ORIGINAL ARTICLE

Stimulation Ranges, Usage Ranges, and Paresthesia Mapping During Occipital Nerve Stimulation

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ABSTRACT

Introduction. Subcutaneous, occipital nerve stimulation has emerged as a potentially effective treatment modality for patients with refractory headache disorders. The purpose of this study was to document occipital stimulation characteristics in 10 patients status post implantation of an occipital nerve stimulator. **Methods.** All possible electrode combinations were tested in each patient, and sensory threshold, discomfort threshold, and associated paresthesia maps were noted. **Results.** Mean perception threshold was 1.07 V and mean discomfort threshold was 3.63 V. The associated paresthesia maps demonstrated that most patients felt stimulation as expected in the occipital regions; trigeminal distribution stimulation occurred but only in a minority of patients. Half of the patients experienced $\geq 50\%$ reduction in headache frequency or severity. **Conclusions.** These results should aid in clinical decision-making and manufacturing requirements for this modality; larger, prospective studies will be needed to determine the safety and efficacy of stimulation techniques for headache disorders.

KEY WORDS: *Headache disorder, migraine headache, occipital nerve stimulation, paresthesia, peripheral nerve stimulation.*

Introduction

Pain in the distribution of the first (ophthalmic) division of the trigeminal nerve and greater occipital nerve (GON) is a characteristic feature of primary and cervicogenic headache disorders. This pattern of pain referral reflects the anatomical and functional coupling between nociceptive dural afferents and cervical afferents in the GON onto neurons in the trigeminocervical complex. Greater occipital nerve infiltration and blockade with local anesthetics and corticosteroids is used as a treatment for patients with primary and secondary headache disorders, including migraine and cluster headache (1–4).

Occipital nerve stimulation has emerged as a potentially effective treatment modality for patients with refractory primary headache disorders. The implantation of subcutaneous leads in the occipital region is an off-label use of spinal cord stimulator technology. The fact that nonpainful stimulation of peripheral nerves can elicit analgesic effects has been exploited using transcutaneous electrical nerve stimulation, spinal cord stimulation, dorsal column stimulation, or subcutaneous stimulation (5–7). The modulatory effect on the pain associated with primary headache disorders may be secondary to local inhibitory circuits in the spinal cord or rostral pain-modulatory

structures, including the periacqueductal gray and thalamus.

The stimulation parameters, sensory thresholds, and paresthesia distribution have not been previously reported for refractory headache patients who have undergone implantation of occipital nerve stimulators (ONS). The influence of these parameters on clinical outcomes also has not been previously reported. The primary purpose of this study is to document occipital stimulation ranges (perception threshold through discomfort threshold), usage ranges (discomfort threshold divided by perception threshold), and stimulation maps for all possible electrode combinations for each of 10 patients with chronic refractory headache disorders who underwent implantation of an ONS. We hypothesize that the majority of patients will experience stimulation in the occipital region and that a minority will report stimulation in the distribution of the trigeminal nerves.

Materials and Methods

This study was approved by the Mayo Institutional Review Board. Patients previously implanted with an ONS were recruited based on their physical proximity to our medical center. The only exclusion criteria were patient refusal.

The following terms will be used throughout: a lead consists of bundled wires covered with inert polyurethane. Metallic contact points along the lead are called electrodes. Each electrode can be neutral or programmed to function as a cathode or anode to direct the flow of current through the surrounding tissue. An electrode array refers to a programmed combination of cathode(s) and anode(s). Perception threshold is the lowest voltage that elicits sensation; the upper end of the stimulation range (discomfort threshold) is defined as the voltage where patients feel stimulation strongly and do not wish the stimulation to be increased any further. The term *paresthesia* refers to any sensation the patient experienced during stimulation regardless of whether a specific nerve was being stimulated. The stimulation range represents the useful amplitudes for any given electrode combination while the usage range "represents the relative size of the therapeutic stimulating window" (8).

Before permanent implantation of the ONS, each patient had undergone a neurologic examination and a headache diagnosis was made using the International Headache Society (IHS) criteria (9). A psychiatric consultation was obtained on all patients. Each patient underwent a five- to seven-day percutaneous occipital nerve stimulation trial. The leads were then removed and the permanent ONS was implanted within one month of the end of the successful trial. A trial was considered successful if the patient obtained at least a 50% decrease in their headache frequency and/or severity. For the permanent implantation, Pisces Quad Plus leads/Synergy Internal

FIGURE 1. Bilateral subcutaneous occipital stimulator leads permanently implanted at the C1 level.

Pulse Generators (Medtronic Inc., Minneapolis, MN, USA) were used in all patients. Headache location determined the laterality of the leads (only patients with bilateral headaches underwent implantation with bilateral leads). Lead placement was accomplished using a technique previously described (10). A Touhy needle, bent to conform to the occiput, was inserted subcutaneously and transversely at approximately the level of the C1 spinous process. For the permanent implantation, the leads were secured to the fascia in the midline at the C1 level and then tunneled to an extension connector site several centimeters inferior to the C1 incision (Fig. 1). The extension was then tunneled to the implanted pulse generator, typically in the upper buttock or low abdomen. Stress relief loops were placed at both the cervical and periscapular sites. Data on frequency and severity of headaches before and after ONS implant were gathered from patient pain diaries and the medical record.

Upon presenting for the study, the following baseline data were gathered through both patient interviews and stimulator interrogation: headache location, average daily ONS use (hours), rate, amplitude, and pulse width. The number of baseline cathodes per side also was noted.
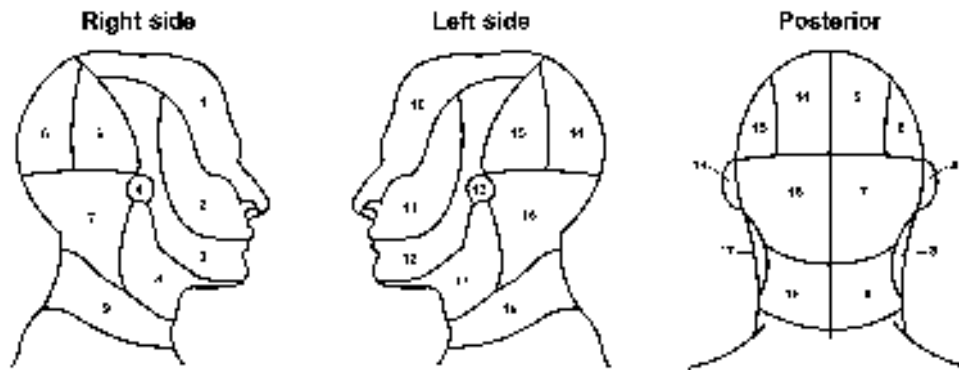
FIGURE 2. Maps used to identify location of baseline headache and stimulation patterns.

Impedances were checked for any system that required high amperage to achieve stimulation, and any electrodes with values greater than 4000 Ω were noted and eliminated from analysis. Next, each possible electrode combination was randomly programmed into the ONS. For unilateral leads, 50 possible combinations of anodes and cathodes exist, while there are 102 possible combinations for bilateral leads. Specifically, for bilateral leads, 50 electrode combinations exist per side plus one additional combination consisting of four cathodes on the tested lead with the anode on the contralateral lead. The patient's baseline rate and pulse width were not altered during the study. The patients were given a stimulation map that we created to divide the head into 18 areas (Fig. 2). They were asked to identify by number the location of their baseline headache and the location of paresthesia during testing of each electrode combination. Paresthesia locations were recorded at both perception threshold and discomfort threshold along with the corresponding amplitudes. At the end of the study, the patient's ONS was returned to its baseline electrode array unless the patient requested a programming change.

Statistical Methods
The percentage of patients with paresthesia at each area of the map was determined for threshold and discomfort voltages.

Results
Eleven patients were invited to participate; 10 agreed and signed informed consent. One patient was moving away from the area and declined to participate. Patient characteristics and outcomes are described in Table 1. The most common baseline headache locations were sites 7 and 16 (see Figure 2 for head map). No patients reported headache at site 8 or 17. One patient was found to have two (of eight) malfunctioning electrodes (impedance > 4000 Ω), and one patient was found to have one malfunctioning electrode. Furthermore, three electrode combinations were inadvertently not tested in one patient. Nine of 10 patients underwent implantation with bilateral leads. A total of 1748 electrode combination data points were gathered (407 right, 467 left, each at perception threshold and discomfort threshold). The mean perception threshold voltage for all electrode combinations tested was 1.07 V,

TABLE 1. Patient Characteristics

Patient	Diagnosis	Right*	Left*	Frequency change (%)	Severity change (%)	Response
21 years old, F	Chronic migraine	2, 3, 7, 9	11–12, 16, 18	0	0	Nonresponder
44 years old, M	Posttraumatic	1–3, 6, 7, 9	10, 15–16	0	−25	Nonresponder
41 years old, F	Chronic migraine		12, 15–16	−100	−100	Responder
34 years old, F	Chronic migraine	1–3, 5, 7, 9	10–12, 14, 16, 18	0	−20	Nonresponder
53 years old, F	Chronic migraine	3–7, 9	12–16, 18	−83	−26	Responder
31 years old, F	Chronic migraine	1, 3, 5–7	10, 12	−83	−60	Responder
29 years old, F	Chronic migraine	7, 9	16, 18	0	0	Nonresponder
46 years old, M	Chronic cluster	2, 7	12, 16	0	−38	Nonresponder
26 years old, F	Chronic migraine	1, 5–7	10–12, 14–16	0	−57	Responder
39 years old, F	Hemicrania continua	1	10, 14–16	−87	−60	Responder

F, female; M, male. Frequency change: percentage change in headache frequency in the 90 days pre- to post-ons. Severity change: percentage change in average headache severity in the 90 days pre- to post-ons. Response: responder ≥ 50% reduction in headache frequency or severity. *Right and left refer to baseline headache location (Figure 2).

TABLE 2. Baseline Stimulator Data (*N* = 10)

Duration since implant (months); mean (SD), range	20 (14), 5–41
Usage (hours/day); mean (SD), range	18.9 (8.5), 2–24
Bilateral implants	9
Number of cathodes per side; mean (SD), range	1.65 (0.82), 1–3
Rate; mean (SD), range	
Right (*N* = 9)	38 (13), 25–60
Left	38 (13), 25–60
Amplitude; mean (SD), range	
Right (*N* = 9)	2.8 (2.0), 0.1–6.7
Left	2.4 (1.8), 0.3–5.6
Pulse width; mean (SD), range	
Right (*N* = 9)	396 (87), 240–450
Left	403 (72), 240–450

TABLE 3. Percentage of Patients With Paresthesia for Any Electrode Combination at Perception (Mean 1.07 V) and Discomfort (Mean 3.63 V) Thresholds (*N* = 10)

	Threshold	Strong	95% CI
Right			
	0	0	0–31
Site 1	0	0	0–31
Site 2	0	20	3–56
Site 3	30	40	12–74
Site 4	20	50	19–81
Site 5	30	70	35–93
Site 6	90	90	56–100
Site 7	20	40	12–74
Site 8	70	70	35–93
Left			
Site 10	0	10	0–44
Site 11	0	10	0–44
Site 12	10	20	3–56
Site 13	20	50	19–81
Site 14	10	60	26–88
Site 15	30	80	44–97
Site 16	100	100	69–100
Site 17	40	50	19–81
Site 18	80	90	56–100

CI, confidence interval.

while the mean discomfort threshold voltage was 3.63 V (stimulation range 1.07–3.63 V). The mean usage range (discomfort threshold divided by perception threshold) was 4.0. One patient requested a new electrode array to be programmed into her stimulator after participating in the study. Other stimulator data are summarized in Table 2, including mean baseline rate, amplitude, and pulse width. Five of the 10 patients reported at least 50% reduction in headache frequency or severity (95% confidence interval 19–81%).

Paresthesia maps are reported in Table 3 and Figures 3 and 4. Sites 7, 9, 16, and 18 had the highest percentage of
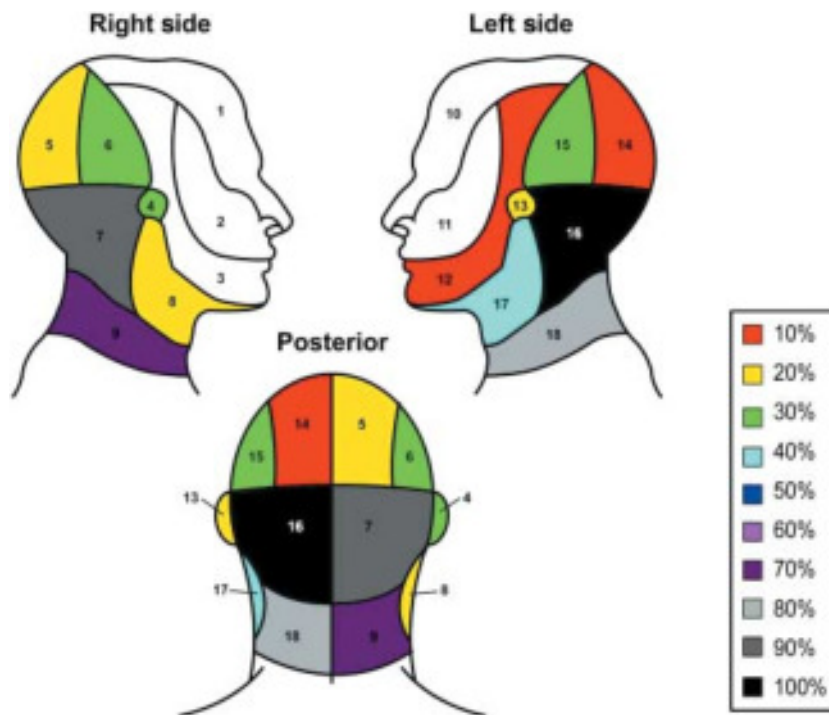

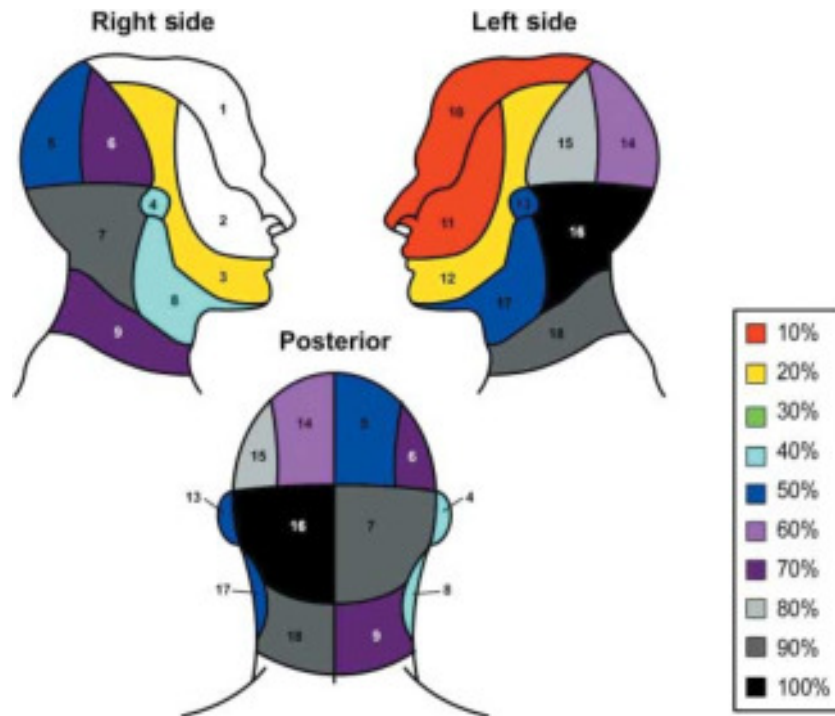**FIGURE 3.** Paresthesia maps at sensory threshold.

FIGURE 4. Paresthesia map at discomfort threshold.

patients with paresthesia. A majority of patients also are likely to have paresthesia at sites 5, 6, 13, 14, 15, and 17.

Discussion

This study documents stimulation and usage ranges, and paresthesia maps for 10 patients who underwent permanent implantation of an ONS. It is not surprising that most of the patients felt paresthesia in the occipital region where the leads were implanted; more remote regions of the head were less reliably stimulated. Paresthesias were reported least often in the trigeminal dermatomes. In terms of treatment efficacy, half of the patients were "responders," defined as $\geq 50\%$ reduction in headache severity or frequency. This is a result similar to other studies (10–15). However, it must be emphasized that outcome of treatment was not a primary endpoint of this study. The patients were not randomized and there was no control group. The primary purpose of the study was to examine stimulation parameters and paresthesia maps in this group of heterogeneous refractory headache patients.

The improvement reported by "responders" may reflect the reduction in trigeminal activation and the mobilization of central pain modulatory centers that occur in response to electrical stimulation of the GON (15,16). Therefore, while sensitization of convergent nociception specific neurons in the trigeminal cervical complex may be the physiologic substrate for the development of the

spread and referral patterns seen in primary headache disorders, the inhibition of these same neurons either from supraspinal centers or direct stimulation of the GON may be responsible for the relief of trigeminal distribution pain after ONS stimulation.

The stimulation provided by quad plus leads most likely represents monopolar stimulation, as the electrodes are set widely apart (12 mm vs. 6 mm for the quad regular leads). Current density is the highest (sharpest) at the edge of the electrode, and is related to pulse width, amplitude, and electrode size. It is possible that closer electrode spacing would produce different paresthesia patterns than the diffuse monopolar stimulation we have studied. However, the current density is quickly attenuated as the distance from the electrode increases. Therefore, we speculate that paresthesia patterns would not change dramatically with closer electrode spacing. Nonetheless, future studies of occipital paresthesia patterns and voltage parameters could include eight contact electrodes per lead or other leads with more "compact" electrode spacing than the quad plus leads we tested. The placement of these leads was done without any effort to ensure that the electrodes were adjacent to specific nerves (eg, greater or lesser occipital nerves). Therefore, we assume that the stimulation patients experience represents tissue stimulation mediated via the distal branches of the C1–3 nerve roots. However, it is possible that some of the electrodes

were positioned such that they could interact directly with the greater or lesser occipital nerve resulting in both local and more remote paresthesia. The clinical utility of direct nerve stimulation in this setting is unknown.

In conclusion, we have documented the stimulation and usage ranges and associated paresthesia maps for patients undergone implantation with widely spaced (quad-plus) electrodes. Unfortunately, the number of patients studied is not sufficient to determine whether and to what extent specific stimulation parameters or paresthesia maps correlate with clinical outcomes. Further prospective, controlled studies are needed to document the efficacy of this modality for refractory headache disorders and determine if certain leads (percutaneous vs. surgical), paresthesia and stimulation patterns, electrode arrays, and/or electrode spacing are advantageous in treating this difficult patient population.

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