

Treatment of medically intractable cluster headache by occipital nerve stimulation: long-term follow-up of eight patients



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Summary

Background Cluster headache is a form of primary headache that features repeated attacks of excruciatingly severe headache usually occurring several times a day. Patients with chronic cluster headache have unremitting illness that necessitates daily preventive medical treatment for years. When medically intractable, the condition has previously been treatable only with cranially invasive or neurally destructive methods.

Methods Eight patients with medically intractable chronic cluster headache were implanted in the suboccipital region with electrodes for occipital nerve stimulation. Other than the first patient, who was initially stimulated unilaterally before being stimulated bilaterally, all patients were stimulated bilaterally during treatment.

Findings At a median follow-up of 20 months (range 6–27 months for bilateral stimulation), six of eight patients reported responses that were sufficiently meaningful for them to recommend the treatment to similarly affected patients with chronic cluster headache. Two patients noticed a substantial improvement (90% and 93%) in their attacks; three patients noticed a moderate improvement (10%, 60%, and 20–30%) and one reported mild improvement (25%). Improvements occurred in both frequency and severity of attacks. These changes took place over weeks or months, although attacks returned in days when the device malfunctioned (eg, with battery depletion). Adverse events of concern were lead migrations in one patient and battery depletion requiring replacement in four.

Interpretation Occipital nerve stimulation in cluster headache seems to offer a safe, effective treatment option that could begin a new era of neurostimulation therapy for primary headache syndromes.

Introduction

Cluster headache is a form of primary headache characterized by bouts during which patients experience many attacks of very severe headache, considered by some to be the worst pain experience. The chronic form of cluster headache is defined as having a bout of no more than a month in every 12 months, unless treatment is given.¹ The 1-year prevalence of chronic headache is about 0.12%, about 10% of this group have chronic cluster headache.² Chronic cluster headache is probably over-represented in headache clinic populations, although the definition itself is probably too restrictive in terms of the length of a mean night gap between bouts for an individual. The devastating nature of intractable chronic cluster headache has encouraged us to explore novel approaches to its management.

Both episodic and chronic cluster headache can be successfully treated with a range of oral and parenteral medical or surgical interventions, but a substantial proportion of patients, all of which have been extensively reviewed,^{3,4} although many patients are treated effectively, a proportion, particularly with chronic cluster headache, present an ongoing challenge. Treatment of episodic and chronic cluster headache by injection of local anaesthetic and steroid into a greater occipital nerve^{5,6} is generally reported to be useful. Adverse events are modest, and further studies are warranted.⁶ Because the effect of greater occipital nerve

injection is limited to weeks, this approach is less useful in chronic cluster headache, where repeated injections are impractical or cease to be effective.

A resolution of patients with chronic cluster headache unrefractory to medical management (although the extent of this problem is unclear, since guidelines to define such patients have only been evolved). That such refractory patients exist is clear from reports of surgical interventions including head-on-ice, external trigeminal nerve or cranial parasympathetic outflow. Destructive or invasive surgical interventions reported include application of glycerol to the trigeminal ganglion,⁷ radiofrequency ablation of the trigeminal ganglion,⁸ gamma knife surgery to the trigeminal nerve,⁹ trigeminal neurectomy,¹⁰ trigeminal sensory nerve neurectomy,¹¹ surgical section of the nerve in its course,¹² radiofrequency ablation of the nerve in its course,¹³ decompressions of nerve sections,¹⁴ decompression of the facial nerve,¹⁵ endoscopic sphenopalatine ganglion blockade with lidocaine and dexamethasone,¹⁶ and radiofrequency lesions of the pterygopalatine ganglion.¹⁷ The reported complications from such procedures include death, permanent neurological impairment, including corneal anaesthesia, which can lead to visual loss, amaurosis fulgens, jaw deviation, and cluster attacks switching sides after a unilateral lesion has been made. In addition to these complications, a case¹⁸ has also been reported of attacks that

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performed on the same side despite unilateral nerve root section.¹² A 7% success rate was reported for microvascular decompression combined with sectioning of the nucleus intermedius without producing a neurological deficit in 28 patients who underwent 39 procedures.¹³ Many of these procedures bear the risks of a craniotomy or the micro-procedure and the attacks may swap sides. With a clear potential side-effects for destructive procedures, non-destructive ways of pain control would be an important advance.

Neurosurgical therapy approaches that target control of peripheral nervous system targets might offer a direction for the development of treatments for medically intractable headache disorders. The approach has been used in other pain indications, including neurocystic pain¹⁴ and was pioneered by Warner and Keel¹⁵ in head pain. Identification of anatomical and structural change¹⁶ in the region of the posterior hypothalamus in cluster headache led to deep brain stimulation of this region being trialed successfully.¹⁷ This procedure is associated with a small risk of fatal haemorrhage.¹⁸ Peripheral stimulation of the occipital nerve for medically refractory headache has been used in severe occipital neuralgia and cases for migraine,¹⁹ occipital neuralgia,²⁰ and other primary headaches.²¹ On the basis of our experience with greater occipital nerve injections,²² our neuroimaging studies of the effects of occipital nerve stimulation,²³ and our concerns about morbidity and mortality of deep brain stimulation for cluster headache, we began to give occipital nerve stimulator implantations to patients with medically intractable chronic cluster headache. We report the systematic long-term follow-up of these patients.

Methods

Selection of patients

Patients with medically refractory chronic cluster headache from the outpatient department at the National Hospital, London, UK, were offered an occipital nerve stimulation. Patients seen at this hospital are referred by

neurologists throughout the UK and represent a wide geographical distribution. These patients were offered the option of a destructive trigeminal nerve procedure or deep brain stimulation. Eight individuals opted for occipital nerve stimulation. All patients were diagnosed with chronic cluster headache and fulfilled the standard criteria,²⁴ with the exception that one patient had long attacks (Table 1, Appendix).

Some hospitals use a temporary percutaneous wire electrode connected to an external generator to stimulate the occipital nerve for a trial period of several days before implantation of a permanent device.²⁵ This practice is not used at our institution and therefore was not a selection criteria. Additionally, although we were aware of each patient's response to occipital nerve block using lidocaine and steroid, this response was not a selection criteria.

The patients were given implants on compassionate grounds and the study was an audit of outcome, and as such under UK guidelines did not require ethics committee approval.

Surgical technique

Occipital nerve stimulation electrodes, leads, and battery were implanted by use of a technique similar to that previously described.²⁶ Implants were bilateral in all patients except the first, who initially had a unilateral bilateral implant followed 9 months later by the addition of a right-side electrode. In brief, a single-stage procedure was used with two parts to allow an intraoperative trial of stimulation. The first part was done under local anaesthesia and gentle sedation, with care taken to avoid undue bending the occipital nerves. The patient was placed in the lateral position and a sterile field was established. A midline posterior cervical incision was made and bilateral cylindrical quad electrodes (Medtronic, MN, USA) were introduced with curved Tuohy needles using an image intensifier to aid position. A dual programmable pulse generator (Medtronic Synergy, Medtronic) was then used to test stimulation and confirm that 'paras'hesia was felt bilaterally. The second part of the insertion was done under a general anaesthetic. The electrodes were looped and anchored to the cervical fascia. Then a tunnel to a second cervical or suboccipital vein course intermediate incision. A left suboccipital or claustrum incision was made (depending on the patient's preference) to form a pocket to implant the pulse generator. Electrodes were carried to the intermediate incision and a pair of extension leads (Medtronic) attached. Silicone sheaths were used to protect the lead connections. Tubical antibiotic cover with gentamicin was introduced around the pulse generator incision and closed.

Patients were provided with remote controls and instructed how to use them to turn remote-wired, the implanted pulse generators. Patients could adjust their stimulator settings with the remote control, although the pulse generators were programmed to provide continuous

	Age (years) at time of implantation	Type of chronic cluster headache	Years since first cluster attack/active of implant	Years since chronic cluster onset/active of implant
1	50N	Primary	7	7
2	32F	Primary	1	1
3	32N	Secondary	1	2
4	40N	Secondary	18	7
5	58N	Secondary	12	8
6	38N	Secondary	27	0
7	50N	Primary	12	12
8 ^a	27(N/39)	Secondary	54(32)	2(20)
Median	36(33-58)		12(5-52)	6(2-20)

Abbreviations: F=female; N=male; N/A=not available.

Table 1 Patients' demographics

stimulation. Patients could turn the stimulator on or off, and vary the pulse width, frequency, or amplitude, although most patients tended only to vary the amplitude. The polarity of the electrodes was adjusted during follow-up visits to reflect non-comfortable bilateral parietal sites in the occipital region. Patients remained in hospital for several days after implantation before discharge.

Follow-up and data collection

The data for this report were obtained from the patients' records, from a patient visit, and by post-mail telephone by one investigator (PB). At the follow-up interviews, patients were asked to compare retrospectively their attacks before and after the procedure, to gain an overall impression of effectiveness. They were also asked whether the use of triptans had altered, and to provide an overall response to the question "would you recommend the procedure to a fellow cluster headache sufferer?" Data on frequency, severity, and duration of headaches were obtained from consecutive mailed questionnaires, then by direct follow-up with the patients. All patients were presented with their own case history and the data, and asked to confirm to the best of their knowledge that the information was accurate.

Results

Seven men and one woman with a median age at operation of 46 years (range 32–57 years) were given implants (table 1). Full case histories are shown in the web-appendix. Median duration of chronic cluster headache at the time of the operation was 6 years, although for the patients with secondary chronic cluster headache the number of years spent with episodic cluster headache was much longer. Five patients had secondary chronic cluster headache (i.e. the chronic form had evolved from an episodic form), and three had primary chronic neurovascular headache, commencing at beginning. Patients all fulfilled new criteria for instability,¹⁰ and would have been suitable for deep brain stimulation by current criteria.¹¹

Before stimulation, frequency of attacks ranged from one or more per day per severity was rated as 10/10 on a verbal rating scale for seven of eight patients, and the duration of attacks was in the range 15–250 min.

These patients had not had sustained benefit from a range of preventive drugs used as monotherapy (table 2) and transitional treatment (table 3). Some patients also tried combination therapy (table 3), which was also ineffective. Two patients had undergone trigeminal

Weight (kg)	Duration (years)	Metoprolol	Topiramate	Neotomin	Gabapentin	Sodium valproate	Other drugs
1	560	1200	200	0	2000	1000	Paraldehyde, propranolol
2	260	1500	200	0	2000	1000	Amoxycillin, paracetamol
3	480	400	NK	NK	0	0	Amoxicillin, paracetamol
4	720	1500	0	0	2000	1000	Paraldehyde, paracetamol, carbamazepine, clonidine
5	1900	1900	0	200	2000	2000	Low-dose diazepam, acetaminophen, carbamazepine, clonidine
6	600	1200	200	0	200	0	0
7	790	NK	0	200	0	NK	0
8	560	1200	0	0	NK	NK	Paraldehyde, propranolol, paracetamol

For all quantities listed, the value shown is the maximum dose used. NK, not known; 0, none; 1000, 10 mg per day.

Table 2: Preventive drugs used without sustained improvement and doses (total mg per day)

Patient	DHE infusion (give 100 µg 4 days)			Prednisolone (a 7 day course)		GON infection (if doubtful use steroid)		
	Cluster headache improved	No. of attacks given	Duration of response (days)	Cluster headache increased?	Eventing (days)	Cluster headache improved?	Subclinical infection	Eventing response
1	Yes	2	2000	No	60	Yes	1	No eventing
2	NT	0	0	Yes	60	No	1	0
3	0	0	0	Yes	60	Yes	1, 2	2 (not the same as no response)
4	0	0	0	Yes	60	Yes	1, 2	2 (not the same as no response)
5	Yes	1	2	Yes	60	No	0	0
6	Yes	1	10	Yes	60	No	1	0
7	Yes	1	2	No	40	No	1	0
8	Yes	1	2	Yes	60	No	1	0

DHE, dihydroergotamine; NT, not treated; 0, none; 1, one; 2, two; 10, 10 mg per day.

Table 3: Transitional treatment tried for cluster headache and response

	Sumatriptan		Oxygen
	Response	Response time (min)	Effect size†
1	No	-	No
2	Yes	10	Yes
3	Yes	10	Yes
4	Yes	10	Yes
5	Yes	20	Yes
6	Yes	10	Yes
7	Yes	10	Yes
8	Yes	10	Yes
Summary	8/8	10 (100%)	8/8

Effect size†

Table 4: Responses to the first dose before implantation

of sterile ganglion injections of local anesthetic without long-term success. If a patient's responses to stimulation in a particular evening are mixed (high/low oxygen) are shown in table 4. Three patients had single-blinded placebo-controlled administration tests that were negative.

Four patients had oral indomethacin at doses from 75 mg to 150 mg daily without resolution. One patient had never had indomethacin (patient 6); his history was most atypical for an indomethacin-responsive headache.

Before stimulation, only three of the eight patients were taking a preventive (paracetamol in all cases). After implantation, two of these three patients continued to use verapamil and one stopped because of side effects. None of the five patients who were not taking a preventive drug before implantation started taking one afterwards.

The median follow-up for headache-free days was 20 months (range 8–27 months). Six of eight (75%) patients rated an improvement in their condition and said that they would recommend an occipital nerve stimulator to other patients with chronic migraine because in similar circumstances. One patient's headache was about the same before and after use of the stimulator but she said that she would still recommend another patient try using the stimulator if they were in a similar situation. One patient who had used the stimulator only for a few days did not find it helpful, and said that he would not recommend it to another patient. None of the patients became pain

	Yes to headache onset	Yes to side effects at follow-up	Patients' overall view of whether headache was worse since implantation	Patients' estimate of % change in headache frequency since implantation	Time since before or after further action	Would not eat even a small amount of stimulator?
1	7	23	Same	-	Same	No
2	5	21	Same	-	Same	Yes
3	5	11	Increased	75%	Low (stoppage)	Yes
4	17	17	Increased	50%	Low	Yes
5	10	21	Increased	20–50%	Same	Yes
6	14	8	Increased	50%	Low	Yes
7	13	17	Increased	25%	Same (initial 2 weeks)	Yes
8	14	27 (27%)	Increased	25%	Same	Yes
Summary	13 (66%)	90 (66%)	23 (61%) increased	36% (20–93%)	28% increased, 28% biphasic	25% recommended not

Table 5: Effectiveness of treatment, side effects, change in headache frequency, and patient's view of stimulator

Table 5: Follow-up for various reasons

	Frequency		Severity (peak intensity)†		Duration (min)			
	Before	After	Before	After	Before	After	After	After
1	1/day	1/week	10/10 data	Some	10	10	0	None
2	1/week	Some	10/10 data	Some	120	10	None	Some
3	1/day	1/day	10/10	10/10	10/10	10	10	None
4	1/week	1/week	10/10	10/10	10	10	10	Some
5	1/week	2/week 1/day	10/10	10/10	10/10	10	10	None
6	1/week	1/day	10/10	10/10	10/10	10	10	CC
7	2/week	1/day (10/10)	10/10	10/10 (10/10)	10/10	10	10/10	Some

† 0 = None, 10 = Worst imaginable (including vomiting).

Table 6: Patients' estimates of headache frequency, severity, and duration of attacks before and after treatment

free, although in one patient, severity of pain was reduced so much that he stopped using triptans.

Of the six patients who improved, two received a marked improvement, of 90% or better, in their attacks (table 6). Three patients received a moderate improvement in their attacks of 40% or better, and one patient received a mild improvement, of 25%. The meaning of the term "improvement" differed between individuals and typically meant a change in frequency or severity rather than duration (table 6). Patients who felt that they improved did so without a change in the use or type of preventive treatment. After stimulator implantation, one patient stopped using triptans completely. Three patients reduced triptan use, and for 1 patient, had no alteration in triptan use (table 7).

The benefit from the stimulator was not immediate and it was necessary to report it in less than weeks. Indeed, the useful effect built up over months. By contrast, when a technical fault in the implanted device developed for one of the patients who reported a 90% benefit from the stimulator, there was an almost immediate worsening in their headache pattern over hours to days, a similar rapid decline was also reported by two other patients when the batteries in their devices failed.

The first patient to undergo implantation had a unilateral, ipsilateral electrode, because 83% of their attacks had been left-sided. After implantation the attacks changed; 40% were right-sided or left-sided, whereas 20% of attacks started on the right and merged into a left-sided attack. After the addition of the right-sided electrode to complete bilateral stimulation, the attacks became 70% ipsilateral and 30% right-sided with an overall 40% improvement compared with attacks before any stimulation. On the basis of this case, we chose to give all subsequent patients bilateral implants.

The parameters produced by stimulating the occipital nerves can be modified and adjusted by altering the stimulation amplitude, frequency or pulse width of the device. A wide range of settings were used for each patient (table 7). We do not know the optimal values for efficacy so far, the most crucial variable seems to be the presence of paroxysmal itself.

Complications are listed in table 8. Eighty-six in total surgical interventions (nine in individual events) needed to be done in these patients. Five were due to electrode migration (all three occurred in the same patient), one was due to electrode failure, and five were related to battery malfunction or depletion (all two battery depletions in the same patient). Because of these complications, the patients had to be seen at the hospital for a diagnostic check by a neurosurgeon followed by a focused admission to the operating theatre. One patient elected not to have a battery replaced after 23 months of bilateral stimulation because they did not want another operation at that time and wanted to see how their attacks altered without use of the stimulator. Lead replacement was done in one patient and battery replacement in four

Table 6. Values of settings in visits*

	Range of values set during inpatient visits†			Patients who indicated that they improved
	Amplitude (V)	Pulse width (µs)	Pulse width (µs)	
1	20-30	20-30	20-30	improved
2	20-30	0-50	20-30	improved
3	20-30	10-30	20-30	improved
4	20-30	20-30	20-30	improved
5	1-50	10-30	20-30	improved
6	1-50	10-30	20-30	improved
7	15-30	0-50	20-30	improved
8	10-30	10-30	10-30	improved

*Values were set at the beginning of the patient's admission to prevent any further changes of the equipment during the inpatient visit. †Values were set with 60-400 µs.

Table 7. Settings used for occipital nerve stimulation

Table 8 also includes one patient who had postoperative pain and another whose device needed to be reprogrammed when a suspected mode-competition developed. In addition to these events, some patients reported neck stiffness or limited neck movements after implantation, and one patient had muscle recruitment from migrated electrodes.

Paroxysmia in the occipital region occurred in all patients and was more evident at times for some patients than for others, but since all patients generally considered this effect to be a reassuring or even a pleasant sensation and a marker of stimulator activity rather than an adverse effect, we have not listed it as a complication in table 8.

Discussion

Our case series provides long-term, albeit open-label evidence that occipital nerve stimulation might have a role in the management of medically refractory chronic cluster headache. That the patients did not respond to medical treatment and had long histories of cluster headache and that attacks returned when technical problems occurred, all suggest that the stimulator had more than a placebo effect. A further strength of the findings is the relatively long duration of follow-up which suggests that the effect is robust and long-lasting. In selected patients whose lives are otherwise so completely wrecked by a constant illness, even a modest response rate would seem to be worthwhile, particularly in view of the very minimal side effect profile for the procedure. Since the alternative for such patients is either destructive, irreversible procedures, such as ablation, or even more risky or deep brain stimulation, which also has complications, this treatment seems to be an attractive next step. The time to onset of effect suggests an interesting neurobiology in terms of brain plasticity. Further studies are warranted, with even longer term follow-up, to understand the place of this potentially important development in clinical practice.

Nerve stimulation therapy for chronic cluster headache has thus far focused on deep brain stimulation.^{28,29} Two

	Months since implantation at review	Complications	Adverse events
1	25	(1) Electrolyte imbalance (hypokalaemia)	(1) Electrolyte imbalance (hypokalaemia)
2	27	(1) Headache (mild), (1) dizziness (mild), (1) nausea (mild), (1) vomiting (mild), (1) dizziness (mild)	(1) Headache (mild), (1) dizziness (mild), (1) nausea (mild), (1) vomiting (mild), (1) dizziness (mild)
3	31	None	None
4	37	(1) Headache (mild), (1) dizziness (mild), (1) nausea (mild), (1) vomiting (mild), (1) dizziness (mild)	(1) Headache (mild), (1) dizziness (mild), (1) nausea (mild), (1) vomiting (mild), (1) dizziness (mild)
5	47	(1) Headache (mild), (1) dizziness (mild), (1) nausea (mild), (1) vomiting (mild), (1) dizziness (mild)	(1) Headache (mild), (1) dizziness (mild), (1) nausea (mild), (1) vomiting (mild), (1) dizziness (mild)
6	57	(1) Headache (mild), (1) dizziness (mild), (1) nausea (mild), (1) vomiting (mild), (1) dizziness (mild)	(1) Headache (mild), (1) dizziness (mild), (1) nausea (mild), (1) vomiting (mild), (1) dizziness (mild)
7	61	None	None
8	67	(1) Headache (mild), (1) dizziness (mild), (1) nausea (mild), (1) vomiting (mild), (1) dizziness (mild)	(1) Headache (mild), (1) dizziness (mild), (1) nausea (mild), (1) vomiting (mild), (1) dizziness (mild)

1 patient with no complications, 1 patient with 1 complication, 1 patient with 2 complications, 1 patient with 3 complications.

Table 5: Complications

cases have been abstracted in which occipital nerve stimulation was used in patients with chronic cluster headache who had had "every conceivable medication", and this approach was said to be "heptual". A patient implanted with a smaller unilateral device (Blou) reported a 70% improvement in frequency and severity of attacks.⁶ By contrast, no benefit was noted in another series of six patients.⁸ Unilateral implants were used in this series and to longevity was short (7 months); longer-term findings (8 months) reported at a meeting⁹ suggest that four of five patients noted an improvement, 1 of which is consistent with our results. Deep brain stimulation for cluster headache was developed after identification of an area of activation ("and's natural target") in the region of the posterior hypothalamus. Deep brain stimulation of the posterior hypothalamic region has been used successfully,¹⁰ but "with a small risk of fatal haemorrhage,"⁹ which has led us to investigate occipital nerve stimulation as an "initial, perhaps screening, option before deep brain stimulation." One might conclude that occipital nerve stimulation should be tried first, since its side-effect profile is so modest, although response rates seem to be better for deep brain stimulation, with 4 of 10 of treated patients reported to be completely pain-free.¹¹

Peripheral nerve stimulation has been used in neuropathic pain with mixed success.¹² In treatment of head pain was first focused on cases described as occipital neuralgia, because of "pain in the distribution in the occipital region".⁵ Our experience with such patients is that most have another underlying primary headache, typically migraine.⁶ Remarkably, the effect of occipital nerve stimulation is not restricted to the peripheral distribution of the greater occipital nerve, although the paroxysmal patients report clear pain syndromes clearly involving extra-occipital territory, such as migraine,⁶ and hemiparesis continua (unilateral and⁶), are also successfully treated with occipital nerve stimulation. This

extra-occipital effect is also seen with greater occipital nerve injection programmes, although response to greater occipital nerve blockade was not a "all or nothing" outcome in occipital nerve stimulation. The probable explanation for this effect is a central modulatory change at least involving the trigeminothalamic complex of neurons where second order neurons have input from both trigeminal and occipital afferents.¹³ Indeed, some functional brain imaging has shown that patients with chronic migraine with occipital nerve stimulation have modulation of thalamic activation rather than deactivation, migraine areas,¹⁴ the effect in chronic headache might be much more central than the trigeminothalamic complex.

In other reports of occipital nerve stimulation for headache common complications have included infection, meningitis, infection, cervical pain, allergy to metal, and muscle recruitment or spasm of the neck.^{5, 6, 15} In this series with a median follow-up of 26 months for bilateral electrodes we see a range of complications, although no infection or allergy, four of eight patients needed a new battery, and two patients needed new electrodes. Muscle recruitment, pain, and electric shock sensations were also noted. Battery depletion is not strictly a complication but it does mean that no patient is required to have an operation, should they choose to have the wires replaced. In previous reported series, battery depletion seems to have been less common, possibly because of shorter follow-up, lower voltage use, intermittent use of the stimulator, or different electrode contacts. Several issues need to be explored, such as selection of patients and predictors of successful outcome. Occipital nerve block did not seem to predict benefit of successful occipital nerve stimulation (see table 3) but the numbers here are small and more data are needed. Other than selection of patients and predictors of outcome, operative technique and equipment improvements are important, electrode migration needs to be minimised,

and battery consumption, or the possibility of a re-chargable battery system, needs to be explored.

In these patients a range of different stimulation frequencies, pulse widths, and voltages were used. The reason for changing the variables was to achieve a comfortable degree of paresthesia in the distribution of the occipital nerves by adjustment of the parameters. We have not been able to identify a trend or pattern for the settings, and this point should be carefully researched in the future.

Although our results are promising, with a lack of high patients reporting that they noticed an improvement in their headache, the study did not have a placebo control. This issue is among the most challenging for trials of device-based treatments, since paresthesia seems to be a requirement of effective therapy. Little doubt exists that placebo effects are seen in cluster headache, but they seem an unlikely basis for the substantial effect that we observed, a resolution of medically intractable symptoms, stable year's or longer-term follow-up, and a return of attacks with electrode migration or battery failure. For the most part, at least, we cannot be sure, although the observation that patients reduced use of triptans and did not start to use another preventive drug suggest a positive outcome. For a condition such as medically intractable chronic cluster headache, where the options are so limited and lack a new treatment to control the problem in just a fifth of patients would be a wonder. In advance. These results open up a more complex question, which our study cannot address: should patients with medically treated chronic cluster headache, whose symptoms are controlled but with a significant side effect, be offered this approach? The mainstay treatments of chronic cluster headache have important and stable anti-side effect patients should be involved in decisions about how to advance this potential option.

In summary, six out of eight patients with stable medically intractable chronic cluster headache had, for their treatment, and would like to improve their condition such that they would like to attend the procedure to similarly treated patients. The effects we noted persisted over a median follow-up of 20 months, do not seem to be predicted by greater occipital nerve blockade with local anesthetic and steroid, and are reversible when the device malfunctions. The procedure itself is relatively straightforward, without substantial morbidity over the time we have observed this group. The fact that syndromes in which the pain is mainly felt in the ophthalmic division of the trigeminal nerve can be modified by stimulation in a connected somatosensory suggests that the underlying principle of this treatment is one of modulation of brain function, while the cause of the therapeutic effect has all the hallmarks of the implication of brain plasticity. If a technique provides hope for patients, and a nice opportunity to understand the biology of primary headache syndromes by careful follow-up of these and other cases.

Contributors

ERB conceived of the initial design of the experimental setup. ERB and JG performed the initial study, and collected the data. ERB conceived of the study, participated in its design and coordination, participated in drafting the manuscript, and was the main author of the manuscript. ERB and JG conceived of the study, participated in its design and coordination, participated in drafting the manuscript, and was the main author of the manuscript. ERB conceived of the study, participated in its design and coordination, participated in drafting the manuscript, and was the main author of the manuscript. ERB conceived of the study, participated in its design and coordination, participated in drafting the manuscript, and was the main author of the manuscript.

Conflict of interest statement

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