measurements may help to characterize chronic pain patients, enabling clinicians to evaluate and monitor the integrity of the nervous system, effects of SCS intervention on the spinal cord, effects of medications, and changes in neural activation and conduction properties over time. CV, chronaxie, and rheobase measurements provide information about the type and excitability of neural fibers stimulated, and further analysis of these data may help improve neural selectivity in programming.

Conclusions: CV measurements collected in the Avalon study indicate that Aβ fibers are primarily activated during SCS. Chronaxie and rheobase values range widely in different studies based on stimulation parameters. No direct comparison exists between the strength-duration data measured in the Avalon study (objective measurement using ECAPs) and previous literature (subjective measurements based on patient-reported threshold). Validation of automated data collection methods against the previous methods shows that automated methods are reliable. Automated methods will allow increased patient numbers and analysis of correlations between therapy results and neurophysiological measurements. A multicenter, double-blind, randomized, controlled trial, currently underway, will also investigate these measurements (ClinicalTrials.gov: NCT02924129).

Figure 1: Distributions of conduction velocity, chronaxie, and rheobase measurements



Objectives

1. Record neurophysiological characteristics of nerves stimulated in SCS.
2. Determine types of fibers activated based on objective characteristics.
3. Build dataset of characteristics and correlate to SCS outcomes in future.

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435. INS19-0094

A PROSPECTIVE GLOBAL REGISTRY OF REAL-WORLD OUTCOMES USING SPINAL CORD STIMULATION SYSTEMS FOR CHRONIC PAIN

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Introduction: Large patient outcome registries are a key part of the compendium of information typically mined to generate real world data and evidence. Real world evidence (RWE) derived from such registries via application of advanced data analytics therefore represents a potentially important aspect of the on-going rational assessment and future development of commercially-available Spinal Cord Stimulation (SCS) devices. We present here a prospective global registry designed to evaluate long-term effectiveness of neurostimulation therapy for pain.

Materials/Methods: This is a prospective, multicenter global registry (RELIEF Registry, Boston Scientific) that aims to assess several various aspects of the pain treatment experience using SCS in up to 1700 participants at up to 80 centers (ClinicalTrials.gov Identifier: NCT01719055). These assessments will encompass pain relief, satisfaction, quality of life, safety, and other aspects associated with the real-world clinical use of SCS. Eligible study participants are trialed for "on label" use only with a commercially-approved SCS system (Boston Scientific) and must sign an IRB-approved informed consent form. All permanently-implanted subjects are followed out to 36-months.

Results: Results of the data analysis from initial cohorts evaluated from the Boston Scientific-sponsored RELIEF registry will be presented.

Discussion: This multicenter, global registry collects and analyzes a large real-world dataset collected from patients using SCS for chronic pain. Previously, SCS has been shown to be an effective treatment option for chronic pain as demonstrated in randomized controlled trials (1-3). This cohort represents the first prospective global registry evaluating the real-world use of SCS as a treatment approach for chronic pain.

Conclusions: This cohort represents the first prospective global registry evaluating the real-world use of SCS as a treatment approach for chronic pain.

Objectives

The RELIEF registry collects and assesses the following: pain relief, satisfaction, quality of life, safety, and other aspects associated with the real-world clinical use of SCS.

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436. INS19-0196

CUSTOMIZATION OF NEURAL DOSE: REAL-WORLD DATA DEMONSTRATING THE RELATIONSHIP BETWEEN FREQUENCY, PULSE-WIDTH, AND AMPLITUDE IN ACHIEVING SUB-PERCEPTION SCS PAIN RELIEF

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Introduction: A recent randomized controlled trial demonstrated sub-perception Spinal Cord Stimulation (SCS) at different frequencies requires titration of pulse-width and amplitude to enable optimal pain relief (1). This putative relationship between stimulation frequency, pulse-width, and amplitude is termed "neural dose". Additionally, initial evaluation of a new algorithm enabling patient-specific customization of stimulation field shape reported effective sub-perception SCS pain relief with reduced device charging (2). We describe validation of the proposed relationship between stimulation frequency, pulse-width, and amplitude using outcomes in previously-implanted patients utilizing sub-perception SCS (≤1.2kHz) combined with a novel field shaping algorithm designed to facilitate specific engagement with dorsal horn targets implicated in mediating the analgesic effects of sub-perception SCS (3).

Materials/Methods: This observational study of permanently-implanted patients (up to N=30) at 2 sites in Europe retrospectively (chart review) assessed SCS outcomes for chronic pain (NCT01550575). Pain relief scores (NRS) were collected at baseline and follow-up after utilization of an algorithm enabling a patient-specific field shape and titration of stimulation-frequency with individualized adjustment of pulse-width and amplitude. Patient charging burden is also under evaluation.

Results: As reported earlier, the relationship between frequency and pulse-width (as derived from most effective programs) demonstrated that shorter mean pulse-widths (~30-40μs) at 10kHz increased as frequency decreased, ultimately resulting in mean pulse-widths of ~100–110μs at 1kHz (1). In this study, a similar trend has been observed as frequency is further decreased. Data collection is ongoing and final results to be presented.

Discussion: We postulate that understanding relationships between stimulation parameters will contribute to better understanding of mechanisms-of-action of sub-perception SCS and foster decreased charge burden while maintaining or improving pain relief outcomes.

Conclusions: This study uses real-world data to verify the relationship between frequency, pulse-width and amplitude ("neural dose") in achieving analgesia. In addition, using the optimized neural dose, in combination with a customized field shape algorithm, may significantly decrease patient charge burden.

Objectives

1. To validate relationship between frequency, pulse-width and amplitude with sub-perception SCS pain relief.

2. To assess charging burden in patients using optimal neural dose (sub-perception SCS) combined with customized field shaping algorithm.

3. To document patient pain relief when combining use of a customized field shaping algorithm with titration of frequency and individualized adjustment of pulse-width and amplitude.

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437. INS19-0213

TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION AS A PAIN RELIEVING APPROACH IN LABOR PAIN – A SYSTEMATIC REVIEW OF RANDOMISED SHAM-CONTROLLED STUDIES

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Introduction:

• Transcutaneous electrical nerve stimulation (TENS) is a non-invasive electrophysical modality, which involves cutaneous application of electrical current that is used extensively to reduce pain and hyperalgesia in acute and chronic pain conditions including labor pain (1,2).

• The effectiveness of TENS for labor pain is still not established (3,4).

• As a result, TENS is not used routinely at clinic for controlling labor pain.

Materials/Methods: A systematic review was conducted according to guidelines from PRISMA and Cochrane.

Eligibility criteria:

• Studies on TENS and labor pain

• Randomised sham-controlled studies

• English and Danish literature

• Full-text studies

Keywords:

• "Transcutaneous electrical nerve stimulation" and "TENS"

• "Labor pain", "labor" and "parturition".

Databases:

• PubMed, Embase, Cochrane Library, Web of Science

Results:

• Ten studies were included in this review involving a total of 1179 parturients.

• Findings showed that the studies suffer from lack of quality in study design, which ultimately lead into lower GRADE.

• Four studies were identified significant positive for effectivity of TENS, while 6 studies were negative.

• Overall, TENS tend to reduce pain scores, the duration of labor and additional use of analgesia.

Abbreviations: publ. = publication, int. = intervention, SD = standard deviation, N/A = non applicable, N.S. = non significant, para0 = nulliparous, para1 = primiparous, para>1 = multiparous, N2O = nitrous oxide.

Discussion: N/A

Conclusions:

• The review showed a predominant effect of TENS compared to sham-TENS in labor pain.

• However, the current evidence is still not sufficient to show if TENS is more effective than sham-TENS in labor pain.

• Therefore, more qualified studies are required with respect to study design, appropriate stimulation parameters and powered studies.

Objectives

To perform a systematic review assessing the effectiveness of TENS compared to sham-TENS in healthy parturients with following outcomes:

• Pain relief

• Duration of labour

• Additional analgesia

1st Author, publ. year (Country)	Pain relief (VAS (cm ± SD)) [int. vs control(s)]	Duration of labor (min. ± SD) [int. vs control(s)]	Additional analgesia [int. vs control(s)]	Outcome	Randomization	Blinding	GRADE
Aghamohammadi 2011 (Iran)	8.1 vs 9.8 VAS score at full cervical dilatation, P<0.0001	180.9 ± 25 vs 238.2 ± 30.7 (first stage), P<0.0001	N/A	Positive	Inadequate (toss with coin only once)	Adequate (double-blinded)	++
Chao 2007 (Taiwan)	31/50 (62%) vs 7/50 (14%) VAS score reduction ≥ 3, P<0.001	122 ± 108 vs 133 ± 115 (first stage), P=0.64, N.S.	N/A	Positive	Adequate (blocks by stratification of parity)	Adequate (double-blinded)	+++
Harrison 1986 (Ireland)	33/49 (68%) voted pain level 3, which lowered after 1 h to 17/46 (37%), N.S.	372 ± 162 vs 300 ± 90 (para0), N.S.	43/49 (88%) vs 44/51 (86%) (para0), N.S.	Negative	Inadequate (not described)	Adequate (double-blinded)	+++
Lee 1990 (Hong Kong)	N/A	459.6 ± 140.4 vs 375 ± 152.4 vs 452.4 ± 195.6 (para0), N.S.	31/46 (67%) vs 18/24 (75%) vs 25/31 (81%), N.S.	Negative	Inadequate (not described)	Adequate (double-blinded)	++
Nesheim 1981 (Norway)	25/35 (71%) vs 19/35 (54%) reporting "some relief", N.S.	525 vs 570, N.S.	49 vs 63 events, N.S	Negative	Adequate (toss with coin)	Adequate (single-blinded)	++
Padma 2000 (Oman)	13/25 (52%) vs 4/10 (40%) (para1) and 16/25 (64%) vs 4/10 (40%) (para>1) reporting "good to excellent relief", P<0.05 (back pain)	Reduced with 120 min. in para>1 (TENS) and 77 min. in para1 (sham), P<0.001	N/A	Positive	Inadequate (not described)	Inadequate (not described)	+
Shahoei 2017 (Iran)	6.4 ± 2.14 vs 8.4 ± 1.38 vs 8.2 ± 1.6, after 1 h, P<0.001 (also 2h, 3h, 4h after, P<0.000)	158.42 ± 136.64 vs 262.5 ± 125.23 vs 257.16 ± 114.10 (first stage), P<0.002	N/A	Positive	Adequate (toss with coin)	Adequate (single-blinded)	+++
Steptoe 1984 (Denmark)	4/11(36%) vs 2/13 (15%) VAS score reduction, N.S.	241 vs 268, N.S.	5/12 (42%) vs 13/13 (100%), P<0.05	Negative	Inadequate (not described)	Adequate (single-blinded)	++
Thomas (1988) (Australia)	3.5 ± 3.4 vs 3.3 ± 3.1, for < 7 cm cervical dilatation (low back pain), N.S.	N/A	120/132 (90%) vs 136/140 (97%) (N_2O), N.S.	Negative	Adequate (list of random numbers)	Adequate (double-blinded)	++
Van der Ploeg 1996 (Netherlands)	6.6 vs 5.8, N.S.	454 ± 213 vs 587 ± 205, N.S. (first stage)	60.8 ± 21.6 mg vs 65.4 ± 15.9 mg, N.S (pethidine)	Negative	Inadequate (not described)	Adequate (double-blinded)	+++

Table 1: Quality and result characteristics of the selected studies

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438. INS19-0062

SPINAL CORD STIMULATION FOR LEG PAIN AND LOW BACK PAIN WITH DEGENERATIVE LUMBAR KYPHOSCOLIOSIS

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Introduction: Degenerative lumbar kyphoscoliosis (DLKS) is associated with leg pain due to stenosis inside and outside the spinal canal, and kyphosis is associated with back pain and quality of life, DLKS patients often chief complaint of leg pain and back pain[(1)]. Spinal cord stimulation (SCS) is one of the minimally invasive surgical procedures, clinical experience and the results of basic research clearly show that the indicated pain is effective for neuropathic pain and ischemic pain[(2)]. We report two cases in which SCS was performed on leg and back pain by DLKS.

Materials/Methods: SCS was introduced in DLKS cases where orthopedic surgery is not indicated.

Results: Case.1 A-88 old woman, height 145cm, weight 42kg.

The patient reported a pain score of 8 out of 10 at rest on a standard NRS. Intermediate claudication (IC) is 1m. Lumbar JOA score is 7 out of 29. She underwent permanent implantation of SCS lead and a generator. It shows the change of ADL after 12 months since SCS was implanted. IC: 1 m → 100 m (using a walker), lumbar spine JOA score: 7 → 14 points.

Case.2 A-79 old Woman, height135cm, weight35kg

The patient reported a pain score of 8 out of 10 at rest on a standard NRS. IC is 50m. Lumbar JOA score is 10 out of 29. She underwent permanent implantation of SCS lead and a generator. It shows the change of ADL after 12 months since SCS was implanted. IC: 50 m → 200m, lumbar spine JOA score: 10 → 10points.

Discussion: DLKS has mixed pain. Causes and types of mixed pain include nociceptive pain due to osteophyte formation, myofascial pain caused by elongation and shortening of spinal column standing muscles with lateral kyphosis, joint pain by sacroiliac joints and facet joints, and neuropathic pain caused by intervertebral foramina and spinal canal stenosis with spinal degeneration(3)

Conclusions: SCS is a minimally invasive operation, it is considered to be a method that can avoid surgery for older DLKS patients with large perioperative complications due to orthopedic surgery.

Objectives

none

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439. INS19-0435

O-ARM GUIDED PERCUTANEOUS BALLOON COMPRESSION FOR TRIGEMINAL NEURALGIA: PERSONAL EXPERIENCE

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Introduction: Percutaneous Balloon Compression (PMC) is widely used for treatment of trigeminal neuralgia (TN) in selected patients, but foramen ovale (FO) is not always clearly identified with classic fluoroscopy devices and sometimes direct puncture is difficult. We report our experience with O-Arm2 navigation PMC for TN in cannulating the FO and determining the position of the balloon

Materials/Methods: O-Arm2 registration and navigatied PMC was performed in 10 consecutive cases. The 3D bone reconstruction of skull base was obtained with stealth-station software after intraoperative O-Arm registration. The FO puncture was obtained with navigated needle with suretrack. The balloon position and compression were verified with fluoroscopy with O-Arm. Time of procedure and FO cannulation is discussed

Results: O-Arm registration and navigation of needle allows quick, safe and easy cannulation of the FO. It provided three-dimensional images which were more elaborate than the classic fluoroscopic images for determining correct positioning in all cases. O-Arm registration and navigation is lmore time-consuming than normal fluoroscopy, but cannulating the FO was in all case achieved, with less attempts and in less than 1 minute. All the patients were pain-free after PMC and no complication reported

Discussion: O-Arm registration and navigation assists PMC in three ways: (1) the FO can be visualized in 3D skull base reconstruction; (2) needle correction or insertion can be performed much more easily because of the direct fluoroscopic control; and (3) low incidence of complications and a good prognosis

Conclusions: We believe that using this new intraoperative system, the overall time of surgery and fluoroscopy could still be reduced in a near future

Objectives

new surgical technique
neuronavigation and neurosurgery
improving results of percutaneous procedures

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Poster Presentations - May 27 - May 30
Spine - Pain

440. INS19-0186

RESPONDER ANALYSIS OF PROSPECTIVE, MULTICENTER TRIAL TO EVALUATE MULTIPLEXED SCS FOR DIFFERENTIAL TARGETS IN SUBJECTS WITH CHRONIC INTRACTABLE BACK PAIN WITH OR WITHOUT LEG PAIN

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Introduction: Differential-Target Multiplexed spinal cord stimulation (DTM-SCS) involves using multiple pulsed signals that are combined spatially and temporally. Neurons in the spinal cord underneath SCS are surrounded in greater number by glial cells. It is now understood that these cells play important roles in establishment and maintenance of chronic pain. Therefore, modulating the neuro-glial interaction may be a promising strategy for SCS. Furthermore, neurons and glial cells behave differently when exposed to electrical pulses. We hypothesize that multiplexing electrical signals to differentially targeting glia and neurons may have beneficial impact on chronic pain relief.

Materials/Methods: Pain relief from DTM-SCS was compared with conventional SCS in a prospective, multi-center, open-label, crossover study. Seven sites in US participated. DTM-SCS was delivered using investigational device (37022-MRS ETS), and programmed by the sponsor's (Stimgenics) representatives. Multiplexed pulses were between 20 and 1,200Hz and under 1ms. Conventional SCS was programmed by device manufacturer's representatives. Subjects evaluated conventional SCS for 4 ± 1 days. After chronic pain returned during the washout period, DTM-SCS was applied for 4 ± 1 days. Analysis was conducted for responders (subjects experiencing ≥50% pain reduction) to DTM-SCS or conventional SCS.

Results: Twenty-five subjects were enrolled. They had predominant back pain with a mean duration of 18 years and mean age of 62.4. Overall, back pain responder rate was 80% for DTM-SCS, and 50% for conventional SCS. In the subset of back pain responders to DTM-SCS, mean baseline back pain was 7.6 with DTM-SCS achieving a mean back pain of 1.8, representing a reduction of 76% reduction from baseline. For back pain responders to DTM-SCS, a 79% reduction in leg pain was attained. In conventional SCS responder subset, back pain reduction of 67% and leg pain reduction of 42% were achieved.

Discussion: DTM-SCS achieved significantly greater back pain relief and back pain responder rate than conventional SCS. Similarly, when evaluating subsets of patients who were responders to respective approaches, DTM-SCS achieved greater back and leg pain relief than conventional SCS.

Conclusions: This multicenter prospective study shows that DTM-SCS is a feasible alternative for treatment of chronic low back pain. A larger, long-term randomized clinical study to confirm these findings in in progress.

Objectives

Introduce DTM-SCS for treating chronic back pain.

Report on feasibility of DTM-SCS.

Compare pain relief of SCS therapies

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441. INS19-0181

PROSPECTIVE, RANDOMIZED, MULTI-NATIONAL STUDY RESULTS TESTING A NOVEL, PULSED STIMULATION PATTERN (PSP) IN THE TREATMENT OF CHRONIC LOW BACK PAIN

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Introduction: For 50 years, spinal cord stimulation (SCS) has primarily used low-frequency (e.g. 40Hz) tonic stimulation to target dorsal spinal cord structures and produce analgesia in chronic pain patients. Recent applications of higher frequencies and burst patterns have expanded the perspective on how stimulation patterns can influence clinical efficacy. In this prospective, randomized, multi-center, multi-national study, we tested a novel, pulsed spinal cord stimulation pattern in the treatment of leg and/or low back pain.

Materials/Methods: A novel, pulsed stimulation pattern (PSP) has been developed to take advantage of multiple and divergent neural mechanisms underlying analgesia with SCS. A prospective, randomized, multi-national, study was conducted to determine if this novel stimulation pattern could provide improved clinical efficacy in comparison to tonic SCS. Standard epidural lead placements were used and both low frequency tonic and the PSP were tested acutely for up to 14 days. Leads were epidurally placed in either traditional physiologic positions (utilizing paresthesia overlap) or an anatomically-based location (below paresthesia threshold), covering the T8-T10 epidural region. Initially, 21 subjects were randomized to anatomic- versus physiologic-based programming with the novel PSP. An additional 27 study subjects were trialed on the novel pattern, with anatomic-based PSP. In all study subjects, standard tonic programming was used as a control.

Results: The anatomic-based programming demonstrated a better responder rate (>50% pain relief) in both the back (70%) and the legs (86%) compared to the physiologic-based programming (30% for back and 40% for legs). When all the anatomic-based programming outcomes were compared to tonic outcomes, among the PSP responders, the novel PSP yielded statistically better pain reduction than tonic in both the back and leg. When compared to baseline within subjects, PSP pain reduction was 77% in the back and 71% in the leg, whereas Tonic pain reduction was 52% in the back and 51% in the leg.

Discussion: These clinical results demonstrate that statistically significant low back and leg pain relief can be achieved when a novel, pulsed SCS pattern is delivered to a discrete anatomic location. Both the responder rate to therapy, as well as the level of response, are significantly better when utilizing PSP as compared to Tonic. Mechanistically, PSP has

demonstrated altered pain responses in dorsal horn neurons thus providing a translational confirmation via the clinical results reported here.

Conclusions: These early findings show strong responder rates and pain relief for a novel, anatomically placed, paresthesia-independent stimulation pattern.

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442. INS19-0253

ELECTROPSYCHOPHYSICAL CHARACTERIZATION OF HIGH-KHZ EPIDURAL SPINAL CORD STIMULATION

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Introduction: 10kHz spinal cord stimulation (SCS) has been successfully used for the long-term treatment of chronic neuropathic pain since the 10kHz spinal cord stimulation system was first made clinically available in 2011. Electropsychophysical characteristics of low frequency (<1.2kHz) epidural SCS (LF-SCS) with have been studied, but the subjective and quantitative responses of patients using high-kHz SCS are unknown. This study will collect basic electropsychophysical data including (1) strength-duration (SD) curves for sensation and (2) quantitative description of paresthesia with supra-perception amplitude, at 5kHz with 20, 30, 50 and 80us pulse widths (PW).

Materials/Methods: Perception threshold (Pth) to SCS was collected at 5kHz with various pulse widths (20us, 30us, 50us, 80us), using both duty-cycled (200ms ON, 1s OFF) and continuous stimulation, using a bipole configuration, from patients implanted with a permanent 10kHz SCS system. The SD curve at 5kHz was compared to that from LF-SCS (Yearwood et al). Using duty-cycled 5kHz SCS, set to 10-20% above Pth, paresthesia intensity perceived by patient was queried every 15sec for 1min.

Results: Data were collected from 8 subjects (7 females). SD curve of Pth at 5kHz showed a typical exponential decay function with PW. However, rheobase and tau were much smaller (1.8mA and 103us, estimated from subjects providing full strength-duration curve within 20-80us pulse width) than LF-SCS (2.5mA and 295us) by Lapique equation. Perceived paresthesia intensity grew weaker during 1 min of duty-cycled 5kHz stimulation, by ~86% at 20us, and ~54% at 80us.

Conclusions: Electropsychophysical characteristics of paresthesia from high-kHz SCS was characterized by a more sensitive SD curve and short-term adaptation. Lower rheobase from high-kHz SCS patients might be the small dCSF distance effect. Shorter tau may imply that neural fibers activated by high-kHz SCS are different populations from those activated by LF-SCS. Short-term adaptation might be a unique characteristic of nerve fibers exposed to high-kHz stimulation. While it is noted that paresthesia-independent 10kHz SCS therapy is applied clinically at much lower intensity than Pth, high-kHz stimulation may modulate nerve fibers in different manner from conventional stimulation.

References

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443. INS19-0274

SPINAL CORD STIMULATION AT 10 KHZ FOR TREATMENT OF CHRONIC PAIN IN A COMPENSABLE SETTING

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Introduction: The treatment of chronic pain with traditional spinal cord stimulation (SCS) in a compensable patient population has caused much contention over the years. Whilst proved efficacious in patients without perceived secondary gain (1,2), prior studies have shed scrutiny over the use of traditional SCS in patients under worker's compensation and similar compensable schemes (3). Paresthesia-independent high frequency spinal cord stimulation at 10 kHz (HF-SCS) has demonstrated superior long-term safety and efficacy in back and leg pain patients when compared to traditional (SCS) (4). Given this, we investigate whether HF-SCS can also be efficacious in a compensable chronic pain patient population.

Materials/Methods: Forty-one patients clinically diagnosed with chronic leg and/or back pain of ≥5 on the numerical pain rating scale (NRS) and intractable to conventional medical management, received a HF-SCS implant following a successful trial phase. Electrode leads were placed epidurally over T9/T10 vertebral levels. Patients were followed up as per commercial practice at end of trial, 3-, 6-, 12- and 24-months post permanent implant. Patient outcomes were recorded and presented as mean ± standard deviation.

Results: Baseline pain scores of 8.3±1.3 NRS (n=41) improved to 2.0±1.5 NRS (n=36), 2.8±2.7 NRS (n=22), 3.8±3.0 NRS (n=18), 2.6±3.1 NRS (n=13) and 3.3±3.8 NRS (n=4) at the end of trial, 1-, 3-, 6-, 12- and 24-month follow-ups, respectively. When surveyed at last follow up, 85.4% of patients reported an improvement in function, 77.8% reported an improvement in sleep and over half (56.4%) of the patients were able to decrease their medication use. No long-term adverse events were observed.

Discussion: This early data reports similar outcomes to those published in a non-compensable cohort (5), encouraging the wider application of HF-SCS therapy, despite the payer conditions under which the therapy was received.

Conclusions: Interim results in this commercial and compensable patient cohort demonstrate that HF-SCS at 10 kHz could potentially provide clinically meaningful pain relief to patients, irrespective of their payer status.

Objectives

To actively consider the use of HF-SCS in a compensable patient setting.

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444. INS19-0281

PRELIMINARY INVESTIGATION OF A NOVEL ULTRAHIGH-FREQUENCY STIMULATION PARADIGM AT SPINAL CORD IN PATIENTS WITH INTRACTABLE BACK PAIN AND/OR LEG PAIN

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Introduction: High-frequency spinal cord stimulation (SCS) at 10 kHz could provide better efficacy at reducing back and leg pain than traditional SCS and does not produce paresthesia.[1] Another high-frequency example is dorsal root ganglion (DRG) stimulation with pulsed radiofrequency paradigm (500 kHz), which exerts temporary analgesia. We thus hypothesized that an implantable modality with ultra-high frequency (UHF) pulses at the spinal cord level may have equal effects.

Materials/Methods: We conducted the SCS study with IRB approval. Eligible patients with intractable back and/or leg pain (with average pain score VAS-ave >5) were included. Two leads were placed at the T8-T12 epidural space and stimuli were maximized to 9 mA, 10-min in duration, once or twice per day during hospitalization. The leads were implanted for 5 days and explanted before discharge. Feeling of paresthesia, leg motor function, analgesics medication, Brief Pain Inventory (BPI), and Oswestry Disability Index (ODI) were evaluated pre- and post-stimulation.

Results: Ten eligible patients (4 males, 6 females) completed the study. Two cases were participants of previous DRG trial with adequate wash-out period. Baseline VAS-max and VAS-ave were 8.9±0.7 and 6.9±0.7. None of the cases felt paresthesia during stimulation. All cases experienced pain reduction >50% and 7 cases had pain reduction >70% during trial period. The responsive duration (with pain reduction > 50%) was from 1 day to the longest 12 days. BPI and ODI showed significantly improvement. No severe adverse events (SAE) was present. Most AEs were injection-induced local pain and all were mild and resolved before the end of study.

Discussion: This is a pilot and the first study to date demonstrating intermittent UHF pulsed at the spinal dorsal column is safe, paresthesia-free, efficacious in attenuating back pain and leg pain, and can normalize functionality. Each stimulus produces temporary analgesia for days, implicating no continuous electrostimulation is necessary. These findings are compatible with our preclinical animal study and worthy of developing next generation of a power-saving or battery-free SCS modality.

Conclusions: We speculate that UHF stimulation at the spinal cord can become a novel implantable neuromodulation modality. We still need evidence from double-blinded, randomized control studies to prove this hypothesis.

Objectives

1. To evaluate whether an implantable stimulation with UHF is safe, paresthesia-free, and feasible for human use.

2. To compare effects of UHF stimulation between the spinal cord and DRG on reducing back pain and leg pain.

3. To evaluate whether UHF stimulation could become a novel neuromodulation modality.

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445. INS19-0284

PRELIMINARY INVESTIGATION OF A NOVEL ULTRAHIGH-FREQUENCY STIMULATION PARADIGM AT DORSAL ROOT GANGLION IN PATIENTS WITH INTRACTABLE BACK PAIN AND/OR LEG PAIN

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Introduction: High-frequency spinal cord stimulation (SCS) at 10 kHz could provide better efficacy at reducing back and leg pain than traditional SCS and does not produce paresthesia(1). Another high-frequency example in use is dorsal root ganglion (DRG) stimulation with pulsed radiofrequency paradigm (500 kHz), which exerts temporary analgesia. We thus hypothesized that an implantable modality with ultra-high frequency pulses (UHF) at the DRG level may produce equal effects.

Materials/Methods: We conducted the DRG study with IRB approval. Eligible patients with intractable back and/or leg pain (with average pain score VAS-ave >5) were included. Only one electrode was implanted and stimuli were sequentially increased but limited below 9 mA, 5-min in duration, and maximally three stimuli during 2 implantation days for safety concern. The lead was implanted for 2 days and was explanted before discharge. Feeling of paresthesia, leg motor function, pain scores, and analgesics medication were evaluated pre- and post-stimulation.

Results: Eleven eligible patients were enrolled and 8 cases (5 males) completed the study. Seven cases were diagnosed with failed back surgery syndrome. The averaged baseline VAS was 6.4±1.1. The most significant pain reduction (VAS: 3.0±1.1, $p<0.001$) occurred one day after stimulation and 4 cases showed pain reduction >70%. The responsive duration (with reduction >50%) was from 3 days to over 2 weeks. The analgesic medications (NSAID, opioid, and antiepileptics) were reduced but no statistical significance. No severe adverse events (SAE) was present. Most AEs were injection-induced local pain (about 30%) were mild and resolved before the end of study.

Discussion: This is a pilot and the first study to date demonstrating intermittent UHF pulsed at the DRG is safe, paresthesia-free, efficacious in attenuating back pain and leg pain, and can normalize functionality. Each stimulus produces temporary analgesia for days, implicating no continuous electrostimulation is necessary. These findings are compatible with our preclinical studies (2) and worthy of developing next generation of a power-saving or battery-free DRG stimulation.

Conclusions: We speculate that UHF stimulation at the DRG can become a novel implantable neuromodulation modality. We still need evidence from double-blinded, randomized control studies to prove this hypothesis.

Objectives

1. To evaluate whether an implantable stimulation with UHF is safe, paresthesia-free, and feasible for human use.
2. To compare effects of UHF stimulation between the spinal cord and DRG on reducing back pain and/or leg pain.
3. To evaluate whether UHF stimulation could become a novel neuromodulation modality.

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446. INS19-0190

OUTCOMES FOLLOWING UTILIZATION OF A DEVICE ADAPTOR IN PREVIOUSLY-IMPLANTED PATIENTS USING SCS FOR CHRONIC PAIN

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Introduction: Patients implanted with spinal cord stimulation (SCS) systems who use continuous or high amounts of power may intermittently discontinue therapy or use lower energy settings to potentially preserve device longevity. This has the potential to extend the therapy and use of their device over time. Alternatively, patients using SCS systems who have endured problems with device longevity and/or loss of efficacy may be able to achieve better outcomes utilizing newer technologies that offer an increased variety of waveforms and programming options to address their chronic pain. In this retrospective study, we examined the outcomes of previously-implanted patients who went on to use a commercially-available adaptor enabling connection to an SCS system that offers multiple neurostimulation based treatment approaches to regain and maintain efficacious therapy.

Materials/Methods: This is a real-world, retrospective study of patients who were previously implanted with an SCS system (commercially-available SCS device, Abbott) who then went on to utilize an adaptor (Precision S8, Boston Scientific) to connect to a new SCS system capable of multiple modality stimulation and/or combination therapy. Pain relief and other associated outcomes with both previously-implanted SCS systems and newly connected commercially available systems (Boston Scientific) are being collected.

Results: Data from a total of 10 subjects have been reported. Seven subjects with overall pain scores using both systems were analyzed. Five out of 7 subjects utilizing a device adaptor reported better pain relief with the use of a multiple waveform SCS system than with their previous system. Additional data to be presented.

Discussion: New technologies now offer a range of options when using SCS to help treat chronic pain specific to one's own needs which many previously-implanted patients are not able to experience. Use of a commercially-available adaptor therefore may provide previously-implanted patients with enhanced neurostimulation-based technological capabilities.

Conclusions: The results of this preliminary study suggest that offering previously-implanted SCS patients a system capable of providing multiple waveforms can improve pain relief. Further analysis is required.

Objectives

1. To evaluate pain intensity associated with a commercially-available adaptor enabling connection to an SCS system that offers multiple neurostimulation based treatment approaches.
2. To evaluate patient quality of life associated with a commercially-available adaptor enabling connection to an SCS system that offers multiple neurostimulation based treatment approaches.
3. To evaluate patient satisfaction associated with a commercially-available adaptor enabling connection to an SCS system that offers multiple neurostimulation based treatment approaches.

References

NA

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447. INS19-0432

BOTH CERVICAL AND THORACIC SPINAL CORD STIMULATION IN SAME PATIENT.

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Introduction: Spinal cord stimulation (SCS) is indicated in several pain related pathologies such as neuropathy, failed back surgery syndrome, chronic regional pain syndromes, peripheral vascular pain etc. (1,2) For the lower extremities and the back pain, the electrodes are often placed between the thoracic 8 and 12 level and for the neck and upper extremities pain the electrodes are placed to the cervical epidural area. Herein, we report a case of persistent neuropathic pain on both the upper and lower extremities treated successfully by cervical and thoracic SCS implantation.

Materials/Methods: A 39-year-old male patient was admitted to our outpatient clinic due to persistent neuropathic pain in the lower and upper limbs and in trunk, which started approximately five years ago. The Visual Analog Scale (VAS) score was 9 at rest. He was diagnosed with diabetes mellitus 10 years ago. Severe motor and sensory axonal neuropathy was observed on electroneuromyography. The patient was being treated with Naproxen sodium (750 mg/d) and gabapentin (2400 mg/d) and the subsequent addition of tramadol (200 mg/d) but there is no response to the treatment. The patient underwent to the surgery. Two separate electrodes was inserted percutaneously under local anesthesia to the cervical and thoracic epidural space (Medtronic Inc., Minneapolis, MN, USA). After successful trial stimulation period, the permanent Implantable Pulse Generator (IPG) was implanted.

Results:

In the trial period the pain (both on upper and lower extremities) was immediately relieved. 1 month after the IPG implantation the VAS score was decreased from 9 to 3. The medication was decreased step by step. The gabapentin dosage lowered to 1200 mg/d. and the Tramadol treatment was discontinued.

Discussion: Spinal cord stimulation is an effective treatment modality in resistant diabetic neuropathic pain. In our knowledge In literature there is no any study about the double target.

Conclusions: If SCS treatment is decided in patients with both upper and lower extremities pain, they could be treated with two separate electrodes on cervical and thoracic epidural spaces.

Objectives

SCS is an effective therapy on resistant diabethic neuropathy.

Two separate electrodes (cervical and thoracic) could be used on same patient.

Two separate electrodes can implant in same surgery.

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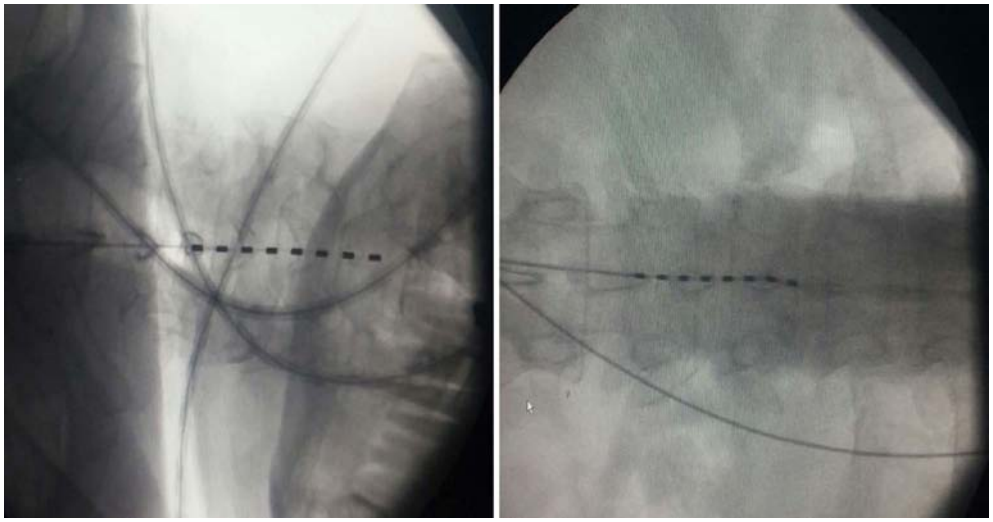

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448. INS19-0167

PATTERNED PULSE TRAINS YIELDED MANIFOLD SENSATIONS PERCEIVED BY PATIENTS DURING ACUTE SPINAL CORD STIMULATION EVALUATION

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Introduction: Spinal Cord Stimulation (SCS) for chronic pain management generally uses tonic pulse trains, where the amplitude, pulse width (PW) and rate of a stimulation program, once set, do not vary with time. Patients experience paresthesia for pain relief during supra-perceptive stimulation, however the variation of sensations induced by conventional SCS may be limited, largely due to the time-invariant nature of stimulation. We hypothesize that stimulation with time-varying pulse trains may enable tailoring of sensation quality. In this work, we evaluated the sensation perceived by patients when acutely stimulated with SCS using several patterned pulse trains.

Materials/Methods: Patients undergoing an on-label percutaneous SCS trial were recruited. An off-the-shelf external stimulus generator (STG4004, Multi-Channel Systems, Germany) was used to generate tonic and patterned stimulations, the latter including amplitude-modulated, PW-modulated and rate/timing-modulated pulse trains. At the end of SCS trial, consented subjects blindly received different stimulations for a few minutes each, and provided assessment of their experience including drawings of perception location, description of sensation, and ratings for comfort and helpfulness to pain relief. Verbal description of experience was audio-recorded from patients consented for this option.

Results: Sensation induced by 65% (41/63) of patterned stimulation were rated as comfortable or very comfortable, and 76% (48/63) were rated as helpful or very helpful to pain relief. Using the same electrode configuration and PW, 57% (36/63) of patterned stimulation achieved greater concordance over pain areas than tonic stimulation. Maximal coverage was achieved by a patterned stimulation in 9/13 patients. More variation in sensation was described by subjects when undergoing patterned stimulation as compared to tonic stimulation, with some distinct sensations achieved only during patterned stimulation. Positive rating of sensation during patterned versus tonic stimulation was found to vary among subjects by age, gender and pain location.

Discussion: The variation in sensation, the positive ratings for patterned stimulation, as well as the desire expressed by subjects to use different stimulation patterns during different activities, suggested that personalization of and access to multiple patterns is valuable.

Conclusions: SCS using patterned pulses has potentials to improve stimulation sensations and provide more options for therapy optimization and personalization. Additional studies are warranted to evaluate their efficacy on pain relief and satisfaction in chronic settings.

Objectives

1) To assess the quality of sensation induced by acute SCS using patterned pulse trains.

2) To assess the stimulation coverage of pain produced by patterned SCS.

3) To assess patient's perception of potential for pain relief using patterned SCS.

References

None

Poster Presentations - May 27 - May 30
Spine - Pain

449. INS19-0151

CERVICAL SCS WITH SUBPERCEPTION MODALITIES: A CASE SERIES

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Introduction: Chronic intractable cervical pain has been treated for decades with drug therapy and eventually surgical approaches. Although spinal cord stimulation has a validated clinical evidence for management of intractable lumbar and leg pain (1), it is currently under-utilized for cervical pain treatment, particularly due to increased risk of complications and uncomfortable paresthesia feeling reported by the patients. We report our experience with cervical SCS using novel subperception waveforms (2).

Materials/Methods: Five patients with diagnosis of cervical radiculopathy, have been implanted with a SCS system capable of current steering, 3D algorithm (Illumina™3D) for pain mapping and multimodal stimulation pattern platform (Boston Scientific, Valencia, CA). Three patients have been mplanted with dual octopolar linear leads, while two patients with a single 16-contact lead (Infinion™CX, Boston Scientific). Patients never experienced paresthesia stimulation but only subperception modalities (Burst3D and 1 KHz), modeled on paresthesia test and optimized during the first weeks after implant. Patients reported pain relief by NRS score, PDI and QOL at 6 – 12 – 24 months

Results: All patients have been successfully implanted with SCS leads in the cervical spine; they reported respectively pain relief of 60% by NRS, PDI scores significantly reduced from baseline and an overall improvement of QOL along 24 months of follow up. They used subperception programs, with a configuration activating a mean of 6 contacts; three patients used a burst3D program (mean Pulse width 600 microsec, mean amplitude 0,7 mA) and two patients a 1 KHz rate program (mean Pulse width 80 microsec, mean amplitude 1,6 mA). No lead migration has been reported

Discussion: Clinical outcomes of these patients implanted with cervical SCS are aligned with our experience with lumbar SCS using the same products. Subperception modalities are definitely an adequate solution for cervical SCS. Moreover, to reduce the probability of complications like lead migration, we decided to use the longer 16 contact lead with 67mm span with optimal contacts placed in the middle line.

Conclusions: Cervical SCS, combined with subperception modalities and proper lead selection should be considered as a valid treatment for cervical chronic pain.

Objectives

Cervical SCS for pain related to radiculopathy
Cervical SCS with subperception waveforms
Use of 16 pole lead in cervical area

References

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Poster Presentations - May 27 - May 30
Spine - Spasticity and Movement Disorders

450. INS19-0051

LATERAL CORD MAGNETIC STIMULATION FOR REFRACTORY SPASTIC CEREBRAL PALSY – DESIGN OF A MULTICENTER DOUBLE BLINDED RANDOMIZED AND CONTROLLED CLINICAL TRIAL

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Introduction: Cerebral Palsy (CP) is a chronic and multi- etiological morbid condition affecting the psychomotor development, as a consequence of perinatal acquired developmental abnormalities.

Manifestations are motor disorders, mental retardation, spasticity, dystonia1, and refractory speech troubles for which there is no currently available therapy 2, these conditions are stable at early adulthood 3.

Additionally, magnetic stimulation is a non invasive method with spreading medical use 4, what can be modeled to adjust the therapeutic target 5.

New therapeutic options are needed for spasticity and the spinal cord is an excellent target for that purpose 6.

Materials/Methods: A double group masked assignment will be done into two different arms, treated and sham (Table1).

Volunteers will be recruited based on inclusion and exclusion criteria (Table2)

Assessments with Modified Ashworth Scale and Functional Independence Measure (FIM)- for speech, as Primary Outcome Measures, and also Barthel Index evaluation) will be performed on day 0 baseline evaluation and one monthly post – interventional evaluation during three consecutive months.

TABLE 1

Patients will be divided into two arms, randomly assigned:

1) **Treated Arm (MS – PKT):** they will receive kinesthetic and phoniatric treatment, and during a period of six months they will receive a magnetic stimulation treatment, stimulations that will have the following parameters, will be performed at 80% of the motor threshold of the cervical musculature (infra liminali, with 10 trains of 100 pulses at 10Hz completing 1,000 pulses in total. Each train will last 10 seconds with an interval of 50 seconds, lasting each session for around 30 minutes. These applications will be repeated twice a week for 3 months, cervical lateral location. The parameters will be modelized in order to focalize the impact on the anatomical region corresponding to the Lateral Spinal Cord.
2) **Sham comparator Arm (fMS – PKT):** they will receive kinesthetic and phoniatric treatment, and during a lapse of 3 months and with equal period city, they will receive a false magnetic stimulation treatment, of equal localization that the previous one, that will be sensitive to the stimulated subject, but of insufficient and irregular parameters so as not to produce any effect on the spinal cord, in order to blind clinical experience.

TABLE 2

INCLUSION CRITERIA
- Age 16 years or older - Spastic Cerebral Palsy with stable condition. - Motor disability unilateral or predominantly unilateral - Clinically evident speech disorders - Normally subnormal normal intellectual coefficien: - Absence of psychiatric disorders
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. - Episodes of Status Epileptucus - Personal history, or in close relatives, of medical legal complaint

At least 20 individuals in all centers, will be recruited. Movements and speech, will be also filmed and recorded monthly.

Results: Statistical tabulation will be carried out, by p calculation, Student's t-tests and analysis of variance, in search of significant differences into the two groups. This study was registered on the National Institutes of Health (NIH) website, NCT 03676439.

Discussion: The rationale of this clinical trial is the decrease of the excitability threshold of the nociceptive response by electrically stimulating the lateral Spinal Cord and its validation as a new method depends on a correct clinical trial design 11 and execution 12. Spastic Cerebral Palsy has been chosen as a targeted therapeutic population, a chronic and irreversible condition, up to the present, which has scarce, ineffective therapeutic options, with frequent complications.

Conclusions: Lateral Cord Stimulation (LCS) was discovered as producer of mean threshold increase for abnormal muscle responses, under experimental conditions, as described and referred. Due to its non-invasiveness and possible efficacy, the use of magnetic stimulation on this target is proposed to prove its therapeutic usefulness.

Objectives

1) To describe the anti abnormal spreading effect of Lateral Cord Stimulation (LCS) as a fundament for antispastic therapeutics and to introduce LCS as a new tool for the treatment of Refractory Spasticity.

2) To analyze the non invasive technique to be employed and its rational in future patients with refractory spasticity treated by means of LCS.

3) To communicate the clinical trial design structures to demonstrate its effectiveness into a limited and circumscribed sample of patients with specific characteristics, Spastic Cerebral Palsy on a chronic and steady condition and to propose the theoretical basis of clinical trial setted up on NIH clinicaltrials.gov, under the number NCT 03676439

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Poster Presentations - May 27 - May 30
Spine - Spasticity and Movement Disorders

451. INS19-0071

STRIDE LENGTH ON UNAFFECTED SIDE AND MODIFIED ASHWORTH SCALE ARE TOOLS TO ASSESS LOWER LIMB SPASTICITY TREATED WITH PERIPHERAL NEUROTOMY ENHANCED BY PERIPHERAL MAGNETIC STIMULATION

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Introduction: Post – stroke Spasticity is released by selective peripheral neurotomy (SPN)1,but is difficult to calculate the amount of lesion to avoid weakness or remaining spasticity2. This issue is outstanding on lower limbs where rigidity3 acts as weight support on gait 4,5. Nevertheless, spasticity can carry to several orthopedic limb dysfunctions6. Our objective is twofold, to analyse the effects of post – operative antagonistic Magnetic Stimulation on improvement of spastic lower limbs treated by SPN of the tibialis posterioris nerve and to evaluate the stride length of unaffected side for treatment's outcome. This work is the continuation of a previous paper 6.

Materials/Methods: Sixteen patients with unilateral post stroke refractory spasticity on lower limbs with inclusion and exclusion criteria (Table 1), were treated by SPN, followed by sessions of kinesics and Magnetic stimulation treatment. A previous anesthetic blockade with a decrease greater than 1,5 in MAS (hip, knee, ankle and toes) was considered positive and underwent SPN on tibialis posterioris nerve, on the affected side. After surgery, patients underwent rehabilitation treatment with parallel MS applications at 80 per cent of infraliminar individual

Inclusion Criteria

- Stroke lasting at least six months
- Harmful Spasticity on gait function
- Refractoriness to medical and rehabilitation treatment, including Botox and maximal Baclofen doses
- Decrease of at least 1,5 points in MAS after Bupivacaine local blockade

Exclusion Criteria

- Severe cardiovascular disease
- Repeated stroke events (not steady condition)
- Bone or articular deformities on the lower limbs (hip, knee, ankle)
- Oncologic diseases with less than a year of life expectancy
- Severe cognitive impairment (mini mental test 16 or lower)

motor threshold, 100 pulses at 10 Hz, each train lasting 10 seconds, with a fifty second interval, done twice a week, during 6 months. Patients were preoperative and monthly postoperatively evaluated by mean score of MAS, related to hip, knee, ankle and toes, and unaffected side Gait stride length assessments (Figure 1)

Results: Patients showed a high improvent on both outcome measures at three months, with a slight increase on measures at 3, 6 and 12 months (See table 2).

Discussion: SPN described by Stofel8 is used to treat harmful spasticity9, 10. Magnetic stimulation is employed in transcranial11 and muscle12 applications. Several works have described its peripheral use13 and we didn't find any publication with our aim. We used this combined method on upper limbs14, this is our study focalized on lower limbs. Stride length on unaffected side is a clinical feature of post stroke condition15,16,17 not currently used for functional assessment on weight support effectiveness. This vicarious mechanism makes treatment of functional outcome difficult18, so we introduce it, as a guide for functional outcome. Our combined method19 had better results than isolated selective peripheral neurotomy2,20, but more experience is needed to demonstrate statistical significance.

Conclusions: Magnetic stimulation is a valuable complementary treatment to improve patients' evolution, avoiding need of extensive surgical lesión, and stride length on unaffected side is useful to assess this condition.

TABLE2:

Measures were made in a SILEMA SYSTEM (Sistema Informático para Laboratorios del Estudio de la Marcha en Argentina)

Preoperative Mean stride length Measures :

32,4 +- 6,8 cm

Post- operative stride length Measures: 41,1 +- 7 cm, 41,6 +- 7,1 cm, 45,2 +- 6,2 cm and 45 +- 7,9 cm, at 3, 6, 9 and 12 months, respectively

Preoperative Mean Ashworth Scale :3,4 +- 0,8

Post- operative Mean Ashworth Scale: 2 +- 0,78, 2,22 +- 0,54, 1,91 +- 0,6 and 1,90 +- 1, at 3, 6, 9 and 12 months, respectively.

Figure 1: Patient being evaluated on the treadmil of the laboratory of gait

Objectives

1)To promote and re – launch the surgical method known as Selective Peripheral Neurotomy as an effective treatment for refractory post stroke Spasticity.

2)To evaluate Magnetic Stimulation as a complementary method for Kinesics and Physics Therapy on Spasticity

3)To employ unaffected stide length on evaluation for post stroke lower limb spasticity assessment

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Poster Presentations - May 27 - May 30
Spine - Spasticity and Movement Disorders

452. INS19-0079

SPINAL CORD STIMULATION FOR THE TREATMENT OF SPASTICITY IN PATIENTS AFTER SPINAL CORD INJURY

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Introduction: Complicated spinal cord injury is one of the most pressing problems of modern neuroscience, neurorehabilitation and neurosurgery. According to the published data, the number of patients having an issue with the spastic syndrome in a year is 36.3%, in 2 years - 23.4% and in 5 years this number had been growing and now amounts to 31.2%.

Materials/Methods: We analyzed treatment outcomes of 19 patients. According to the severity degree of spinal cord injury according to the ASIA scale, the group included 16 patients of group A (84.21%), 1 patient of group C (5.26%) and 2 patients of group D (10.52%). On the level of spinal cord damage, patients were divided as follows: 2 patients with the upper cervical level (C1-C4) of spinal cord damage; 4 patients with lower cervical level (C5-C8); 5 patients with upper thoracal level (Tn1-Tn6) of damage; 4 patients with lower thoracal (Tn7-Tn12). All patients had the spasticity level from 3 to 5 points on the Modified Ashworth Scale(3.89 ± 0.76), from 2 to 4 (2.66 ± 0.71) points on the Penn Spasm Frequency Scale, on the scale of motor functions the level was from 0 to 4 points (0.29 ± 0.9), on the reflexes scale the level was from 3 to 5 points (3.89 ± 0.69).All patients underwent trial SCS, according to the results of which, the spasticity level, according to the Modified Ashworth Scale, was (0.84 ± 0.49) points (average tonus decrease by 3.05 points). According to the result of which implantation of a neurostimulator was performed in patients.

Results: In twelve months of neurostimulation, the level of spasticity according to the Modified Ashworth Scale was (1.20 ± 0.41) points, on Penn Spasm Frequency Scale 1.13 ± 0.35, on the scale of motor functions the level was 0.57 ± 1.17, on the reflexes scale, the level was 2.47 ± 0.73.

Discussion: The obtained results allow for the conclusion that SCS is a high-efficient treatment option for the spastic syndrome in patients after spinal cord injury.

Conclusions: SCS for spasticity requires further in-depth study

Objectives

The aim of our work was to study treatment efficacy of the severe pharmacoresistent spastic syndrome in patients who had spinal cord injury by the system implantation for chronic SCS.

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Poster Presentations - May 27 - May 30
Spine - Spasticity and Movement Disorders

453. INS19-0475

INTRAVENTRICULAR BACLOFEN THERAPY FOR DYSTONIC-SPASTICITY: SERIES OF 3 CASES

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Introduction: Intrathecal spinal infusion is the leading technique to baclofen delivery into the intradural space. However, almost 78% of GMFCS V Cerebral Palsy (CP) patients develop scoliosis and may require spinal fusion, which hardly can be done with intrathecal catheter route. Besides that, severe dystonic-spastic patients may present intense abnormal postures that may preclude Cerebrospinal Fluid (CSF) puncture and intrathecal catheter delivery. In both situations intraventricular baclofen (IVB) therapy may be a secure and valuable alternative to baclofen infusion into the CSF.

Objective: To report the efficiency and safety of IVB therapy in dystonic-spastic patients.

Results: CASE 1: A nineteen-year-old male had CP GMFCS V. Due to spastic-dystonia on four limbs and trunk he underwent to intrathecal baclofen (ITB) therapy. After two years, his thoracolumbar scoliosis became severe and surgical treatment was indicated. Before this, a procedure to commute catheter placement into cerebral ventricle was performed. Pump was kept on abdominal place. Ventricular puncture was performed free-handed and a ventricular drainage catheter was placed in a sub-optimal position into the left lateral ventricle, close to its lateral wall. Due to the lack of response of therapy in next week, patient underwent to a revision surgery and pump spinal catheter was found disconnected from ventricular one. After reconnection, the catheter tip was stereotactically located into the third ventricle. Family reported great improvement, even better than that acquired with intrathecal infusion.

CASE 2: A nineteen-year-old male had hypoxic-ischemic encephalopathy secondary to a cardiac arrest after a convulsive episode. Due to that an intrathecal baclofen trial was proposed. Since patient had a high dose response during test (200mcg) it was decided for primary IVB therapy. Catheter was placement stereotactically into the third ventricle. Patient presented pneumonia on postoperative period, which was solved after antibiotic treatment. Patient evolved with spasticity improvement on whole body.

CASE 3: A boy with six-years-old suffered a cardiac arrest after electrical shock when he was nine months-old. He became dramatically spastic with dystonia associated, in a minimal consciousness state. He presented pathological hyperextension posture almost touching his hips with his head and had painful spasms. Patient was submitted to an intrathecal baclofen test (30mcg) with great improvement and then was submitted to an intraventricular baclofen pump, guided by neuronavigation. Patient presented great and sustained improvement, became from Penn 3 to 0 and Modified Ashworth Scale (MAS) from 3 to 1+. Patients treated with intraventricular baclofen therapy. MAS: Modified Ashworth Scale; IVB: intraventricular baclofen

Conclusions: Intraventricular baclofen therapy may be an efficient and safe treatment for dystonic-spastic patients and seems to have better response in dystonic patients compared to ITB one. It is recommended to use neuronavigation or stereotactic apparatus to guide ventricular catheter placement.

Table 1

Patient	Diagnosis	MAS pre	MAS post	Follow-up (months)	IVB dose (mcg)
M, 19a	Kernicterus	4	2	6	572
M, 19a	Anoxic encephalopathy	4	3	6	120
M, 6a	Anoxic encephalopathy	3	1+	3	78

Poster Presentations - May 27 - May 30
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454. INS19-0476

INTRATHECAL MORPHINE THERAPY FOR SPASTICITY

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Introduction: The most used intrathecal therapy for spasticity is baclofen one. In Brazil, the public health system does not provide intrathecal baclofen, so, other medications are used intrathecally to promote spasticity improvement, like morphine.

Objective: Report efficacy and efficiency of intrathecal morphine therapy for spasticity treatment.

Materials/Methods: Eleven patients with diverse spasticity etiologies, who remained refractory to best clinical treatment, underwent intrathecal drug delivery system implantation (Synchromed II – Medtronic). Patients were evaluated for pain (numeric rating scale - NRS); spasticity (Modified Ashworth Scale – MAS and Penn scale) and Patient Global Impression of Improvement (PGI-I).

Results: Clinical data, etiologies and results are summarized on table 1. Morphine dosage varied from 0,4mg/day to 2,6mg/day, by continuous or flex flow mode. From eleven patients reported here, eight presented spasticity improvement. Two patients presented also vesical spasticity improvement. Two patients who had no improvement after intrathecal morphine had therapy switched to intrathecal baclofen. One patient referred spasticity improvement, but worsening of global function after morphine infusion. Cerebral palsy patients didn't present good responses with intrathecal morphine therapy. One case presented pump pocket infection, which demanded pump explantation. This patient had multiple sclerosis and improved of spasticity and pain after intrathecal morphine therapy. Another patient presented worsening of consciousness level and it was decided to keep morphine infusion at minimum-rate.

Conclusions: Intrathecal morphine therapy is an option for spasticity treatment, presenting better results when associated with pain and secondary to spinal cord injury and multiple sclerosis. Intrathecal baclofen is an expensive treatment for spasticity in developing countries. Intrathecal morphine may be as effective and much cheaper than baclofen. Table 1:

SCI: spinal cord injury; MS: Multiple Sclerosis; CP: cerebral palsy; MAS: Modified Ashworth Scale; NRS: numeric rating scale for pain and PGI-I: Patient Global Impression of Improvement

Table 1.

Patient	Sex	Age	Etiology	Pre-MAS	Pos-MAS	Pre-NRS	Pos-NRS	Pre-Penn	Pos-Penn	PGI-I	Follow-up (months)
1	M	44	SCI	4	2	7	1	4	3	2	
2	M	30	SCI	4	0	8	5	2	0	1	
3	M	53	MS	3	2	9	4	NA	NA	2	
4	M	18	CP	4	4	NA	NA	4	2	3	
5	M	58	Spinal tumor	3	1	7	5	3	2	5	
6	M	20	MS	4	4	8	0	1	1	2	
7	M	41	SCI	2	1	10	10	1	1	3	
8	M	31	SCI	2	0	10	2	4	0	1	
9	M	16	CP	4	4	8	6	3	3	4	
10	F	38	SCI	3	0	2	0	1	1	1	
11	F	60	SCI	3	0	10	0	3	2	1	

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455. INS19-0129

WHY DO PATIENTS DISCONTINUE INTRATHECAL BACLOFEN TREATMENT? A RETROSPECTIVE SERVICE ANALYSIS

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Introduction: Intrathecal baclofen (ITB) is an established and effective treatment for the long term management of severe spasticity. We have experienced a number of individuals who have discontinued ITB treatment. Although common, this is poorly reported or investigated. This study aims to explore reasons for discontinuing treatment, what alternative methods are used to manage spasticity and who may manage without ITB.

Materials/Methods: Patients in the Nottingham adult ITB service were retrospectively reviewed over 10 years to identify those who discontinued treatment, reasons why and the success of their ongoing spasticity management plan.

Results: Thirteen out of eighty patients discontinued ITB treatment. Diagnoses were cerebral palsy, multiple sclerosis, glutamic aciduria and hypoxic brain injury. All had a successful test dose prior to treatment. ITB was stopped due to patient request or medical complication. All patients were commenced on oral baclofen. Without the ITB pump, 23% of patients had minimal spasticity which was easily managed, 31% of patients had moderate spasticity which was managed by oral medications and 46% of patients presented with severe spasticity but chose alternative intervention.

Discussion: ITB treatment was discontinued due to planned and unplanned reasons with requests to discontinue most common prior to pump renewal. Following a period of time with an ITB pump, some individuals presented with minimal spasticity or chose to manage their spasticity by alternative methods. Successful management was more likely for those on lower doses and following a planned weaning programme. Some patients declined re-insertion of an ITB pump despite poorly controlled spasticity. Adults whose pump was inserted as a child should be given the opportunity to discuss a pump free management plan prior to renewal.

Conclusions: Despite the presence of a long term condition, some individuals no longer preferred or required an ITB pump to manage their symptoms.

Objectives

Individuals are reviewed at 12 months prior to pump renewal.

Treatment options are discussed with potential outcomes and risks.

A trial of weaning establishes how one is likely to manage without ITB.

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456. INS19-0273

IMPROVED CHRONIC WIDESPREAD PAIN AND MOTOR FUNCTION USING HIGH FREQUENCY SPINAL CORD STIMULATION (HF-SCS) AT 10 KHZ: A CASE STUDY

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Introduction: Chronic widespread pain (CWP) including fibromyalgia is traditionally difficult to treat (1). Paresthesia-independent high frequency spinal cord stimulation at 10 kHz (HF-SCS) has demonstrated long-term safety and efficacy in back and leg pain patients when placed within the epidural space (2). Here, we report on a complex pain patient receiving HF-SCS.

Materials/Methods: A 63-year old female presented with a 40-year history of CWP in the right upper limb and right facial region over the trigeminal nerve. Right hemibody dysaesthesia with clinical elements of central sensitisation and secondary hyperalgesia was observed with MRI results depicting mild thoracic kyphosis with grade 1 anterolisthesis of the L4/L5 level, and no visible cord compression. Allodynia in the right thumb and middle finger was of significant concern for the patient. The patient also had a diagnosis of Parkinson's disease, with symptoms mostly non-motor. Ineffective conservative therapies included pharmacological approaches (Trileptal 300 mg, Endone 10 mg and Gabapentin 300-600 mg).

Results: Two electrode leads were placed epidurally, top of C1 and C2 vertebral levels. During the trial, facial pain completely resolved and function in the hand improved, with the ability to move her thumb and middle finger and maintain a flat position of her upper arm and hand. Within three weeks of having the HF-SCS system removed, the patient's pain and dysaesthesia had returned to pre-trial levels. The patient proceeded to an HF-SCS implant. Two-weeks post-implant, improvement in fine motor function of the fingers and improved range of movement in the shoulder, elbow and wrist was reported. At 12-months, speech and swallowing were markedly improved. Improvements in her pain were also reported (Arm: 9.0 vs. 5.5 (numerical rating scale [NRS]); Facial 7.0 vs. 0.0 NRS; Back: 10 NRS vs. only on mobilizing). No adverse events were observed.

Discussion: CWP is thought to relate predominately to central sensitization mechanisms with approximately a third of patients experiencing severe and disabling symptoms that are relatively resistant to current therapies (3). The results shown depict an improvement in both pain and motor function.

Conclusions: High frequency spinal cord stimulation at 10 kHz may prove to be a viable treatment alternative in this intractable and difficult to manage pain condition.

Objectives

To assess the effectiveness of HF-SCS in a complex pain condition, not traditionally indicated for neuromodulation.

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457. INS19-0423

RETROSPECTIVE CROSS SECTIONAL ANALYSIS OF DECISION MAKING AND OUTCOMES FOR INTRATHECAL CONTRAST STUDIES IN PATIENTS RECEIVING INTRATHECAL BACLOFEN THERAPY

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Introduction: Patients receiving intrathecal baclofen therapy (ITB) for the treatment of spasticity require ongoing continuous monitoring of medication response and periodic assessment of catheter integrity, connections, and distal position. Recent advances in catheter technology (e.g. tubing material, pin connector) have reduced rates of previous types of complications such as disrupted flow due to kinking and catheter detachment from the reservoir stem in recent years. Procedural interventions to assess the catheter component of an ITB drug delivery system prior to planned pump reservoir replacement or when troubleshooting possible loss of therapeutic effect remain a technical mainstay of providing intrathecal therapy.

Materials/Methods: Patients seen at the Neuromedicine Pain Management Center were identified through the University's electronic medical record system who were receiving ITB between 1/1/2010-5/31/2018. A standardized protocol including pump reservoir and catheter visualization under multiple views of fluoroscopy, aspiration of CSF from the catheter access port, and inspection of omnipaque spread following by bolus and reprogramming were performed in each patient in this series.

Results: This search method identified 22 intrathecal catheter studies in 35 patients with implanted drug delivery systems over 8 years. The clinical indication for dye test increased symptoms of spasticity, preoperative planning prior to pump replacement, and unexpected residual reservoir volumes.

Discussion: This case series provides preliminary support for possible changes to the prevailing diagnostic approach when catheter-related dysfunction tops the differential diagnosis or elective pump reservoir replacement is planned.

Conclusions: Additional research is needed to optimize the use of contrast studies in patients undergoing intrathecal drug delivery with baclofen.

Objectives

1. Recognize indications for catheter dye study. 2. Interpret results of intrathecal catheter dye study. 3. Identify alternative and supplementary diagnostic approaches to intrathecal catheter dye study.

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458. INS19-0280

REMODULATION OF MOTOR CORTICAL ACTIVITY AFTER LONG-TERM CONTINUOUS INTRATHECAL BACLOFEN DELIVERY IN CHRONIC SPINAL CORD INJURY

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Introduction: Intrathecal baclofen (ITB) is commonly used for severe spasticity due to chronic spinal cord injury (SCI). Clinical effect of ITB on reduction of spasticity is well known; however, mechanism of long-term administration of ITB on the motor cortex is not fully elucidated. We tried to determine which cortical processes are activated using functional magnetic resonance imaging (fMRI).

Materials/Methods: Ten subjects (8 males, aged 20-69 yrs) with chronic thoracic lesion were selected from 15 SCI patients enrolled in our fMRI study. All of them presented with no voluntary movements on lower limbs. 1.5T fMRI with mental movement simulating foot flexion on the dominant side (2 left-handed subject was flipped in x axis) were performed before, 12 weeks and one year after ITB pump implantation. FMRI data processing was carried out using FEAT (FMRI Expert Analysis Tool) Version 6.00, part of FSL. Second-level analysis was carried out using FLAME stage 1 and 2. Level of spasticity was assessed by Modified Ashworth scale (MAS). The study obtained Institutional Review Board approval.

Results: ITB treatment significantly decreased limb spasticity in all subjects (group MAS knee spasticity dropped from 2.8 to 0.4). Second-level analysis (Z=2, cluster significance threshold p=0.05) revealed increase of activation of primary sensorimotor cortex of the foot; however, broader activation was observed 3 months after pump implantation.

Discussion: Neural connectivity has recently been shown to be altered after SCI also in the brain (1). In animal studies, the functional connectivity between the primary motor and primary sensory areas significantly decreased (2). In this study, we observed more pronounced increase of sensorimotor cortex activation of plegic lower limb three months after ITB administration followed by a decrease in activation one year after pump implantation.

Conclusions: This finding may reflect distant functional reorganization due to long-term neuroplastic changes with a time-dependent compensatory adaptive changes of sensorimotor cortex.

Supported by Research Project of Charles University Progress Q35.

Objectives: Continuous ITB administration relieving spasticity in SCI patients was associated with increase of activation of sensorimotor cortex of plegic legs reflecting functional reorganization of cortical sensorimotor network due to positive neuroplastic changes.

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459. INS19-0102

LONG TERM FOLLOW UP OF INTRATHECAL BACLOFEN THERAPY FOR SPASTIC AND DYSTONIC PATIENTS

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Introduction: ITB (intrathecal baclofen) therapy is garnering attention as a non-destructive, reversible, and programmable treatment method that induces neuromodulation. We report the surgical methods and therapeutic outcomes of 38 spastic and dystonic patients who underwent ITB therapy, together with an investigation of the effects on metabolic and respiratory functions

Materials/Methods: 38 patients who exhibited improvement in spasticity with hemiplegia, paraplegia, or tetraplegia presenting with severe spasticity. Patients comprised 33 cases with spasticity and 5 cases with secondary generalized dystonia. The effect of ITB therapy was evaluated using the Ashworth scale. And also respiratory gas analyzer was used to measure resting metabolic rate, and effects on respiratory function using polysomnography, were also measured before and 1 month, 6 months and over 1year follow up periods after the procedure in 13 patients.

Results: Lower limb spasticity improved markedly in all patients following ITB therapy. Some patients, especially traumatic brain injury patients, showed marked reductions in resting metabolism following ITB therapy, and this correlated with the degree of improvement in spasticity. Sleep apnea thus improved or remained unchanged in all cases, and did not worsen in any patients.

Discussion: Weight gain has been observed clinically in patients undergoing ITB therapy, although published reports of this side effect are rare, but weight gain constitutes a major cause of hypometabolism. Our results also suggest that the reduction of spasticity and metabolic rate may be involved, and that adjusting the dosage of baclofen may enable better control of spasticity and dystonia. We also confirmed that ITB therapy improved the Apnea Hypopnea Index, indicating that ITB therapy does not necessarily have negative effects on respiratory function.

Conclusions: Intractable spasticity and dystonia are complicated by severe hypermetabolism and sleep apnea, which necessarily has negative effects on activities of daily living and quality of life, and we have confirmed that these measures are improved in long-term period when spasticity and dystonia are alleviated by ITB therapy. ITB therapy may be further expected to serve as a neuromodulation treatment in functional neurosurgery.

Objectives: ITB therapy can greatly improve activities of daily living (ADL) and quality of life (QOL) due to spasticity and dystonia, and this treatment is attracting attention as a neuromodulatory therapy that also affects metabolic and respiratory functions.

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460. INS19-0346

COMPLETE RELIEF OF TWO CASES OF SEVERE NECROTISING RAYNAUD'S PHENOMENON WITH CERVICAL SPINAL CORD STIMULATION

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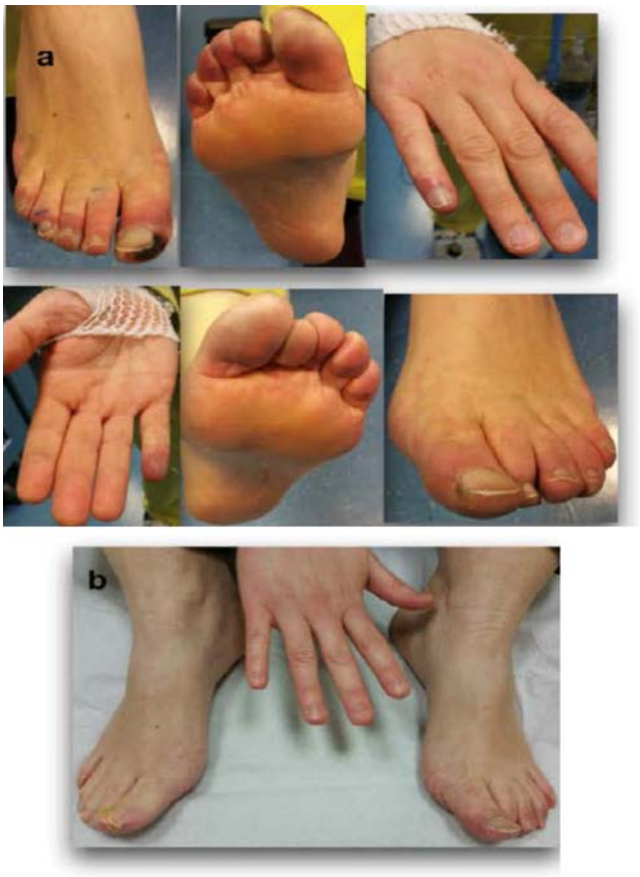
Introduction: Raynaud's phenomenon is a vasospastic condition affecting primarily the distal resistance vessels, that seems to be related to high levels of sympathetic activity and low levels of calcitonin gene-related peptide expression in the local sensory fibers. We present two cases of severe necrotising Raynaud's phenomenon successfully treated with cervical SCS electrodes.

Materials/Methods: Two women, aged 37 and 60, were diagnosed necrotising Raynaud's phenomenon at both feet and hands. The pain was tearing with a mean rating of 8/10. It did not respond to any kind of therapeutic maneuver or behavioral factors. Both patients had been immediately treated with vasodilators iv, with scarce clinical response and increasing pain and necrosis (figure 1, panel a). Indication of amputation was therefore made. Before amputation, a trial of SCS was performed. An octopolar SCS lead was implanted in cervical region, in order to obtain an analgesic and vasodilator effect on both hand and feet.



Results: The patients referred in subsequent days a net improvement of symptoms, with a reduction of mean pain ratings until 2/10. Also perfusion in hands and feet significantly improved, so that necrosis completely reversed and amputation was no longer necessary (figure 1, panel b). The systems were therefore totally implanted. The patients are still followed up every month for iloprost infusion and no more Raynaud's phenomenon is observed.

Discussion: It has been proposed that SCS increases cutaneous blood flow by antidromic activation of afferent fibers in the dorsal roots. It has a direct inhibitory effect on peripheral vasoconstriction maintained by efferent sympathetic activity including nicotinic transmission in the ganglia and the postganglionic alpha-1-adrenergic receptors. Furthermore, it is believed that pain relief is mediated by suppression of nociceptive transmission via descending inhibitory pathways.

Conclusions: In both our patients SCS allows a rapid and persitent pain control, as well as the preservation of extremities.

Objectives: The present case once more highlights that SCS is a promising therapeutic option for severe Raynaud's phenomenon, suggesting that SCS improves cutaneous blood flow, thus reducing the risk of amputation, and allows rapid pain relief, maybe by suppression of nociceptive transmission via descending inhibitory pathways.

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461. INS19-0210

DIAGNOSTIC AND PROGNOSTIC VALUE OF TRANSCRANIAL MAGNETIC STIMULATION IN MUCOPOLYSACCHARIDOSIS-RELATED CERVICAL MYELOPATHY

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Introduction: Mucopolysaccharidosis (MPS) are lysosomal diseases due to defective catabolism and storage of glycosaminoglycans in the skeleton and soft tissues. Cervical myelopathy (CM), the main cause of neurological morbidity and disability in MPS [1], is caused by atlanto-axial subluxation, odontoid hypoplasia, periodontoid soft tissue masses, and spinal canal narrowing, eventually leading to spinal cord compression. Given that early CM detection is associated with best surgical and post-operative outcome, accurate diagnosis and strict monitoring are recommended [2]. We applied Transcranial Magnetic Stimulation (TMS) in MPS-related CM.

Materials/Methods: Eight patients (two males), median age 14.5 years (range 13.0-41.0), were included. Four of them, with clinical and MRI signs of CM, had previous surgical decompression, although three still complained symptoms. The other subjects did not have significant clinical or radiological evidence of CM. Motor evoked potentials (MEPs) to single-pulse TMS were recorded from the first dorsal interosseous (FDI) and tibialis anterior (TA) muscles, bilaterally. MEPs latency, shape, and amplitude, as well as central motor conduction time (CMCT) were recorded at rest and during moderate isometric voluntary contraction [3].

Results: Among those underwent surgery, MEPs were absent from FDI of two patients and TA of one patient. Motor latencies were prolonged in all treated patients; in three of them, MEPs had also reduced amplitude and polyphasic shape. CMCT was increased in two of treated subjects from both upper and lower limbs, whereas responses to cervical root stimulation could not be evoked in the other two. Among the four apparent neurologically normal subjects, MEPs were abnormal in terms of reduced amplitude, increased latency, or altered shape in at least one of the examined muscles.

Discussion: Abnormal TMS findings from both upper and lower limbs were consistent with diffuse axonal damage and demyelination, suggesting that a spinal disease was clinically present before the occurrence of an overt CM and might persist despite surgery. However, MEPs analysis also revealed functional impairment even in patients without a clear evidence of CM, thus allowing a preclinical diagnosis.

Conclusions: TMS was able to detect MPS-related CM, even subclinically, and to provide reliable electrophysiological data after surgical decompression.

Objectives

TMS is a safe, painless, and non-invasive neurophysiological technique assessing excitability and conductivity of the cortical-spinal tract.

TMS screening for CM should be performed in MPS.

Baseline and longitudinal exams are helpful for an early diagnosis and prognosis.

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