Increasing Collaboration between Headache Medicine and Plastic Surgery in the Surgical Management of Chronic Headache

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Introduction: Chronic headache is one of the most disabling conditions afflicting humankind. The management of chronic headaches has, to date, been only partially successful. The goal of this paper is to highlight the importance of collaboration between surgeons and headache physicians in treating this condition.
Methods: We present a narrative review of migraine pathophysiology, its medical and surgical treatment options, and the important role of collaboration between headache physicians and surgeons.
Results: Migraine headaches can be treated with both medication-based regimens and surgery. Novel medications such monoclonal antibodies directed at the CGRP molecule or its receptor have recently been FDA approved as an effective treatment modality in chronic migraines. However, these medications are associated with a high cost, and there is a paucity in data regarding effectiveness compared to other treatment modalities. The pathophysiology of headache likely exists along a spectrum with peripheral — extracranial and meningeal — factors at one end and central — brain — factors at the other, with anatomic and physiologic connections between both ends. Recent evidence has clearly shown that surgical decompression of extracranial nerves improves headache outcomes. However, appropriate patient selection and preoperative diagnosis are of paramount importance to achieve excellent outcomes.
Conclusions: Surgeons and headache physicians who are interested in providing treatment for patients with chronic headache should strive to form a close collaboration with each other in order to provide the optimal plan for migraine/headache patients. *(Plast Reconstr Surg Glob Open 2022;10:e4479; doi: 10.1097/GOX.0000000000004479; Published online 24 August 2022.)*

INTRODUCTION: HEADACHE PREVALENCE, DISABILITY, AND COST

Chronic headache is one of the most disabling conditions afflicting humankind.[1] The International Classification of Headache Disorder (ICHD)[2] lists the diagnostic criteria for the two most common causes of chronic headache, namely, chronic migraine (CM), which affects approximately 1%–2% of the population,[3] and chronic tension-type headache (CTTH), which affects about 2%–3% of the population.[4] Of these two headache types, CM[5] is usually considered to be the more disabling, due to the greater severity of pain typically encountered, as well as the presence of associated symptoms, including photophobia, phonophobia, and nausea. However, CTTH, while less intense in severity, can also be very problematic at the society level, as it is more common than CM,[6] and may also pose significant disability due to the unrelenting nature of pain, even in the absence of associated symptoms. Additionally, it is common for CTTH and CM to exist simultaneously. The management of chronic

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headaches has, to date, been only partially successful. There is a wide array of both medical and surgical treatment options available for this condition, which highlights the importance of collaboration between headache physicians and surgeons to provide our patients with the highest standard of care.

For many years, the mainstay treatment regimen consisted of medications such as antidepressant and anticonvulsants, which are directed at the stabilization of neuronal membranes. These medications, which are still widely used today, have not been found to be highly effective, and their use is often abandoned.[7] Botulinum toxin was found to be effective in the prevention of CM,[8] and entered into the treatment armamentarium in the United States in 2010. More recently, a new and widely heralded class of medications for migraine prevention, monoclonal antibodies (mabs) directed at calcitonin gene-related peptide (CGRP), a protein that plays an important role in inflammation and pain processing, entered the market in 2018. The introduction of the CGRP mabs was quickly followed in 2019 by FDA approval of another class of agents that block the action of CGRP, this second class being a smaller molecule called "gepants." Gepants (ubrogepant and rimegepant) were initially approved for acute treatment of migraine, and rimegepant and another gepant, atogepant, have also subsequently earned FDA approval for preventive use. The CGRP mabs on average provide about 2–3 fewer headache days per month compared with placebo, a figure which is very similar to that of the botulinum toxin studies; the price for the CGRP mabs and for Botox is also similar, at a monthly cost of approximately $600. The preventive use of rimegepant and atogepant provided on average 1–1.7 fewer day of headache per month compared with placebo,[9] at a monthly wholesale cost of approximately $1000–$1800.[10] There is, therefore, clearly significant cost associated with the use of preventive medications for CM, a condition which by its very name speaks to the long duration of the condition. Neither botulinum toxin nor the CGRP mabs nor the gepants have been studied or approved by the FDA for the treatment of CTTH.

The overall effect of these expensive treatment options with respect to headache disability and the economic expense of chronic headache is, as yet, unclear. FDA approval of botulinum toxin for the treatment of CM in 2010 did not seem to significantly alter global levels of disability due to headache, according to the Global Burden of Disease (GBD) study published in 2016.[1] According to this global study, headache continues to be the second most disabling condition globally for those under the age of 25, and in the top five disabling conditions for those aged 25–50. According to the 2017 publication of Global Burden of Disease,[1] CM and CTTH were the first and second most disabling neurological conditions, respectively, in Western Europe and the United States, despite widespread access to botulinum toxin.[11] It remains to be seen if medications directed at blocking the effect of CGRP will have more of an effect on disability; the effect on cost will likely not be to reduce the cost of headache management significantly.

Takeaways

Question: How important is the collaboration between headache medicine physicians and plastic surgeons?

Findings: Chronic headaches have complex pathophysiology, and for some patients with chronic headache, surgical treatment is a necessary component of pain reduction. It is important for headache medicine specialists and surgeons to work together to identify patients for whom surgical treatment is appropriate.

Meaning: Collaboration between headache medicine physicians and plastic surgeons in the surgical treatment of chronic headache ensures the best outcome for patients by optimizing patient selection for surgical treatments, advancing knowledge regarding pathophysiology of chronic headache, establishing a common nomenclature, and providing optimal patient care.

Underlying the complexity of the management of chronic headache is the even more intricate pathophysiology, which is simultaneously accepted to be both multifactorial and poorly understood. One of the most common yet most challenging clinical situations encountered in the tertiary Headache Medicine clinic is the patient with unremitting head and neck pain (UHNP).

HEADACHE PATHOPHYSIOLOGY

Unremitting Head and Neck Pain and Occipital Nerve Compression

UHNP can accompany CH and CTTH.[12] In some patients with UHNP, a mechanical etiology in the neck is suggested by the constant presence of neck pain, as well as tenderness to palpation of soft tissue in the upper neck and occiput, and aggravation of pain by provocative maneuvers, including prolonged neck flexion or head turn. A possible mechanical cause of UHNP is congenital compression of the occipital nerves (ONs). Compression of the ONs in the posterior cervical musculature has been described in numerous cadaver series,[13–17] and placement of ONs within cervical muscles seems to be a common embryologic anomaly, even in the absence of headache.[18] It is unknown why nerve compression may lead to pain in some individuals but not all. An analogous situation exists with classical trigeminal neuralgia; while vascular compression of the trigeminal nerve is reported in asymptomatic individuals,[19] it also widely accepted as an etiology of trigeminal neuralgia, and trigeminal nerve decompression is widely accepted as an effective treatment.[20] Moreover, recent evidence demonstrated a high correlation between patients with head and neck nerve compression syndromes (such as ON compression) and other nerve compression syndromes such as carpal tunnel syndrome.[21]

Compression of ONs by other tissues, including vasculature,[13] lipoma,[22] and reactive lymph nodes,[23] has also been described, and if ONs are surgically decompressed, flattened ONs and fibrotic and inflamed fascial tissues are

often noted.[24,25] Embryologic placement of muscle fibers within the nerve is an example of one of the many anomalies of ONs encountered. Inflammatory tissue is usually observed around compressed nerves, potentially further contributing to nerve compression. Inflammation associated with nerve compression is associated with periosteal changes as well, as was reported in 2016,[26] with the finding that individuals with UHNP and ON compression had a significant increase in proinflammatory markers in the periosteum compared with nonheadache controls.[24] This finding was the first evidence of extracranial pathology in chronic occipital headache.

As with compression of nerves throughout the body, such as the median nerve in a crowded carpal tunnel, or of the spinal nerve roots by an extruded disc, pain may be present solely at the site of compression or may radiate distally along the pathway of the nerve. Accordingly, individuals with ON compression may experience pain solely in the posterior neck, subocciput, and occiput, or radiate retroorbital or up the posterior head to the vertex, in the distribution of the greater ONs, or to the temples, in the distribution of the lesser ONs. As also seen with other types of nerve compression, pain may be aggravated by provocative maneuvers of the surrounding tissue, in this case the neck.[27] This clinical presentation may meet the ICHD criteria for cervicogenic headache,[2] with ON compression serving in the role of the required "lesion" in the soft tissue of the neck.

UHNP does not always indicate the presence of nerve compression. Other causes of UHNP include hemicrania continua, medication overuse headache, and CM that is purely central in origin. The possible presence of these conditions should be carefully assessed by a provider with training in headache medicine before arriving at a diagnosis of nerve compression.

MIGRAINE PATHOPHYSIOLOGY: THE POSSIBLE ROLE OF ON COMPRESSION IN THE GENERATION OF CHRONIC MIGRAINE

Over a decade ago, Oleson et al[28] stated in *Lancet Neurology* that "despite the attention paid recently to the role of central sensitization in migraine pathophysiology, in our view, neuronal hyperexcitability depends on activation of peripheral nociceptors." The source of the proposed activated peripheral nociceptors that may cause neuronal hyperexcitability has not been definitively identified to date, although it has been hypothesized that anatomic compression of ONs in the neck may provide the necessary peripheral nociceptive activation that may lead to central sensitization. This is similar to the "double crush hypothesis," which theorizes that mechanical impingement as well as systematic nerve neuropathies, such as diabetic neuropathy, can prime nerve axons to be more susceptible to dysfunction when compressed by nearby structures.[29–31]

This hypothesis aligns with several observations about CM. First, the persistent, anatomic mechanical compression of a peripheral nerve is likely to result in persistent, unremitting pain of the sort that has been noted in two large, epidemiological studies of migraine. Persistent CM in extended follow-up was present in 33.9% of subjects with CM in the American Migraine Prevalence and Prevention Study,[32] and in 26.6% of subjects with CM in the Chronic Migraine Epidemiology and Outcome Study.[32] Thus, a large minority of patients with CM have persistent, unremitting pain that may be due to a constant, mechanical activation of peripheral nociceptors. Second, circumstantial evidence for the possible role of a mechanical factor in the soft tissue of the neck in escalating migraine frequency may be reflected in the high frequency of neck pain in the population of individuals with EM,[33] particularly in those who progress to CM.[34] Third, the association of ineffective acute treatments, which is more likely to occur with anatomic compression of a nerve, with the progression from EM to CM.[35] Fourth, the observed poor efficacy of treatments directed at stabilizing neuronal membranes in patients with CM.[36] Additional supporting information for this theory includes the observations that (1) head pain due to ON compression can meet ICHD criteria for CM, and (2) CM can resolve after ON decompression.

The pain experienced by patients with suspected ON compression is often not limited to the neck or the proximal radiation of the ONs. Occipital pain often refers to frontal locations in the head, including the forehead, retro-orbital, and temple regions.[12] Interestingly, such frontal radiation of pain was also included as criterion in the 2000 Sjaastad and Fredriksen criteria for cervicogenic headache,[37] which required pain radiating to the frontotemporal region. The reason why pain that originates in the occiput should spread frontally is not entirely clear, although it is likely that this occurs either via the trigeminal cervical complex (TCC) or through extracranial–intracranial connections. The TCC, a caudal extension of the trigeminal nucleus caudalis, plays a primary pathophysiologic role in pain in migraine.[38] Afferent projections from the trigeminal nerve, conveying nociceptive inputs from the meninges and cerebral vasculature, converge in the TCC along with afferent signals from C1-2 innervated structures, including skin and musculature[39]; it has been previously proposed that occipital pain in CM may represent referred pain from the TCC. Pathways from the TCC ascend to a number of nuclei in the brainstem, diencephalon, and basal ganglia,[40] which, in turn, project to a variety of cortical areas that are involved in the sensory and emotional aspects of headache, including photophobia, phonophobia, and emotional and cognitive symptoms of migraine.[41] The involvement of the trigeminovascular pathway in migraine pathophysiology is a likely explanation for pain location in the eye and the periorbital area,[41] and this primary pain location is one of the most prominent distinguishing factors between pain from ON compression in which the predominant pain location is typically neck and occipital, and that of migraine, in which the predominant pain is usually frontal. An additional potential mechanism by which pain that originates extracranially may refer to trigeminal-innervated areas of the head involves possible anatomic connections in the extracranial space between the ONs and extracranial extensions of trigeminal branches, which exit through calvarial suture lines to reach extracranial tissues

including periosteum, as described by Kosaras et al[42] in 2009. Such extracranial–intracranial connections may lead to increased trigeminal nociceptive activation in the meninges.

Both proposed mechanisms provide a means by which trigeminal afferents, either intracranially or extracranially, may lead to the central neuronal hyperexcitability that causes photophobia, phonophobia, and nausea. The fact that extracranial factors may be causative of CM[43] additionally aligns with the growing role of peripherally directed treatments including botulinum toxin and monoclonal antibodies directed at the action of CGRP. In patients in whom extracranial factors may be prominent in the development of CM, it similarly seems reasonable that reduction of nociceptive inputs by elimination of pressure on the extracranial nerves would result in reduced activation of ascending pathways from the TCC. Blake and Burstein[12] proposed that headache pathophysiology may exist along a continuum, with peripheral, extracranial factors at one end of a spectrum, and central, brain factors at the other. The spectrum pertains to both the clinical presentation as well as to nerve anatomy. Headache due solely to nerve compression would be at the peripheral end of the spectrum, presenting as a constant, tight occipital pain that meets criteria for CTTH, while at the other, central, end of the spectrum, low-frequency episodic migraine with aura would be located. Many patients would reside somewhere on the middle of the spectrum, with both peripheral and central elements. The further to the peripheral end of the spectrum, we theorize, the more likely it is that nerve decompression would provide benefit.

ON DEACTIVATION SURGERY

The earliest report of ON deactivation surgery (ONDS; alternately referred to as "neurolysis") utilizing local anesthesia in a series of 58 patients was reported in *Headache* in 1992.[18] The authors reported that 1 year after surgery, 28 of the 50 patients had continued reduction in pain and "felt that they had benefitted from the operation." A second study from another group published in *Headache* in 1996[44] also showed reduction in headache following 72% of operations at mean follow-up of 28 months. Reports of headache reduction have subsequently appeared in the plastic surgery literature[45–47] and in headache medicine literature.[48]

THE PROCESS OF ONDS

Step 1: Patient Selection

The experience of the authors is that ONDS can provide significant relief for a subset of individuals with UHNP. As with the management of all other medical conditions, correct patient selection is the first critical step for successful treatment. The diagnosis of ON compression as the suspected cause of UHNP is made based on the history and physical examination and requires a careful assessment by a knowledgeable clinician. Additional diagnostic modalities, such as nerve blocks and Botox injections, are useful adjuncts to help identify trigger sites/areas of nerve compression.[49,50] The clinician not only must be able to identify the symptoms that suggest that ON compression is present, but must also be able to rule out as much as possible the role of other causative factors.

Step 2: Nerve Deactivation Surgery

After induction with general anesthesia and with the patient in prone position, a posterior midline occipital incision is preformed, and tissue is dissected down to the midline raphe. A six-point decompression of the greater occipital nerve (GON) is performed.[51,52] This involves identifying and releasing the nerve from the oblique capitus, rectangular segmental resection of the semispinalis muscle between the median raphe and the GON, triangular partial resection of the semispinalis muscle lateral to the GON, and release of the trapezial tunnel. Moreover, due to the close proximity of the occipital artery to the GON, an exploration and identification of the occipital artery is then performed, and branches are ligated or resected to free the nerve from any adjacent vessels.[16] If the third occipital nerve is encountered, it is decompressed. However, previous studies have shown that third occipital nerve decompression does not improve migraine outcomes, and therefore, it is not addressed if not easily encountered during the dissection.[53] Inferiorly based three-sided subcutaneous flaps are transposed and used to shield the decompressed GON to help prevent impingement, much like in ulnar nerve subcutaneous transposition.[54] The skin is then closed in multiple layers over a surgical drain. (**see Video** [online], narrated step-by-step greater occipital nerve deactivation surgery.)

The lesser occipital nerve's (LON) anatomical location is more variable than the GON. It is usually located more caudal and lateral to the GON. Given the anatomical inconsistency of the LON, a separate incision is often required for adequate exposure. Patients are often asked to identify the point of maximum pain preoperatively. A longitudinal or transverse incision is preformed over this area, and the LON is identified deep to the trapezius fascia. The nerve is deactivated, and any adjacent vessels are cauterized or ligated.

Step 3: Postoperative Management

The objectives of close and frequent postoperative management include the following: the monitoring of the reduction in preoperative headaches; the management of typical postoperative symptoms, including numbness, paresthesia, and sometimes cervical muscle spasm; the management of the introduction of physical activities that will engage the cervical muscles for patients who undergo ON deactivation; the monitoring and treatment of any other comorbid headache disorders such as migraines; the management of the return-to-work period; the taper of analgesic and preventive medications that have been used for nerve compression headaches as pain levels reduce; and importantly, education regarding the triggers for and management of flares of pain that may occur, even in the setting of overall favorable response to surgery. In our experience, manageable flares of pain may occur even years after surgery, usually

predictably triggered by either excessive engagement of cervical muscles or emotional factors. We, therefore, continue to see postoperative patients regularly, even if only annually, to continue patient monitoring. Finally, there is a more unusual but often puzzling circumstance that we consider "the unexpected effects of headache reduction," meaning the challenges of adapting to a pain-free life. This circumstance may be unexpectedly difficult for a patient whose life has been structured around the condition of chronic pain, and which also requires education and management, typically in the form of supportive psychotherapy.

COLLABORATIVE ROLE OF HEADACHE MEDICINE AND PLASTIC SURGERY

It is clear in the preceding passages that the management of patients with ON compression is a complex, multidisciplinary effort that requires close collaboration of headache medicine, plastic surgery, psychology, and physical therapy. Headache medicine practitioners should conduct the initial assessment to rule in or out other headache conditions and to identify and treat comorbid conditions. The development of a therapeutic alliance with the patient is a particularly important step, as the process of surgery and the postoperative management of pain can be lengthy and stressful. The communication of the suspected extracranial nerve pathology by the headache medicine practitioner to the plastic surgeon is critical, and an approach to surgery should be planned and agreed upon by both physicians. If a patient is seen first in plastic surgery, the surgeon should refer the patient to the headache medicine specialist for an evaluation before deeming the patient to be a surgical candidate. It is also important and very useful for the two physicians to have a shared language and presentation of concepts to the patient, particularly in a still-emerging field such as nerve deactivation surgery.

Practitioners of headache medicine have embraced the role of nerve deactivation surgery with varying levels of enthusiasm. There are several reasons for this, including (1) the fairly recent proposed mechanism of extracranial factors in chronic headache, which is firmly at odds with the long-held, and often still prevailing, concept that extracranial factors (such as nerve compression) do not have a role in CM; (2) lack of understanding of the anatomy of nerve compression and also of the anatomic connection between the extracranial and intracranial spaces; and (3) the robust presence of the pharmaceutical and device industries in headache medicine—industries that exist in opposition to the elimination of a pain-causing condition. Finally, doubts that headache medicine specialists may have about the role of a surgical treatment can be reinforced by a belief, correct or not, that plastic surgeons are singlehandedly attempting to treat a condition without adequate understanding of pathophysiology. Fortunately, these factors can all be addressed with enhanced collaboration between the subspecialties, as recommended below. The authors have each benefitted from close collaboration with experienced specialists in the complementary fields for many years and

have learned that such collaboration results not only in improved clinical outcomes but also in enhanced professional satisfaction.

Finally, a name for the procedure should be settled. For many years, the term "migraine surgery" was used, before the fuller understanding of the complex anatomy of extracranial and intracranial factors in headache. There are limitations with the term "migraine surgery," as not all patients with nerve compression meet the ICHD criteria for migraine, and many individuals with migraine are not candidates for surgery. For these reasons, we recommend that a broader and more general term such as nerve deactivation surgery for headache should be adopted for the use of this valuable treatment for the common, disabling, and costly condition of chronic headache.

RECOMMENDATIONS

- We recommend that physicians who are interested in providing this treatment for patients with nerve compression headache strive to form a close collaboration with a complementary physician. Identification of such physicians can usually be made through a subspecialty organization such as the Migraine Surgery Society or the American Headache Society. Additionally, the authors are available to assist with identification and education of such complementary physicians.
- Multidisciplinary programs should be developed to address all the critical areas of management that have been introduced above. The interested reader is referred to the textbook *The Surgical Treatment of Headache and Migraine* for a more comprehensive consideration of the important topics.
- A standard for Centers of Excellence for Headache Surgery should be reached and such centers established and certified by the appropriate body.
- We recommend that the surgical procedure be referred to as nerve deactivation surgery for headache.

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