We are IntechOpen, the world’s leading publisher of Open Access books
Built by scientists, for scientists

4,100
Open access books available

116,000
International authors and editors

120M
Downloads

154
Countries delivered to

TOP 1%
Our authors are among the most cited scientists

12.2%
Contributors from top 500 universities

WEB OF SCIENCE™
Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com
Chronic Headache and Neuromodulation

Vicente Vanaclocha-Vanaclocha, Nieves Sáiz-Sapena, José María Ortiz-Criado and Leyre Vanaclocha

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.72150

Abstract

The immense majority of patients with chronic headaches can be controlled with medical treatments. However, there is a subset of them with poor response, and it is for those patients that new therapeutic strategies are being designed. Neuromodulation has been used for chronic pain management in many areas for the past 50 years. The application of these techniques to the treatment of the most refractory chronic headache disorders has offered hope to these patients. There is a large variety of different techniques, each of them particularly suitable to specific types of chronic headaches. The surgically implanted devices are still in use in some particularly recalcitrant cases. Nevertheless, new percutaneous devices allow new treatment strategies. Percutaneous devices do not always show the same effectiveness as surgically implanted stimulating devices, but they are user friendly and have no serious adverse effects. Thus, they are becoming the treatment of choice once the pharmacological means are no longer effective. In case of failure, the surgical procedures would still be available as a last resort.

Keywords: chronic headache, chronic migraine, cluster headache, neuromodulation, neurostimulation

1. Introduction

Chronic headache is one of the most frequent pain syndromes, affecting 3% of the population. It can be rather disabling [1, 2], particularly for young people who are most affected by it. The International Classification of Headache subdivides headaches into 300 different entities [3], each of those with a different pathophysiology and involving different anatomical structures. Pain can originate from the central nervous system, the cranium or the cervical area [4].
Primary headaches like tension headache, migraine (CM) or trigeminal autonomic cephalalgias (TACs) show the highest incidence. TACs are particularly incapacitating [5]. Most cases can be controlled with medication and physiotherapy. Abuse of medication is common with these patients, via the dose, the drugs or both [6]. When the pharmacological and conservative treatments fail, surgery may be considered. In the past, ablative surgical techniques have been applied. These techniques have been replaced by neuromodulation techniques. In them, the anatomical structures are not lesioned, but instead, the electric impulses block the nervous structures in a reversible fashion [7]. These techniques can be subdivided into two broad categories: noninvasive and invasive [1]. The noninvasive options include transcranial stimulation either electric [8–10] or magnetic [11–13] and transdermal stimulation of occipital [14, 15], supraorbital [9, 14–19] or vagus [20–23] nerves. Invasive procedures include stimulation of occipital [5, 17, 24, 25–35], supraorbital [19, 31, 36], infraorbital [31] or greater auricular [37] nerves as well as sphenopalatine ganglion [38–44], cervical spinal cord [45–48] or hypothalamus [4, 25, 27, 49–52].

Noninvasive neuromodulation techniques are user friendly and have low costs and few and minor side effects [8–15, 19–23]. Unfortunately, their effectivity is lower than their invasive counterparts. Invasive neuromodulation is reserved for the most refractory cases, as they are associated with increased aggressiveness, more severe adverse events (AE) and higher costs [7]. All costs have to be taken into consideration. The full cost of neuromodulation would include the disability grants, as well as further possible treatments for AEs [33, 34, 53].

Taking the net expenditure into consideration, some have reported that the reductions in cost are evident at 5-year postimplantation [53]. In any case, invasive neuromodulation must only be used in the most refractory cases and only after all other medical and noninvasive treatments have failed [46]. This is particularly important due to the high incidence of AEs and the possibility of new surgical procedures to solve them [29, 33]. A trial of temporary stimulation is required to evaluate the possible response of a definitive implant [45, 46, 54] to avoid wasting time and resources.

These techniques present promising new treatment strategies. The available evidence will be analysed, describing the possible future trends.

2. Historical aspects of neuromodulation

Electricity to treat chronic headaches was first used in ancient Rome [55], but it was not until the 1950s that neuromodulation was used in the treatment of chronic pain disorders [55, 56]. Thalamic stimulation to treat chronic headaches was introduced in 1976 [57] and percutaneous peripheral nerve stimulation a year later [58]. At the beginning of the 1990s, hypothalamic deep brain stimulation (hDBS) was applied to the treatment of some chronic headache syndromes and particularly in TACs [59]. The first report of occipital nerve stimulation (ONS) to treat occipital neuralgia was in 1999 [60]. In the year 2000, the hypothalamic stimulation was applied in the treatment of drug-resistant cluster headache (CH) [61]. The first two cases of supraorbital nerve stimulation (SONS) were reported in 2002 [62]. The first cases of hDBS in the treatment of CH were reported in 2003 [61]. In 2004, the ONS was applied in the treatment...
of CM [63]. The first case reported with cervical spinal stimulation (SCS) in the treatment of CH was in 2008 [64]. The first report on stimulation of the sphenopalatine ganglion was presented at 2009 [38]. Ever since, there has been an explosion of reports on the effectiveness, indications and AEs of all these techniques. Simultaneously new devices that allow percutaneous stimulation have reached the market, allowing new solutions to old problems.

3. Indications for neuromodulation

The first step is to diagnose the patient and select an appropriate treatment by an experienced team that is familiarised with all available treatments. Neuromodulation techniques are indicated in cases that have failed all other medical treatments available for this specific headache type. It is also recommended that patients receive a psychological assessment.

The next step is to attempt noninvasive neuromodulation techniques particularly useful in this type of chronic headache. Should all fail, a period of temporary trial stimulation is suitable [33]. Patients showing no response are not implanted and are redirected to other forms of treatment. This temporary stimulation also helps to predict the results to be expected if the definitive implant is attempted [32, 46].

4. Classification of the different techniques

4.1. Noninvasive procedures

4.1.1. Transcranial electric stimulation (TES)

This technique involves applying a low amperage continuous electric stimulation directly to the scalp [10]. In most cases, the electric stimulus spreads out of the area covered by the electrodes [10]. AEs have been moderate, such as skin burns due to inadequate electrode skin contact, fatigue or local prickling and burning sensation during the stimulation [8, 10]. Its effectiveness and experience are limited [8, 10].

4.1.2. Transcranial magnetic stimulation (TMS)

A magnetic field is applied to the head, inducing depolarization and electrical activity of the underlying brain cortex [65, 66]. Most have applied it to the left frontal motor area [11, 67, 68], but some have done it to the occipital region, particularly in migraine patients [69]. In chronic headache related to mild posttraumatic head injury (MTHI-HI), it has shown ≥50% improvement in pain intensity and frequency in 58.3% of the patients [11]. In migraine, some have reported a reduction of 31.2% in pain frequency and 37.8% in attack duration [70] in two-third of the patients [66]. The acute variant, with or without aura, seems to have a better response than the chronic one [67–72]. There seems to be a cumulative effect, so that the longer this treatment modality is applied, the greater is the attack duration reduction [69]. In migraine
patients, a randomised study comparing transcranial magnetic stimulation versus placebo showed a 76.6% versus 27.1% pain improvement [75], but these data were not confirmed by others [68]. Another study in this same disease compared this treatment modality with botulinum toxin injection, finding that although both treatment modalities provide pain relief, the last one is more effective [76]. In atypical facial pain, trigeminal neuropathic pain and cluster headache, it has shown ≥30% pain reduction in 73% of the patients [77]. Interestingly, enough older age and longer treatment duration were associated with a better response, while the type of facial pain showed little influence [77]. It has been applied to pregnant migraine patients with no untoward side effects [69]. Complications are rare and include a case of induced trigeminal autonomic cephalalgia that ceased after stopping the transcranial magnetic stimulation [78]. Some patients have reported transient drowsiness [75]. A continuous application is required for the effects to be persistent [69].

4.1.3. Transcutaneous supraorbital-supratrochlear stimulation

This technique involves a special equipment that looks like a pair of glasses, which has to be worn on the forehead. It provides a 50% chronic headache pain reduction, including CM [14, 16, 18]. When used for CM prevention, it reduces the number of attacks but not their intensity [16, 18]. In episodic CM, patients induced a 50% headache frequency reduction in 38.2% of the patients [18]. Although not very effective, the only side effects are local discomfort, redness or temporary skin irritation [16].

4.1.4. Transcutaneous vagus nerve stimulation (VNS)

The first reports entailed electrodes implanted surgically around the vagal nerve in the neck [79]. However, it never gained acceptance because the procedure was invasive and the results are limited. In 2013, a percutaneous VNS device was introduced, showing promising results in the treatment of chronic CM (CM) [20, 23]. Its best advantage is that it is applied directly to the neck by the patient him/herself [21, 23]. Its main drawback is its low effectiveness (22%) [22, 23, 80]. It is well tolerated with minor side effects like neck twitching, raspy voice or redness at the application site [22, 23, 81].

In CH, it is helpful in the episodic but not in the chronic type [80, 81]. In the episodic type, it induces a positive response in 26.7% of the cases [80]. Some have used it in the acute treatment of the chronic variant of this disease with a higher than 50% pain reduction in 40% of the patients [81]. In CM, it provides a 50% or more pain reduction in 22–56.3% of the patients, which is better in the episodic than in chronic variant [20, 22, 82]. It has been helpful in a single case of hemicrania continua (HC) unresponsive to indomethacin [83].

4.2. Invasive procedures

4.2.1. Sphenopalatine ganglion stimulation (SPGS)

The sphenopalatine ganglion has been a target in the treatment of chronic headaches for over a century. Initially, destructive lesions were applied [84], but since 2009, neuromodulation is also available [38]. It is effective in two thirds of episodic CH cases, preventing at least 50% of attacks, showing a decrease in intensity of at least 50% or both [38, 41–43, 73, 74].
SPGS is both preventive and therapeutic in acute phases [85, 87]. About 30% of the patients can stop the medication [85, 87]. A transoral technique has been described with a remote powering system that avoids extension leads and the need to replace the batteries [86], where patients switch-on the stimulation with a handheld remote controller when the pain attack starts [85]. This markedly reduces the incidence of AEs [86]. Some patients use the stimulation continuously to reduce the attack incidence [85]. Bilateral stimulation is more effective than unilateral [39], but it is not so effective in the chronic variant of this disease [85]. AEs are uncommon and mild, including sensory loss in the maxillary region (81%) [87], that may last over 1 year (2–28%), epistaxis (13%), facial numbness (25%), and local pain (4%) [86]. SPGS has also been used successfully in CM [44].

4.2.2. Occipital nerve stimulation (ONS)

ONS is the stimulation of the distal branches of C_2 and C_3 nerve roots (greater and lesser occipital nerves). The electrodes (one at each side) can be inserted either through a 2 cm midline skin incision at C_1 level and tunneled subcutaneously through a bent Touhy needle inserted laterally from the mastoid area or alternatively from a lateral approach with a bilateral mastoid area skin incision and the electrodes inserted from a lateral to medial direction with the Touhy needle [14, 60, 88]. As ONS only covers 85% of the head leaving the forehead uncovered, some have combined it with SONS [15, 89, 90]. Percutaneous ONS is recommended to foresee the results of a permanent implantation [91]. In any case, a temporary external stimulation must be performed before definitive implantation [35]. Those with no positive response are referred to other treatment modalities.

ONS has been used in chronic CH [5, 24–26, 28, 29, 32–35, 40], CM [29, 32, 33], TACs [5], hypnic headache (happening regularly sleep) [92], SUNCT/SUNA [93, 94], and occipital neuralgia [32]. In chronic CH, it reduces the attack incidence in over 50% in 70% of patients [5, 24, 25, 28, 33, 40]. In CM, its average success rate is 65.4% in 67.9–80% of the cases [29, 95]. In SUNCT/SUNA, bilateral ONS induced a 69% pain improvement in 77% of the patients [93, 94]. In idiopathic intracranial hypertension, it has been used to treat the associated headache and the residual headache once the intracranial hypertension is resolved, with higher than 75% pain improvement [89], but it requires bilateral stimulation [89].

AEs plague 33–70% of the cases [24, 25, 29, 33, 96]. Among them are lead erosion [19, 89], local infection [29, 33], electrode emigration [96, 97], lead breakage [28, 30, 33], hardware-related discomfort [98], hardware/stimulation dysfunction [25], and early battery depletion related to high energy consumption [25, 33]. Some technical modifications have been devised to reduce the chance of lead migration [97] that in some series reaches 24% [99]. These include using silicone glue with silicone anchors [100], 2-point anchoring stimulator leads with a tension-relief loop [26], narrow paddle electrodes [101] and to insert the impulse generator as close as possible to the leads (i.e., supraclavicular area) [96]. Unfortunately, solving the AE entails additional surgical procedures in 26–40.7% of the cases [25, 29].

Simultaneous ONS and SONS in CH provide more than 50% pain reduction in over 70% of patients [14]. This dual stimulation has also been successful in HM [15] and TACs [19]. Although the results are promising, the number of cases is too small to draw any statistically significant conclusions.
4.2.3. Great auricular nerve stimulation (GANS)

Pain relief was reported using this technique in a single case of persistent MTHI-Ha 90% [37]. Further studies are needed.

4.2.4. Supraorbital nerve stimulation (SONS)

The first case was reported in 2009 in the treatment of CH [36]. In this disorder, SONS produced more than 50% pain reduction in 71% of the patients [19, 36, 90]. In a series of five patients with TACs, it improved the pain in all of them, but the series is too short to draw any conclusions [19]. It can be used alone or associated with ONS [14, 15, 19, 90].

4.2.5. Cervical spinal cord stimulation (SCS)

The electrode is introduced in the epidural space at the upper thoracic level and advanced to the cervical spinal cord until its distal tip is at the C2 level. One or two electrodes are inserted. The leads are connected to a subcutaneous impulse generator inserted at the infraclavicular area [46].

SCS has been used in CM [46, 47], SUNA [54], CH [45, 64], and MTBI-HA [48], reducing the headache frequency and/or intensity by ≥50% in 71% of the patients [45–47]. In CM, it improves the headache by >30% in 50% of the cases [46, 47, 102]. The AEs are frequent (71%) and usually require system explant and replacement in a second surgery [102]. Among these AEs are infections (13%) and lead rupture or migration (17%) [45–47, 89].

4.2.6. Hypothalamic deep brain stimulation (hDBS)

hDBS was introduced in 2000 to treat drug-resistant CH [61]. It is useful in many types of chronic headache disorders like HC, CH, SUNCT/SUNA, and in TACs [4, 50]. In chronic CH, it results in reduction of ≥50% of the attacks in 60% of the patients [5, 40, 50, 52]. The response rate in HC and SUNA is 82% [49]. In TACs, the improvement rate is >50% in 69.9% of patients [50].

AEs include incision site pain, subcutaneous dislodgement of the impulse generator, transient gaze disturbance (oscillopsia, diplopia), autonomic disturbances, myosis, dizziness, wound infection, cervical dystonia, intracranial haemorrhage, and lead disconnection or rupture [40, 49, 52]. Many of these complications require system explant [49]. hDBS is reserved for those very few cases, in which everything else has failed as death has been reported [50].

The target was initially in the posterior hypothalamus [103, 104], but other areas have also been used like the mesencephalic grey substance, the red nucleus, the fasciculus retroflexus, the dorsal longitudinal fasciculus, the ansa lenticularis, the medial longitudinal fasciculus or the medial thalamus superficialis [104]. In the latest years, the ventral tegmental area is used to decrease the chance of haemorrhages [49, 52].
5. Indications and results for specific chronic headache disorders

5.1. Cluster headache (CH)

CH consists of bouts of unilateral periorbital pain lasting between 15 minutes and 3 hours that follow an annual pattern [105]. It is considered as the most painful headache type, with 0.12% prevalence. About 10% of the cases cannot be controlled with medical treatment [34]. CH has two variants: chronic and episodic [106]. In the episodic, headache periods alternate with others of remission, and the attacks last between 7 days and 1 year with a pain free period lasting at least 1 month [105]. The chronic variant represents 10–15% of the cases [34, 86] and has free pain periods shorter than 1 month or attacks that are present nonstop through at least 1 year [105].

Percutaneous VNS has been used in the acute treatment of the chronic variant of CH with a higher than 50% pain reduction in 40% of the patients [33, 42, 81, 107]. Although not universally effective, it is minimally invasive and with very minor and reversible AEs. Both ONS [25, 26, 34] and SPGS [40–43, 73] are the first options among the invasive techniques [5, 86]. About 70% of patients respond to these treatments with 48% of excellent responders [25, 34]. ONS together with SONS has been applied with >50% pain reduction in 71% of the patients [90]. Cervical SCS has also been used with some success [102]. hDBS should be left as the very last resource as its complications are more severe and potentially life threatening [5, 52].

5.2. Hemicrania continua (HC)

It is a continuous and unilateral headache (it only affects one side of the head), associated autonomic symptoms and episodes of increased headache intensity [105]. Indomethacin is the drug of choice, but some patients do not tolerate it due to side effects like hypertension, gastrointestinal problems (particularly when combined with aspirin), vascular events, or bronchial spasms [83]. In a single case, it was found to respond to noninvasive percutaneous VNS [83]. Others tried repetitive sphenopalatine ganglion block [108]. The data are not statistically significant, and no definite conclusions can be drawn.

5.3. Chronic migraine (CM)

CM is described as having migraine headaches 15 or more days in every month [99]. Worldwide, it is the seventh cause of disability [109]. It affects 2–5% of the adult population [3, 105, 110].

The transcranial stimulation has contradictory results, so no recommendations can be offered [9]. The cervical percutaneous VNS shows promising but moderate results, better in the episodic than in chronic variant [20, 111]. Transcutaneous SONS reduces the number of attacks but not its intensity [18, 111]. Much more efficient is the ONS via implanted electrodes [5, 24, 29, 46], with a success rate of 65.4% in 67.9–80% of the cases [29, 95].
Unfortunately, 70% of the patients suffer AEs, 40.7% of which require a new surgical procedure [29]. Some have combined the ONS with the SONS with ≥50% pain reduction in >70% of the patients [14]. The SCS has also been applied with 30% pain reduction in 50% of the cases [46].

5.4. Hemiplegic migraine

It is a very severe migraine variant, refractory to most known therapies and that often evolves to a very debilitating state. It has been treated with combined SONS and ONS with a 92% average decrease in the number of attacks [15]. The number of cases is limited, so further studies are needed.

5.5. Trigeminal autonomic cephalalgias (TACs)

TAC is a group of headache disorders characterised by unilateral headache accompanied by cranial autonomic symptoms. Although SONS has been attempted [19], ONS is the first option [27], reserving the hDBS to the most recalcitrant cases [49, 50, 52].

5.6. Short-lasting unilateral Neuralgiform headache attacks with autonomic symptoms (SUNA) and short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)

These consist of primary headache attacks associated with cranial autonomic dysfunction. In refractory cases, bilateral ONS induced a 69% pain improvement in 77% of the patients [93, 94]. Deep brain ventral tegmental area stimulation achieved a 78% headache rate improvement in almost all patients but with frequent AEs that at times required to explant the system [49].

5.7. Mild traumatic head injury-related headache (MTHI-H)

MTHI-H represents about 4% of the chronic headaches [112]. Transcranial magnetic stimulation has shown a 57% improvement in the intensity and frequency in this disorder [11–13]. SCS or GANS [37] stimulation has been used, stimulating the left prefrontal cortex [11]. In both cases, there was a 90% headache frequency reduction. Unfortunately, only two case reports exist, and no conclusions can be drawn.

6. Availability and usefulness of ambulatory techniques that can be practiced at home

All noninvasive procedures can be safely practiced at home. Their only drawback is low effectiveness, but they induce no harm in those in whom no beneficial results are obtained. Further studies are necessary. The AEs are minor and completely reversible once the device is no longer used. The biggest problem may arise from the economical point of view, as health providers could choose not to pay for treatments that show moderate response.
7. Conclusions

Although the immense majority of chronic headache disorders can be controlled with pharmacological means, there is a subset of patients that are refractory to all of them. A thorough diagnosis of the specific headache subtype is essential to provide an effective treatment. For those few refractory patients to the current available drugs, there are other treatment possibilities. We have now a wide array of noninvasive techniques that can be tried as a first attempt. In case of failure, surgically implanted stimulating systems can be of help. We should choose the more suitable option to the specific headache variant, keeping in mind the effectiveness possible incidence of AEs of each treatment. hDBS should be considered the very last resource, as it is associated with some serious AEs and potentially to death.

Appendices and nomenclatures

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE</td>
<td>Adverse event</td>
</tr>
<tr>
<td>CH</td>
<td>Cluster headache</td>
</tr>
<tr>
<td>CM</td>
<td>Chronic migraine</td>
</tr>
<tr>
<td>GANS</td>
<td>Great auricular nerve stimulation</td>
</tr>
<tr>
<td>HC</td>
<td>Hemicrania continua</td>
</tr>
<tr>
<td>hDBS</td>
<td>Hypothalamic deep brain stimulation</td>
</tr>
<tr>
<td>HM</td>
<td>Hemiplegic migraine</td>
</tr>
<tr>
<td>MTHI-H</td>
<td>Mild traumatic head injury-related headache</td>
</tr>
<tr>
<td>ONS</td>
<td>Occipital nerve stimulation</td>
</tr>
<tr>
<td>SCS</td>
<td>Spinal cord stimulation</td>
</tr>
<tr>
<td>SONS</td>
<td>Supraorbital nerve stimulation</td>
</tr>
<tr>
<td>SPGS</td>
<td>Sphenopalatine ganglion stimulation</td>
</tr>
<tr>
<td>SUNA</td>
<td>Short-lasting unilateral neuralgiform headache attacks with autonomic symptoms</td>
</tr>
<tr>
<td>SUNCT</td>
<td>Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing</td>
</tr>
<tr>
<td>TACs</td>
<td>Trigeminal autonomic cephalagias</td>
</tr>
<tr>
<td>TMS</td>
<td>Transcranial magnetic stimulation</td>
</tr>
<tr>
<td>tSNS</td>
<td>Noninvasive transcutaneous supraorbital neurostimulation</td>
</tr>
<tr>
<td>VNS</td>
<td>Vagus nerve stimulation</td>
</tr>
</tbody>
</table>
Author details

Vicente Vanaclocha-Vanaclocha*, Nieves Sáiz-Sapena, José María Ortiz-Criado and Leyre Vanaclocha

*Address all correspondence to: vvanaclo@hotmail.com

1 Department of Neurosurgery, Hospital General Universitario Valencia, Spain
2 Hospital 9 de Octubre, Valencia, Spain
3 Anatomy, Universidad Católica San Vicente Mártir, Valencia, Spain
4 Medical School, University College London, London, United Kingdom

References


[28] Bermejo PE, Torres CV, Sola RG. Occipital nerve stimulation for refractory chronic migraine. Revista de Neurologia. 2015 Jun 1;60(11):509-516


[70] Zardouz S, Shi L, Leung A. A feasible repetitive transcranial magnetic stimulation clinical protocol in migraine prevention. SAGE Open Medical Case Report. 2016;4 20503 13X16675257


