

Neurostimulation and Headache Disorders

Medically Refractory Migraine, Cluster Headache, and Occipital Neuralgia

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Can Neurostimulation Be Used for Headaches and Migraines?

Yes, neurostimulation of the peripheral nerves of the head and face are emerging as a potential treatment option for patients with chronic, intractable and disabling primary headache disorders like chronic migraines, chronic cluster headaches, occipital neuralgia and even some forms of chronic daily headaches.

Three headache conditions and their treatment – migraine, cluster headache, and occipital neuralgia – are presented in this document. This overview is intended for patients, family members, caregivers, practitioners, referring physicians, and the general public. Additional resources are listed at the end. In addition, a 2016 table in *Nature Reviews Neurology* summarizes current and emerging neuromodulation therapies for headache, at: <http://bit.ly/neuromodulation-chart>.

Safety and efficacy data are limited in quantity but there is accumulating experience of the use of neurostimulation for the treatment of refractory occipital neuralgia, chronic cluster headache, chronic migraines and other headache disorders.

What Does “Refractory” Headaches Mean?

Refractory means when *no treatments seem to help reduce the pain or suffering*.

Peripheral nerve stimulation for treatment-resistant headaches appears safe, effective, and well-tolerated

The medical definition for ‘refractory pain’ is when:

1) Multiple evidenced-based biomedical therapies used in a clinically appropriate and acceptable fashion have failed to reach treatment goals that may include pain reduction and/or improvement in daily functioning or have resulted in intolerable adverse effects and when 2) psychiatric disorders and psychosocial factors that could influence pain outcomes have been assessed and appropriately addressed. (1)

What Is a Migraine?

A migraine is a chronic neurological disorder characterized by episodic attacks of head pain with associated symptoms.

Migraine sufferers may experience the following:

- A pulsating pain to one side of the head of moderate to severe pain intensity
- Attacks that last from a few hours to several days
- Aggravation from routine physical activities

- Other symptoms may include nausea, sensitivity to light (photophobia) or sensitivity to sound (phonophobia)
- In 20% of people migraines may occur with an *aura* (reversible changes in vision and other sensations like coordination and speech)
- If migraines occur with any weakness of the body, this is a danger sign and medical help should be sought immediately

A migraine can be incapacitating!

Who Gets Migraines?

Migraines affect anyone:

- Up to 18% of women
- Up to 8% of men
- Up to 15% of children under age 18
- About 12% of us will experience a migraine headache at some point in our lives

More than half of migraine sufferers have at least one attack per month.

For some migraine sufferers, certain activities or foods may bring on an attack. Migraine attacks have been linked to consuming red wine or beer, cheese, chocolate, citrus fruits like oranges, and tea or coffee. Foods that may trigger an attack are relatively high in amines, which can alter blood flow in the brain.

Stress can also be a trigger for migraines.

What Is the Impact of Migraines?

Migraines can dramatically impact work, family and social life. Estimates place the annual cost of migraine at \$14 billion, according to the U.S. National Academy of Sciences' 2011 report "Relieving Pain in America".

Today, researchers are still uncovering new information about the condition. We now know there can be a genetic component to migraines. (2)

How Are Migraines Treated?

An approach to managing migraines should include:

- Education
- Lifestyle changes e.g. stopping caffeine, increasing exercise, stress management and improving sleep hygiene
- Recognising triggers and avoiding them
- Determining the type and frequency of migraine attacks using use headache calendars and diaries where appropriate
- Detecting and treat co-morbidity e.g. depression, anxiety commonly co-exists
- Individualised treatment should be provided by specialist neurologists and pain specialist physicians
- Combination medication therapy should be used where possible

What Is the Treatment for Acute Migraine Attacks?

Medications to treat acute migraine attacks include: non-steroidal anti-inflammatory drugs, paracetamol (acetaminophen), triptans and anti-nausea medications.

Routine use of opioid analgesics is not recommended for the treatment of acute migraine due to the potential for medication-overuse headache and worsening the problem.

What Is the Preventative Treatment for Migraine Attacks?

Combination preventative medication therapies might include: antiepileptics, antidepressants, beta-blockers, and anti-hypertensives.

For prevention of migraines, opioid analgesics should not be routinely used due to the potential for development of medication-overuse headache.

What Are Some of the Non-Medication Therapies for Migraines?

- Lifestyle changes e.g. stopping caffeine, increasing exercise, stress management and improving sleep hygiene
- Recognise triggers and avoid them
- Botulinum toxin A injections at the back of the neck, where the occipital nerves may play a role in chronic migraines. Not everyone finds benefit from the injections, however, and repeat injections are required
- Neurostimulation

Non-invasive Neurostimulation for Chronic Migraine

In 2013, the U.S. Food and Drug Administration (FDA) approved a portable, single-pulse transcranial magnetic stimulator to halt the onset of migraine with aura. Then in 2014, the FDA approved a headpiece designed to prevent

migraines. The crown-like band is worn across the forehead for several minutes a day and stimulates the supraorbital nerves. (3)

Emerging Neurostimulation Methods to Treat Chronic Migraine

In 2015, the FDA permitted a clinical study of a miniaturized neurostimulator as a potential chronic migraine treatment. The implant works wirelessly and is inserted beneath the skin of the forehead to stimulate the occipital and supraorbital nerves. Another neurostimulation approach, vagus nerve stimulation, has also been studied as a potential way to prevent chronic migraine. (4 – 8)

Research Into Occipital Nerve Stimulation (ONS) for Chronic Migraine

ONS stimulates the occipital nerves, which run from the base of the skull and wrap around to the forehead. A 2015 review of 12 research studies about medication-resistant (“refractory”) migraine concluded in 2015 that “short-term results indicate that the effect of ONS is, on average, modest among patients with chronic refractory migraine although the observed effects may still be clinically important given the refractory nature of the condition.” (9)

What Is a Cluster Headache?

Cluster headache is a relatively rare, but severe, condition that has been described as the most painful experience known, like being stabbed in the eye with a red-hot poker. The pain is so extreme, the condition is sometimes called “suicide headache”.

Who Gets Cluster Headaches?

Unlike migraine, cluster headaches mostly affect men, striking six times as many men as women. Cluster headaches affect about 1 in 1,000 people.

How Are Cluster Headaches Diagnosed?

As the name of the condition implies, the cluster headache attacks comes in waves, or clusters, over days or months. The headaches last from about 15 minutes to three hours. Cluster headaches strike multiple times a day or every day or two, often at the same time of day.

The pain usually occurs around the eye and on one side of the head. On the affected side, the eye may water and the nose may become stuffy or runny. Due to that, the disorder is sometimes called a histamine headache.

What Is the Cause of Cluster Headache?

The cause of cluster headache is not fully known. Two chemical messengers, histamine and serotonin, may play a role. The hypothalamus, which helps orchestrate sleep cycles, is also thought to be involved in these cyclical attacks.

How Are Cluster Headaches Treated?

Cluster headache treatments aim to limit how many attacks there are, and how severe they are. Medications to prevent cluster headache attacks include: beta-blockers, anticonvulsants, divalproex, tricyclic antidepressants, nortriptyline, and calcium channel blockers. (10)

Medications to halt or limit a cluster headache attack once it has begun include ergots, acetaminophen-isometheptene-dichloralphenazone, dihydroergotamine injection, and triptans. In addition, some over-the-counter migraine treatments can be used for cluster headache.

Breathing pure oxygen during a cluster headache attack may also bring some relief, especially when attacks occur at night.

Cluster Headaches and Neurostimulation

When other forms of treatment fail to bring relief for cluster headache, neurostimulation may be considered.

Early experience with neuromodulation techniques for chronic pain first started in the 1950s with recognition of the role of the hypothalamus – a structure deep in the brain. Later, other less-invasive neuromodulation targets were tried in the spinal cord and facial or scalp nerves outside the skull – such as the upper spinal cord, the sphenopalatine ganglion (a facial nerve bundle), or occipital nerves.

Although neurostimulation treatments are still evolving, in 2013 the European Headache Federation recommended occipital nerve stimulation and sphenopalatine ganglion stimulation as first-line therapy in cluster headache patients whose condition is medication-resistant. (11)

Sphenopalatine Ganglion Stimulation

The sphenopalatine ganglion (SPG) is a nerve bundle near the cheek and upper jaw that has long been a target for other cluster headache therapies, such as local anesthetic or lesioning. SPG stimulation has been available in Europe for episodic and cluster headache since 2012. In the U.S., a clinical trial prior to application for regulatory approval was expected to finish in 2017. (12)

Occipital Nerve Stimulation

Occipital nerve stimulation has been investigated in nearly 100 patients with cluster headache. About 60% of them experienced at least a 50% reduction in headache frequency and/or intensity. (8, 11)

Deep Brain Stimulation

Currently, deep brain stimulation is mainly used to decrease motor symptoms of movement disorders such as Parkinson's disease.

Still, by 2016, at least 64 patients with medication-resistant cluster headache were reported to have received DBS, and recommendations for patient selection have been developed. (9, 13) Deep brain stimulation targets for cluster headache are different than those for movement disorder; they include the hypothalamus or the associated ventral tegmental area, which also plays a role in this "pain circuit".

Vagus Nerve Stimulation

Finally, since the vagus nerve influences the balance of nervous system activity, non-invasive vagus nerve stimulation (VNS) has also been developed as a cluster headache treatment. (14)

What Is Occipital Neuralgia?

Occipital neuralgia, also known as Arnold's neuralgia, is defined by the International Headache Society as a unilateral or bilateral paroxysmal, shooting or stabbing pain in the posterior part of the scalp, in the distribution of the greater occipital nerve, lesser occipital nerve, or third occipital nerve, sometimes accompanied by diminished sensation or dysesthesia in the affected area and commonly associated with tenderness over the involved nerve(s). (15)

If occipital neuralgia fails to respond to the simple therapies like medications, local anaesthetic and steroid injections around the occipital nerve(s), botulinum toxin A injection, and occipital nerve pulsed radiofrequency, then neurostimulation could be considered.

What Treatment Is Available If Headaches, Migraines and Occipital Neuralgia Are Medication-Resistant (Refractory)?

About 20% of the population can experience incapacitating headaches that are resistant to medical therapies. Migraines, cluster headaches, and occipital neuralgia can all become *refractory*.

If the pain is considered refractory, occipital nerve stimulation could be considered.

Occipital nerve stimulation was originally used to treat occipital neuralgia but has application for other refractory headache disorders. (16)

Occipital Nerve Stimulation Explained

The technique of neurostimulation delivers mild electrical currents through small electrodes that are embedded in a thin and soft flexible wire that is placed under the skin, through a needle. The wire (lead) sits just under the skin, at the base of the skull, near the occipital nerves.

Patients receive a small handheld remote control that they use to turn stimulation on and off, using settings adjusted by their pain specialist.

A neurostimulation system is first tried on a temporary basis for up to two weeks and if the pain reduction during this time is greater than 50% or if the migraine severity and/or frequency is greatly reduced, then a permanent implant of the device could be considered. When permanently implanted, the electrical impulses are delivered by a small, pacemaker-like battery that is placed under the skin usually under the skin on the chest wall, near the collarbone, like a pacemaker used for heart conditions.

It has been shown that electrical stimulation of nerves stimulates the release of natural chemicals that cause pain reduction by quieting over-excitability nerves. Electrical stimulation of nerves may also enhance local blood circulation. (17)

When we stimulate nerves with current, we *modulate* the nerve function, hence the term *neuromodulation*. Often neuromodulation therapies refer to the location of stimulation. For instance, when we stimulate the spinal cord, we call it spinal cord stimulation (SCS). When we stimulate small nerves outside the spinal cord we call it peripheral nerve stimulation (PNS).

Occipital nerve stimulation is a type of peripheral nerve stimulation developed for pain relief. In 2003, occipital nerve stimulation was used to treat chronic and refractory migraine. (18) Occipital nerve stimulation has also been used to treat cluster headaches. (19) In addition, occipital nerve stimulation was investigated as a form of therapy for fibromyalgia. (20)

A Bit More Detail on Occipital Nerve Stimulation

In 1999, the International Neuromodulation Society's journal *Neuromodulation: Technology at the Neural Interface* published clinical observations describing use of neurostimulation to reduce the severe head pain of occipital neuralgia that generally occurs to the rear of the head, in areas supplied by the occipital nerves. The authors noted that, similar to treating neuropathic pain with spinal cord stimulation, using peripheral neurostimulation on the occipital nerves induced a pleasant tingling sensation. They report the effect relieved the lightning-like pain condition by at least half in the patients whose conditions were monitored from 18 months to 6 years. (16)

Recent clinical results have seemed to support the expectation of some clinicians that applying a peripheral nerve stimulator to a combination of the occipital nerves and nerves that supply the face might result in a better outcome. (21-23) (A partial convergence of these two systems occurs at the trigeminocervical complex.)

Indeed, the response rate for patients with refractory head-wide pain who were treated with neurostimulation to the occipital and trigeminal nerve systems is reported to be better than 90%. (21-23)

This is an improvement from using only stimulation to the occipital nerves for head-wide pain syndromes, which is reported to bring about just a 40% response. (24) (On average, patients who only have pain in the rear of the head, a posterior occipital syndrome, show improvement averaging 88% from occipital nerve stimulation, with the range running from 71 – 100%.)

Complications of occipital nerve stimulation are usually minor. These include medical complications, such as infection, bleeding or fluid collection under the skin (seroma). The device and the connections can sometimes be the cause of complications and might include movement of the electrical lead (lead migration is one of the commonest complications), breakage/fracture of the leads, or battery (pulse generator) problems.

The results seem best when the tingling sensation (paresthesia), occurs in all the primary nerve distributions involved (occipital and/or trigeminal). There is a growing body of literature supporting these techniques, although continued high quality studies are needed to further assess their long-term effectiveness.

In summary, clinical evidence and medical experience shows that peripheral nerve stimulation, when used for medically refractory head pain syndromes like migraines and occipital neuralgia, appears to be safe, effective and well tolerated.

Please note: This information should not be used as a substitute for medical treatment and advice. Always consult a medical professional about any health-related questions or concerns.

Resources

American Chronic Pain Association

P.O. Box 850
Rocklin, CA 95677-0850
ACPA@theacpa.org
<http://www.theacpa.org> 
(916) 632-0922; (800) 533-3231

National Headache Foundation

820 N. Orleans Suite 411
Chicago, IL 60610-3132
info@headaches.org
<http://www.headaches.org> 
(312) 274-2650; (888) 643-5552

-  Magis D, Jensen R, Schoenen J. Neurostimulation therapies for primary headache disorders: present and future. *Curr Opin Neurol.* 2012;**25**:269-76.
-  Miller S, Sinclair AJ, Davies B, Matharu M. Neurostimulation in the treatment of primary headaches. *Pract Neurol.* 2016;**16**:362-375.
-  Schuster NM, Rapoport AM. New strategies for the treatment and prevention of primary headache disorders. *Nat. Rev. Neurol.* 2016;**12**:635-50.
-  Slavin KV, Colpan ME, Munawar N, Wess C, Nersesyan H. Trigeminal and occipital peripheral nerve stimulation for craniofacial pain: a single-institution experience and review of the literature. *Neurosurg Focus.* 2006;**21**:E5.

For further information see: WIKISTIM at <http://www.wikistim.org> – This free-to-use collaborative, searchable wiki of published primary neuromodulation therapy research was created in 2013 as a resource for the global neuromodulation community to extend the utility of published clinical research. The goals of WIKISTIM are to improve patient care and the quality of research reports, foster education and communication, reveal research needs, and support the practice of evidence-based medicine.

References

1. Deer TR, Caraway DL, Wallace MS. A Definition of Refractory Pain to Help Determine Suitability for Device Implantation. *Neuromodulation* 2014; 17: 711-7152.
2. Wessman M1, Terwindt GM, Kaunisto MA, Palotie A, Ophoff RA. Migraine: a complex genetic disorder. *Lancet Neurol*. 2007 Jun;6(6):521-32.
3. "FDA Allows Marketing of First Device to Relieve Migraine Headache Pain" (Press release). Dec. 13, 2013. Accessed Oct. 14, 2016.
4. <http://www.massdevice.com/fda-approves-breakthrough-migraine-prevention-device> Arezu Sarvestani (March 12, 2014). "FDA Approves Breakthrough Migraine Prevention Device". Mass Device. Accessed Oct. 14, 2016.
5. <http://www.univadis.com/viewarticle/migraine-prevention-transcutaneous-supraorbital-nerve-stimulation-effective-316399?s1=news> Laurie Barclay (Oct. 14, 2015). "Migraine Prevention: Transcutaneous Supraorbital Nerve Stimulation Effective". Univadis. Accessed Oct. 4, 2016.
6. <http://www.medicaldaily.com/new-device-stimrelieve-halo-migraine-treatment-385856> Lecia Bushak (May 12, 2016). "Tiny New Forehead Device, 'StimRelieve Halo,' Provides Migraine Treatment With Electric Pulses". Medical Daily. Accessed Oct. 14, 2016.
7. Silberstein SD, Calhoun AH, Lipton RB, Grosberg BM, Cady RK, Dorlas S, Simmons KA, Mullin C, Liebler EJ, Goadsby PJ, Saper JR; EVENT Study Group. *Chronic migraine headache prevention with noninvasive vagus nerve stimulation: The EVENT study*. *Neurology*. 2016 Aug 2;87(5):529-38. doi: 10.1212/WNL.0000000000002918. Epub 2016 Jul 13. PubMed PMID: 27412146; PubMed Central PMCID: PMC4970666.
8. Neurostimulation for Treatment of Migraine and Cluster Headache. Schwedt TJ, Vargas B. *Pain Med*. 2015 Sep;16(9):1827-34. doi: 10.1111/pme.12792. Epub 2015 Jul 14. Review. PMID: 26177612
9. Chen, Y.F., Bramley, G., Unwin, G., Cernat, D.H., Dretzke, J., et al (2015). Occipital Nerve Stimulation for Chronic Migraine - A Systematic Review and Meta-Analysis. *PLoS One*, 10 (3), e0116786.
10. http://www.emedicinehealth.com/cluster_headache/pages_em.htm Edward Lubin (April 4, 2016). "Cluster Headache". eMedicineHealth. P. 5. Accessed Oct. 14, 2016.
11. Martelletti P, Jensen R, Antal A, et al. Neurostimulation of chronic headaches: Position statement from the European Headache Federation. *J Headache Pain*. 2013;14:86.
12. Pietzsch JB, Garner A, Gaul C, May A. Cost-effectiveness of stimulation of the sphenopalatine ganglion (SPG) for the treatment of chronic cluster headache: a model-based analysis based on the Pathway CH-1 study. *The Journal of Headache and Pain*. 2015;16:48. doi:10.1186/s10194-015-0530-8. doi:10.1177/0333102412473667.
13. Sillay KA, Sani S, Starr PA. Deep brain stimulation for medically intractable cluster headache. *Neurobiol Dis*. 2010;38:361-8.
14. <http://www.medscape.com/viewarticle/878763> "FDA Approves Vagus Nerve Stimulation Device for Cluster Headache". Medscape. Accessed Sept. 12, 2017.
15. Manolitsis N, Elahi F1. Pulsed radiofrequency for occipital neuralgia. *Pain Physician*. 2014 Nov-Dec;17(6):E709-17.
16. Weiner RR, KL. Peripheral Neurostimulation for Control of Intractable Occipital Neuralgia. *Neuromodulation: Technology at the Neural Interface*. 1999;2(3):217-221.
17. 5. 5aum Shaparin, MD, Karina Gritsenko, MD, Diego Fernandez Garcia-Roves, MD, Ushma Shah, MD, Todd Schultz, MD, and Oscar DeLeon-Casasola, Peripheral neuromodulation for the treatment of refractory trigeminal neuralgia *Pain Res Manag*. 2015 Mar-Apr; 20(2): 63-66.
18. Popeney CA, Alo KM. Peripheral neurostimulation for the treatment of chronic, disabling transformed migraine. *Headache*. Apr 2003;43(4):369-375.
19. May A, Leone M, Afra J, Linde M, Sándor PS, Evers S, Goadsby PJ; EFNS Task Force. EFNS guidelines on the treatment of cluster headache and other trigeminal-autonomic cephalalgias. *Eur J Neurol*. 2006 Oct;13(10):1066-77.
20. Plazier M, Dekelver I, Vanneste S, Stassijns G, Menovsky T, Thimineur M, De Ridder D. Occipital nerve stimulation in fibromyalgia: a double-blind placebo-controlled pilot study with a six-month follow-up. *Neuromodulation*. 2014 Apr;17(3):256-63; discussion 263-4.
21. Reed KL, Black SB, Banta CJ, 2nd, Will KR. Combined occipital and supraorbital neurostimulation for the treatment of chronic migraine headaches: initial experience. *Cephalalgia*. Mar 2010;30(3):260-271.
22. Slavin K, Wess C. Trigeminal branch stimulation for intractable neuropathic pain: technical note. *Neuromodulation: Technology at the Neural Interface*. 2005;8:7-13.
23. Mammis A, Gudesblatt M, Mogilner A. Peripheral neurostimulation for the treatment of refractory cluster headache, long-term follow-up: Case Report. *Neuromodulation: Technology at the Neural Interface*. 2011;14(5):432-435.
24. Saper JR, Dodick DW, Silberstein SD, McCarville S, Sun M, Goadsby PJ. Occipital nerve stimulation for the treatment of intractable chronic migraine headache: ONSTIM feasibility study. *Cephalalgia*. Feb;31(3):271-285.