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The Impact of Peripheral Nerve Stimulation on Disability and Depression

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Background: Peripheral nerve stimulation (PNS) of the named nerves of the head has been shown to be effective in reducing pain levels in patients with chronic pain refractory to other treatments. However, the impact of cranial PNS on depression and disability has not been well documented.

Objectives: We prospectively examine the impact of PNS on quality of life via validated survey scores which assess symptoms of depression and daily functional capacities within patients.

Methods: Patients who underwent permanent PNS implantation completed five validated questionnaires: Oswestry Disability Index (ODI), the Beck's Depression Inventory (BDI), the Pain Catastrophizing Scale (PCS), McGill Pain Questionnaire (MPQ), and the visual analog scale (VAS) score. These were completed at baseline, six months, and one year to assess changes in functioning levels. Results were analyzed via repeated measures ANOVA and bivariate analysis.

Results: Compared with baseline, at six months patients showed significantly less depression on BDI ($F = 7.9$, $p = 0.021$), and at one year, a significant decrease in disability was observed on the ODI ($F = 6.1$, $p = 0.036$). At both six months and one year, patients showed a significant decrease in pain on VAS ($F = 16.5$, $p = 0.012$). We noted a trend for ODI to correlate with BDI at six months ($R = 0.616$, $p = 0.077$).

Discussion: Our prospective data show PNS to be an effective modality in improving overall life quality by limiting depression and disability as well as pain.

Keywords: Depression, disability, peripheral/occipital nerve stimulation, quality of life

Conflict of Interest: Dr. Julie G. Pilitsis is a consultant for Medtronic, St. Jude, and Boston Scientific, and receives grant support from Medtronic, Boston Scientific, St. Jude, and NIH 1R01CA166379. She is a medical advisor for Centauri and has stock equity. All other authors have no conflict of interest or financial disclosures related directly to this manuscript.

INTRODUCTION

In the 1960s, the gate theory of pain was proposed to suggest that electrical stimulation of large-caliber myelinated non-nociceptive fibers can override pain from small nociceptive afferent fibers. The same decade, Wall and Sweet clinically demonstrated this theory by providing electrical stimulation to eight patients with cutaneous pain, all of whom experienced pain relief. The initial trials of peripheral nerve stimulation (PNS) involved open surgery until 1999 when Weiner and Reed successfully introduced percutaneous leads. Henceforth, PNS gained increasing popularity as a minimally invasive technique providing focal neuromodulation. Numerous studies since then have shown PNS to provide long-term pain relief for a carefully selected patient population (1,2).

PNS refers to stimulation performed on named nerves anywhere on the body. For pain in the head, PNS has been used to treat chronic migraine, headache not otherwise specified (NOS), trigeminal neuropathic pain, cranial incision pain, temporomandibular joint dysfunction pain, and other indications. Occipital nerve stimulation (ONS) for C1-2-3 transformed migraine and for occipital neuralgia has been shown to have long-term clinical effectiveness in reducing pain (3–7).

Additional benefit with combined occipital and supraorbital nerve stimulation has recently been proposed (8). The impact of PNS of nerves of the head on quality of life (QOL) has been less defined. We do know the migraine disability index and Short Form-36 questionnaire scores improve in patients who undergo ONS for migraines (9–12). Prospective assessment of QOL measures in real-world practice, where PNS is used for multiple diagnoses including neuropathic pain, is lacking.

We utilized the visual analog scale (VAS), Oswestry Disability Index (ODI), Pain Catastrophizing Scale (PCS), and Beck Depression Inventory (BDI) to assess the impact of PNS on pain, disability, catastrophic thinking, and depression, respectively. Our study reflects

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real-world practice of application of PNS stimulators to patients with neuropathic pain of the head. Specifically, we prospectively follow our patients who underwent PNS for chronic migraine or cranial neuropathic pain preoperatively to their one-year visit.

METHODS

Patients with chronic pain who were refractory to other noninvasive and invasive therapies, and had a syndrome amendable to PNS were considered for a PNS trial. Failed previous treatment modalities included but were not limited to: nerve blocks, botulinum toxin injections, acupuncture, medications, radiofrequency ablations, and physical therapy. Prior to a PNS trial, all patients received psychological clearance. Those patients with a PNS trial demonstrating greater than 50% relief were candidates for permanent implantation of PNS and all were offered to participate in this study. All surgeries were performed by the senior author (Fig. 1). Patients were enrolled consecutively in this prospective study. Patients were followed preoperatively, at six weeks, three months, six months, and one year. The Albany Medical College IRB approved this study.

After giving informed consent, patients completed several self-assessment questionnaires, including the ODI, BDI, PCS, VAS, and the McGill Pain Questionnaire (MPQ). The ODI is a condition-specific assessment of functional outcome in patients with chronic pain. The questionnaire presents scenarios found daily such as sitting, walking, and lifting heavy weights, and patients choose statements most reflective of their functional levels. Rating occurs from 0 to 5, with 5 corresponding to the greatest amount of disability. The survey has been shown to have a good level of internal consistency and to correlate with pain measures such as the VAS and MPQ (13).

The BDI contains 21 questions assessing a patient's severity of depression. The survey is shown to have a high internal consistency for psychiatric and nonpsychiatric patients and be able to discriminate subtypes of depression (14). Depression causes greater impairments in chronic pain, while pain may often mask the symptoms of depression and hinder diagnosis. Therefore, BDI is an important outcome measure in any treatment for chronic pain.

The PCS encompasses three aspects of catastrophic thinking related to pain: rumination, magnification, and helplessness. Patients are asked the degree to which they experienced certain thoughts or feelings while in pain. As with depression, catastrophic thinking leads to greater pain intensity and worse functional outcomes (15). In addition to QOL measurements, pain measurements were taken to assess correlations. The MPQ contains descriptive words used by patients to describe their pain.

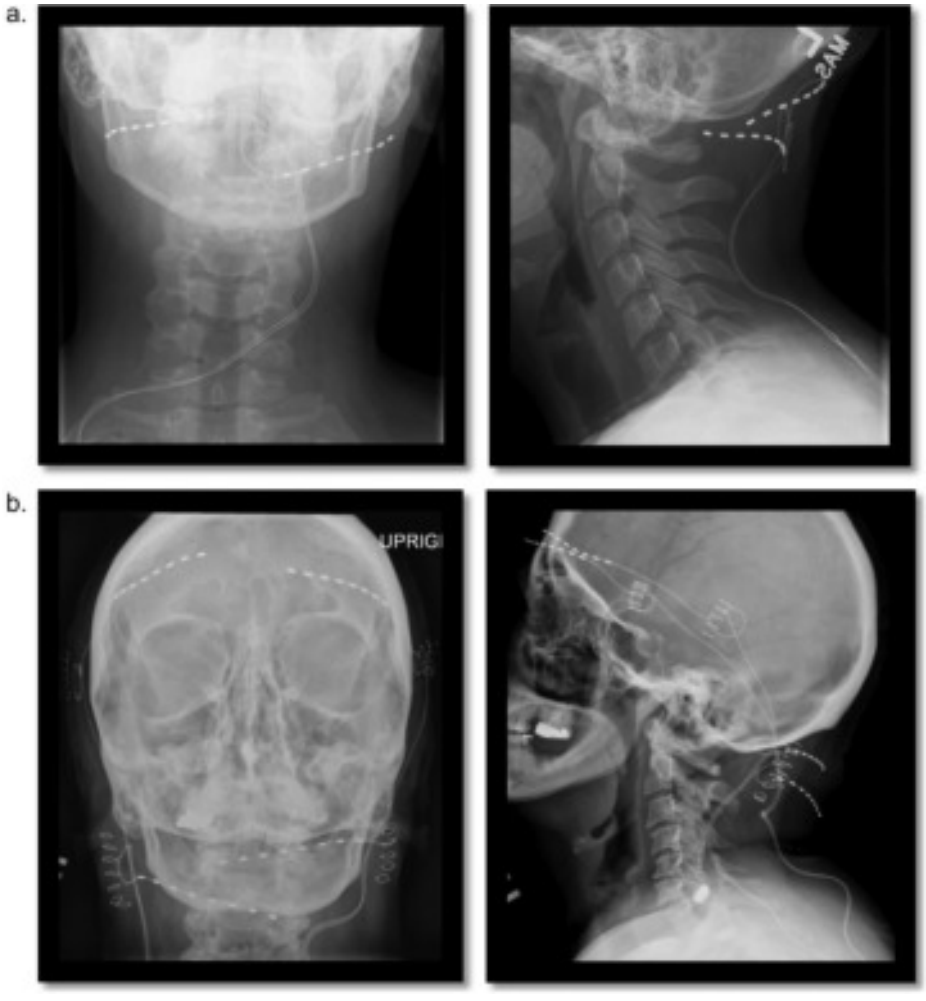

Figure 1. a. Anteroposterior (left) and lateral (right) radiographs of occipital nerve stimulator. b. Anteroposterior (left) and lateral (right) radiographs of hybrid treatment with bilateral occipital and supraorbital nerve stimulators.

Results were collected by a blinded third party and then analyzed via repeated measure ANOVA with Bonferroni post hoc test to compare multiple scores to baseline, paired *t*-test to compare each score to baseline, and correlation analysis.

Patients were implanted with one of three Food and Drug Administration (FDA)-approved systems intended to provide tonic stimulation to the peripheral nerve, off label. Bilateral procedures with percutaneous electrodes were performed in all cases. In cases of occipital nerve stimulators, stimulators were placed in the prone position through a midline occipital incision. We placed the leads at the level of the fascia and confirmed intraoperative placement at the C1 arch, regardless of pain distribution. The devices were tacked to the fascia using 2-0 silk suture and a strain relief loop. A skip incision was always used to allow for an additional strain relief loop and an extension when needed. Implanted pulse generators (IPGs) were placed in the flank region.

In cases of combined occipital/supraorbital lead placement, the patient was positioned laterally on a beanbag. An incision was made behind the hairline for the supraorbital lead, secured in place, a strain relief loop made and then tunneled to the lateral occipital incision where the occipital lead was placed, sutured, and a strain relief loop placed. The leads were then tunneled to an incision midway down the back toward the opposite flank. All incisions were irrigated and closed and then the patient was repositioned and draped for the same procedure on the opposite side. The IPG was placed on the ipsilateral flank.

RESULTS

Demographics

Nineteen patients underwent PNS trials over a two-year period. There were 17 of 19 patients who had successful trials. We were only able to obtain insurance authorization for permanent implantation in 11 of 17 patients. Patients were aware that insurance coverage may pose a difficulty at the time of the trial, but opted to continue. Nine of 11 patients consented to participate in this study. These patients completed validated surveys at baseline, six months, and one year (Table 1) at routine clinical visits. No patients had stimulators removed at one year. The patients had a mean age of 44 years (range: 25 to 68). Majority were female and had chronic pain for more than five years. Most patients had transformed migraines with or without trigeminal extension (Tables 2 and 3). Stimulation parameters varied by patient, but when leads were used independently either an end-to-end bipole or alternating cathode and anode through the entire length of the lead was used. Cross-talking between leads was used when needed. Patients were programmed with standard tonic stimulation starting with low frequencies and low pulse widths. Slowly, pulse widths were increased to get full coverage, and then frequencies were increased if needed.

Outcomes

From the preoperative period to one year, ODI and BDI scores decreased significantly from 41 to 31 ($t(\text{df}) = 3.625(7)$, $p = 0.008$), and

Table 1. Average Scores for Five Self-Assessment Surveys at Baseline, Six Months, and One Year Postoperative ($N = 9$).

Outcome measures at six months vs. one-year follow-up vs. baseline	Baseline	Six months ($N = 9$)	One year
ODI (SD)	40.88 (15.1)	32.13 (14.4)	30.75 (10.9)*
BDI (SD)	18.38 (8.7)	10.75 (9.5)*	10.88 (7.2)
PCS Total (SD)	27.63 (13.8)	19.25 (13.0)	15.38 (12.5)
MPQ Total (SD)	5.63 (3.1)	4.63 (2.2)	3.75 (2.4)
VAS (SD)	6.67(2.0)	2.67 (2.4)**	2.17(1.3)**

Repeated measures ANOVA with Bonferroni post hoc test was performed to compare each score to baseline. Asterisks have been placed near statistically significant values: *$p < 0.05$; **$p < 0.01$, and ***$p < 0.001$.
BDI, Beck's Depression Inventory; MPQ, McGill Pain Questionnaire; ODI, Oswestry Disability Index; PCS, Pain Catastrophizing Scale; VAS, visual analog scale.

Table 2. Specific Demographic Data Were Collected for Each Patient ($N = 9$).

	Lead location	Etiology	Duration (years)	Lead type	Comorbid
Patient 1	Occipital	Transformed migraines	4	Bilateral Octrode leads	Anxiety, depression, muscle spasm
Patient 2	Supraorbital and occipital	Transformed migraines with trigeminal extension	8	4 quad leads	Fibromyalgia, depression
Patient 3*	Occipital	Headache and neck pain following car accident	>5	2 quad leads	Seizures, anxiety
Patient 4*	Occipital	Transformed migraines	4	2 quad leads	Dizziness
Patient 5*	Occipital	Chronic head and neck pain	>5	Bilateral Octrode	Neuritis, fibromyalgia
Patient 6	Occipital	Transformed migraines	>5	Bilateral Octrode	Insomnia
Patient 7	Occipital	Transformed migraines	>5	Bilateral octrode	Arnold Chiari malformation type 1, anxiety, depression
Patient 8	Supraorbital and occipital	Transformed migraines with trigeminal extension	12	4 octrodes	Anxiety, depression
Patient 9	Supraorbital and occipital	Transformed migraines with trigeminal extension	>5	4 octrodes	Anxiety, depression

*Indicates patients who had hybrid treatment with spinal cord stimulation.

Table 3. Demographics Were Collected for Patients Who Underwent Permanent PNS ($N = 9$).

General demographics ($N = 9$)	
Male (%)	3 (33)
Female (%)	6 (67)
Age (STD)	44 (14)
Lead location	
Supraorbital and occipital	3 (33)
Occipital	6 (67)
Pain etiology	
Migraines	6
Occipital neuralgia	4
Headaches NOS	2
Head and neck pain	2
Pain duration	
Two to five years (%)	2 (22)
>Five years (%)	7 (78)
Primary pain distribution	
Bilateral (%)	9 (100)
Comorbid pain conditions	
Depression	5
Anxiety	5
Fibromyalgia	2
Insomnia	1
Seizures	1
Neuritis	1
Chiari I	1

from 18 to 11 (t(df) = 2.578(7), $p = 0.037$), respectively (Table 1). PCS also significantly decreased at the one-year mark (t(df) = 2.711(7), $p = 0.030$). VAS showed significant improvement from 7 to 2 (t(df) = 5.316(5), $p = 0.003$). However, MPQ did not significantly decrease (t(df) = 2.007(7), $p = 0.085$). A greater improvement was seen at one year, compared with six months, as scores on the majority of questionnaires continued to decrease. We attempted to analyze data from patients with supraorbital and occipital leads; however, as we had three patients, not surprisingly we were unable to find significance. In our patients who received occipital leads only ($N = 6$), we found significance between baseline and six months for VAS (t(df) = 0.500(4.5), $p = 0.009$) and BDI (t(df) = 2.064(2), $p = 0.029$). We noted a trend in correlation between ODI and BDI at six months ($R = 0.616$, $p = 0.077$).

DISCUSSION

Our results show PNS to significantly improve disability, depression, catastrophic thinking, and pain at one-year follow-up in PNS patients with cranial neuropathic pain and migraines. While a vast body of work has shown the positive impact of PNS on pain relief, much less data are available on disability and mood improvements in PNS patients and thus this finding contributes to the existing PNS literature. We opted to use the ODI as we routinely use this scale in our spinal cord stimulation (SCS) patients. Thus, this survey allows clinicians to conduct outcome studies with a single set of data sheets, improving ease of performing such studies in a busy office setting. There is some precedent of this in PNS as ODI had been used as a measure of outcome in cases of peripheral field stimulation of the lumbar region, where it showed benefit (16).

Our findings of improvement in depression in PNS prospectively and longitudinally confirm previous retrospective evidence of improvement in BDI at three months (17). Interestingly, the only other prospective data on PNS effect on depression are from a randomized control trial examining 10-week outcomes of PNS in fibromyalgia patients which found BDI to decrease from a mean of 22 to 16.74, and PCS to decrease from 20.55 to 13.2 (18). Our one-year improvements in PCS and BDI suggest that these are lasting and not due to placebo effect.

While our patients showed improved disability, depression, mood and pain levels, we found no significant correlations between these scales. We did note a trend for ODI to correlate with BDI at six months, indicating that disability and depression may be related, which could provide us with future methods for treatments. We realize the small nature of our study and believe that a double-blinded randomized clinical trial using subparesthesia waveforms could allow for confirmation of these finding. We also found no direct correlation between pain improvement and reduction in disability. A prospective study observing the relationship between pain and QOL in patients with nonoperative chronic low back pain also found that improvements in pain may be separate from changes in disability (19).

Our results demonstrate the beneficial impact of PNS on depression, catastrophic thinking, disability, and pain at one-year follow-up in a real-world practice where PNS was utilized for various etiologies when other methods of treatment have failed to be effective in treatment of pain. With a minimal complication rate, relatively short and straightforward recovery period, and prolonged positive impact on pain and overall QOL, PNS remains a viable option for treatments of head pain (20).

Authorship Statements

Tina Ramineni and Dr. Julie G. Pilitsis designed and conducted the study, including patient recruitment and data collection, with help from Priscilla De La Cruz, Lucy Gee, Vignessh Kumar, Meghan E. Wilock, Jessica Haller, Chris Fama, and Samik Patel. Tina Ramineni, Dr. Julie G. Pilitsis, and Julia Prusik prepared the manuscript draft and statistical data analysis. All authors approved the final manuscript. Input for statistical support in analyzing the data came from Priscilla De La Cruz and Lucy Gee.

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