lidocaine infusions. Primarily, this patient had the most positive responses greater occipital nerve, supratrochlear nerve and scalp trigger point injections.
The choice was made to trial SON and ON stimulation simultaneously using a commercially available spinal cord stimulation (SCS) system. Painful trigger points along the hemicranium were mapped offered an opportunity to place a third subcutaneous lead for PFNS (Figure 1). During the trial 70-80% relief was obtained in the entirety the pain distribution, including the region affected by PFNS. The patient then proceeded to permanent implant with similar lead placements connected to a sub-clavicular generator and post-operatively has done equally as well, with continued relief of 70% of chronic neuropathic pain in the affected distributions.

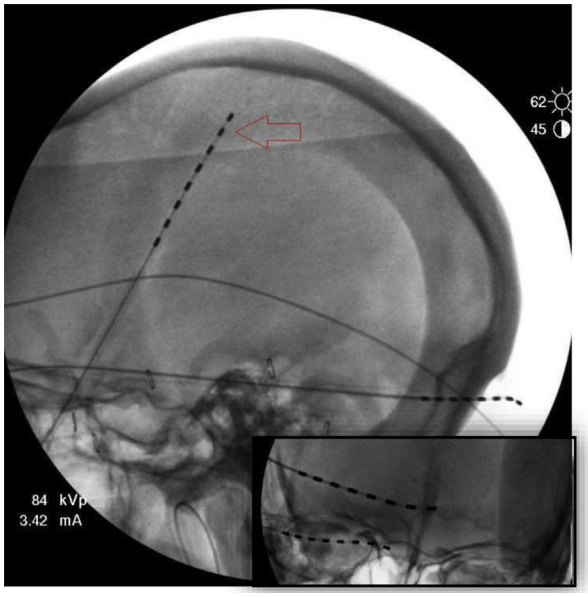

Figure 1. Lateral X-ray showing location of stimulator array, which was placed percutaneously underneath the patient's scalp based on pre- operative mapping of trigger points. AP insert showing occipital and supraorbital nerve leads.

4. RESULTS AND DISCUSSION

Neurostimulation for trigeminal distribution pain is an established therapeutic option for patients with refractory pain. Sphenopalatine ganglion stimulation has long been used for the treatment of refractory facial pain and headaches.[2,3,5] Peripheral nerve stimulation for trigeminal pain and headaches from various pathologies has shown significant improvements in many patients, despite a moderate complication rate.[4]
While PNS for this and other headache syndromes is not a novel concept, this case illustrates a few technical nuances of clinical value. Combined PNS and PFNS techniques allowed for maximal coverage of this patient's pain patterns. Cutaneous mapping of trigger points (particularly those where relief was obtained with anesthetic injections) was important to position the PFNS lead to achieve greatest clinical efficacy. Use of a quad- lead SCS generator allowed for minimal wiring complexity while maximizing options for number of leads (SON/ON/PFNS) and stimulation options (PNS/PFNS). As always, care to properly anchor subcutaneous leads and leave adequate strain relief loops are essential to preventing lead migration.

5. CONCLUSION

Neurostimulation continues to be a promising paradigm for chronic headache management. Multimodality therapy under the guidance of a neurologist or pain management specialist remains the mainstay of treatment. However, use of neurostimulation in emerging and creative patterns may leverage this therapy as a useful tool for patients with refractory, intractable headache syndromes. For example, using a patient's trigger points to guide lead placement was a useful adjunct in surgical planning. Ultimately, attention to the underlying pain pattern, success of lesser invasive methods, and the inherent limitations of peripheral stimulation can help the surgeon map appropriate and successful lead placement. Familiarity with the technical nuances of cranial PNS/PFNS is important for durable clinical outcomes. RCTs with long-term follow-up for this therapy continue to be lacking in the literature and are needed to further advance this therapy.

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PROCEEDINGS #50: DIRECTIONAL DEEP BRAIN STIMULATION LEAD PLACEMENT IN A PATIENT WITH SEVERE OBSESSIVE-COMPULSIVE DISORDER

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1. Abstract

Background: Obsessive-compulsive disorder (OCD) is a pervasive and often chronic disorder. Deep brain stimulation (DBS) of ventral capsule/ventral striatum (VC/VS) is the most commonly selected target in OCD.
Method: We recorded local field potentials (LFPs) from an 8-contact directional lead targeted to VC/VS in an OCD patient and explored their spatio-spectral patterns by Welch periodogram method during offline analysis.
Results: The final position of the lead was 1.93 mm and 2.53 mm inferior on the left and right, respectively. Power spectral density (PSD) of LFPs demonstrated peak activities at theta and beta bands in both hemispheres with different theta/beta power ratios. One month following the initial programming session, the patient reported significant improvement in OCD tendencies and no adverse effects with stimulation at 160Hz/60μs/3.5-5.5V with Case+1- and Case+9-. Yale Brown Obsessive Compulsive Scale (YBOCS) of OCD severity score was improved from 38 to 24.
Conclusion: Our preliminary findings show the local spectral dynamics of VC/VS in OCD. The question of how these spatio-spectral dynamics play a role in compulsion warrants further assessment in larger series of patients.

2. Introduction

OCD affects 2-3% of the population [1]. However, 40-60% of the patients do not respond to conventional treatment approaches [2]. DBS has gained attention as a promising therapeutic approach in therapy-resistant psychiatric disorders. Patients who are candidates for DBS for OCD have had a score of >28 on the YBOCS of OCD severity and fail to obtain benefit with three or more types of medications at optimal dosing in addition to behavioral therapies [3]. Even though the successful ablative approaches in OCD have suggested the VC/VS [3] as DBS target [4], issues remain suggesting that this target may need to be finetuned, including high amplitudes needed for stimulation, resulting in the need for frequent battery changes [1].
Directionality enables energy to be focused toward areas where beneficial effects occur and away from areas where adverse events occur [5-6]. This focused delivery of energy allows for larger therapeutic window. Further, only delivering energy to the area needing therapy allows for more

efficient delivery which may extend battery life [6]. Given the availability of directional leads, we opted after discussion with our IRB and ethics to offer this advanced technology to our patient. Intraoperatively, we recorded LFPs and performed macrostimulation with our directional lead.

3. Methods

A 22-year old female who has suffered from a severe OCD with a YBOCS score of 38 in addition to a medical history of major depression underwent DBS surgery. Patient gave informed consent before her participation to the study in accordance with the Declaration of Helsinki. The study protocol was reviewed and approved by the Institutional Review Board (IRB) of Albany Medical Center.

Based on a standardized DBS protocol using a stereotactic frame and previously reported targets at the relative center of the nucleus accumbens (NAcc) [1,3,7], the AC-PC coordinates were planned as 7 mm lateral to the AC-PC line, 2 mm anterior to the anterior commissure and 3 mm below the AC-PC line and an 8-contact directional lead with 0.5 mm spacing (Infinity-6172, Abbott Laboratories, Illinois, USA) was implanted accordingly (**Fig.1A**).

Following the confirmation of the lead position by macrostimulation, LFPs were recorded at rest using Guideline4000LP Neuromodulation System (FHC Inc, Bowdoin, ME) and analyzed offline in in Matlab (Mathworks, Natick, Massachusetts). To eliminate the common activity among contacts, the LFPs in each hemisphere were decorrelated using a least mean square (LMS) algorithm [8]. The spectral features of the oscillations were computed by Welch periodogram method with 1024-sample Hanning window with 50% overlap. The PSD of decorrelated LFPs were explored between and within hemispheres.

4. Results

Our postoperative imaging showed that the targets were 7.66 mm lateral and 1.73 mm anterior to AC on the left and 6.85 mm lateral and 1.97 mm anterior on the right; 1.93 mm and 2.53 mm inferior on left and right, respectively. When the common activity among contacts was eliminated by using LMS algorithm, the distinct PSD patterns were unmasked. In **Fig.1B**, all contacts indicate theta (4-7Hz) and beta band (13-30Hz) activity. While the peak frequency is in theta range in contacts 1, 2, and 4, it is in beta range in the rest. It is also noted that beta activity in these contacts is skewed to lower beta (15-17Hz) which is similar to the pathological oscillations in parkinsonian subthalamic nucleus (STN) [9]. We observe the highest power in contact-6, which is facing medial and appears to be capturing portions of the VC, caudate and anterior globus pallidus internus (**Fig.1C**). PSDs of available contacts on the right, except 12, are higher in beta band (**Fig.1B**, right-panel). The activity in contact-12 shows visibly lower beta and slower rhythms with a peak at 5Hz. Contact-10, which appears to be facing the NAcc situated more medially, indicates faster peak frequency in theta range and more skewness towards 17Hz. On the right side, the peak frequencies are more divergent (15-to-20Hz). The lead is placed 2.5 mm below AC-PC line on the right and appears to be placed within the central and posterior gross structure of the NAcc. The contacts 10 and 13 are facing anterior and therefore appears to be targeting the centro-lateral posterior portion of the NAcc, the spectrally distinct pattern might be an activity of the shell portion of the NAcc (**Fig.1D**).

Based on monopolar review and previously reported cases [3], initial programming parameters were bilaterally set to 60 μs, 160 Hz, and 3.5 mA by choosing contacts 1 and 9 as anodes. One month following the initial programming session, the patient reported significant improvement in OCD tendencies. Compulsions involving a need to close drawers had resolved. She had re-gained the ability to drive and throw a softball, tasks that she had previously been unable to perform due to excess worry. In subsequent programming sessions, current was ultimately increased to 5.5 mA. She had continued improvement in her symptoms. Notably she had lost the need to perform a post-shower ritual that she had been performing since childhood. After every session her family noted several days of excessively elevated mood followed by resolution. She otherwise tolerated adjustments well.

5. Discussion and Conclusion

Studies reported significant oscillatory changes in STN [9-10], the bed nucleus of stria terminalis [11], and caudate nucleus [12] in patients with OCD. Given the key role of VC/VS in cortico-striatal-thalamo-cortical circuit [4], the spatio-spectral dynamics of LFPs in this region might reflect the pathophysiological activities of the disease and/or its compensatory mechanisms. For instance, the spectral differences between hemispheres might be emerged due to slightly more inferior placement of the lead on the right side; and more improvement in mood by macrostimulation on the right might be the modulations of certain beta oscillations by DBS. However, we know little about the oscillatory neuronal activity in the structures targeted by DBS in OCD. Our report can be the first evidence of spatio-spectral nuances in the VC/VS region in OCD.

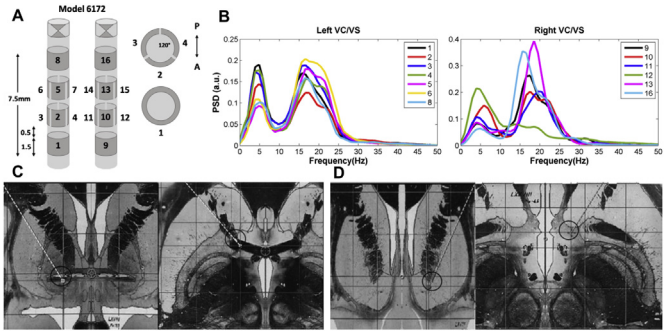

Fig. 1. (A) The schematic of directional lead shows the 1-3-3-1 (ring-side-side-ring) configuration. The contact size is 1.5 mm with 0.5 mm spacing. The side contacts are separated by 120°. The marker ideally indicates anterior direction. **(B)** Power spectral density (PSD) generated from LFPs recorded in left and right VC/VS, respectively. Contacts 1-8: Left; Contacts 9-16: Right. Atlas overlay of the electrode placement in the left **(C)** and the right VC/VS **(D)** demonstrates the location of the electrode tip and the surrounding anatomy.

We obtained exceptional benefits following traditional programming with dramatic increases in return to function. YBOCs scores decreased from 38 pre-operatively to 24 post-operatively. Our programming amplitudes were essentially equivalent to those reported in the literature (2.5-to-10.5V) [1, 3]. Based on the international experience, we noted that the target became more posterior and medial over time [3]. One hypothesis was that the posterior location allowed for targeting of a more compact zone of CSTC networks as they course to the inferior thalamic peduncle [13-14].We attempted to apply directionality by incorporating the second deepest contact (2/10) and turning off the lateral division to drive the stimulation posterior and medial. Unfortunately, this was unsuccessful in our patient. In future cases, we hope to further refine directionality to optimize battery life and will place the lowest directional lead at target to allow for more flexibility.

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Conflicts of Interest

Dr. Pilitsis is a consultant for Medtronic, Boston Scientific, Nevro, Jazz Pharmaceuticals, Neurobridge Therapeutics, and Abbott and receives grant support from Medtronic, Boston Scientific, Abbott, Nevro, Jazz Pharmaceuticals, GE Global Research, and NIH 1R01CA166379. She is medical advisor for Centauri and Karuna and has stock equity. All other authors have no conflict of interest or financial disclosures related directly to this manuscript.

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PROCEEDINGS #51: 4 MA ADAPTIVE TRANSCRANIAL DIRECT CURRENT STIMULATION FOR TREATMENT-RESISTANT DEPRESSION: EARLY DEMONSTRATION OF FEASIBILITY WITH A 20-SESSION COURSE

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1. Abstract

Background: Evidence supporting the use of transcranial direct current stimulation (tDCS) as a treatment for major depressive disorder (MDD) remains inconclusive. One suggested reason is that commonly used treatment protocols fail to deliver enough current to adequately modulate the neural targets.
Methods: Single-blind clinical trial of high-dose (4 milliamp) tDCS targeting the prefrontal cortex to assess for safety, tolerability, and efficacy.
Results: tDCS was safely applied to two patients with medication-resistant MDD. Both patients experienced significant improvements in depressive symptoms.
Conclusions: Based on a short case series, this paper is the first to demonstrate that 4 mA tDCS can be safe, well-tolerated, and potentially efficacious in the treatment of MDD. We present some promising preliminary findings of safety and treatment efficacy for two patients who failed multiple antidepressant medications.

2. Introduction

Major depressive disorder (MDD) is a worldwide problem, afflicting 1 in 23 people with a lifetime prevalence of 20.6%[1]. It is the leading causes of disability in the world[1]. New treatment options are desperately needed, as approximately 1/3 of patients fail to respond even after numerous pharmacotherapeutic trials[2]. Neuromodulation therapies have grown in popularity with the FDA approval of transcranial magnetic stimulation for MDD in 2008. Another form of neuromodulation, transcranial direct current stimulation (tDCS), has been studied extensively for the treatment of MDD with mixed results[3]. tDCS involves the application of low-intensity electrical stimulation to different targets on the scalp. Usually the current delivered is in the range of 1 to 2.5 mA, with application for 20-30 minutes daily for several weeks. Some studies have suggested that higher current intensities, on the order of 4.5 mA or more, are needed to adequately modulate neuronal activity in the brain, whereas those 3 mA and lower failed to do so[4]. Similarly, a meta-analysis of tDCS studies for MDD has proposed that higher tDCS "doses" would lead to greater clinical effects[5]. To date, no studies have attempted to apply currents greater than 2.5 mA to the prefrontal cortex of patients with MDD[6]. This dose has been demonstrated safe in other populations, such as stroke patients[7–9]. This trial aimed to investigate the safety, tolerability, and efficacy of 4 mA tDCS applied to the prefrontal cortex of subjects suffering from a major depressive episode.

3. Methods

Subjects: This was a single-blind (rater blinded) clinical trial conducted with IRB approval at Washington University in St. Louis and registered with Clinicaltrials.gov. Patients were recruited from the Washington University Treatment Resistant Depression Registry and advertisements placed around the hospital campus. Patients were screened by phone and then by expert psychiatric interview using the Mini-International Neuropsychiatric Interview (MINI) prior to enrollment, and met criteria for a DSM-5 diagnosis of major depressive disorder. Other medications were continued with treatment as usual.
Device and Stimulation: The tDCS device used was a tDCS 1x1 model 1300A (Ybrain, Republic of Korea) and the headband and stimulation pads (5x5 cm) were Soterix Medical SNAPstraps and SNAPpads (Soterix Medical, New York, NY). Anode was placed over the left dorsolateral prefrontal cortex (DLPFC) scalp region, and cathode was placed over the right DLPFC region. The stimulation protocol was 4mA current delivered for 20 minutes duration with a brief 30-second ramp-up and ramp-down for tolerability. Subjects had continuous access to the Ybrain Android-based tablet software that gave them the ability to temporarily ramp down ("RELAX") the stimulation intensity by pressing a button if it became uncomfortable. Stimulation was delivered 5 days per week for 4 weeks. Task engagement was standardized - all patients were given adult coloring books and instructed to color for the duration of stimulation.
Evaluations: Evaluations were conducted by trained, blinded psychiatrists at the following time points: pre-stimulation; post-10 stimulations (halfway point); post-20 stimulations; 1-week follow-up; 2-week follow-up. The raters were not told the specifics of the study and led to believe that some patients may receive sham treatments during the trial. The primary outcome measure was a change in Montgomery-Asberg Depression Rating Scale (MADRS) scores. Additional outcome measures included the Hamilton Depression Rating Scale (HAMD-17), the Hamilton Anxiety Rating Scale (HAM-A), the Clinical Global Impression Scale (CGI), the Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR), the Montreal Cognitive Assessment (MOCA), the NIH Toolbox Cognitive and Emotional Batteries, the Temperament and Character Inventory (TCI), and the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q), amongst other tests. Physical and neurologic exams were conducted weekly, and patients were assessed daily by a physician to monitor for side effects. Pain visual analog scales (VAS) were recorded six times during each stimulation session to ensure safety and tolerance of the treatments (baseline, 2 mins, 5 mins, 10 mins, 15 mins, and 18 mins into stimulation).

4. Results

No statistical analyses were conducted as this is an ongoing clinical trial. At the time of this writing, two patients (n=2) had successfully completed the tDCS protocol

Demographics	Pt. 1	Pt. 2
Age	56	58
Gender	M	M
Failed Medication Trials	4	5
MADRS Change (Pre to Post, %)	↓100%	↓61%
Change in Q-LES-Q (Pre to Post)	↑59%	↑37%
Average Pain VAS	1.1	1.6
Max Pain VAS	3	3
Total Uses of "RELAX" Feature	0	0
NIH Toolbox Z-Score Change, Fluid Intelligence	↑1.1	↑0.8
NIH Toolbox Z-Score Change, Crystallized Intel.	↑0.2	↔0
HAM-D Change (Pre to Post, %)	↓100%	↓41%
QIDS-SR Change (Pre to Post, %)	↓100%	↓64%
HAM-A Change (Pre to Post, %)	↓100%	↓50%
CGI-S Baseline to Final Score	4 → 1	4 → 3

Table 1. Demographics & outcome measures. Changes are represented as a percentage change from the baseline score to the immediate post-stimulation score. Green boxes indicate an improvement in symptoms. Orange boxes highlight measures related to tolerability of the stimulus.