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SECONDARY HEADACHE (M ROBBINS, SECTION EDITOR)

Myofascial Head Pain

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Abstract Muscle nociception is mainly characterized by local tenderness and referred pain. The neurophysiological basis of muscle pain supports a role of sensitization mechanisms. From a clinical viewpoint, muscle pain is represented by the presence of myofascial trigger points (TrPs). Evidence suggests that TrPs are able to start a peripheral nociceptive mechanism and hence contributing to changes in the central nervous system. Several studies demonstrated that the referred pain elicited by TrPs reproduces the headache pattern in patients with tension-type headache (TTH), migraine, cervicogenic headache and, in some individuals, with cluster headache. In fact, sensitization of nociceptive pain pathways in the central nervous system due to prolonged nociceptive stimuli from TrPs seems to be responsible for the conversion of episodic to chronic TTH. In other headaches, TrPs may be able to stimulate the trigeminal nucleus caudalis and hence triggering a migraine or cluster headache attack. Proper treatment directed towards TrP inactivation has documented positive effects in individuals with these headaches; however, longitudinal studies are needed to further determine the role of TrPs in head pain.

Keywords Muscle pain · Trigger points · Referred pain · Migraine · Tension-type headache

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Introduction

In the twenty-first century, the percentage of the adult population suffering from headache is around 46 % in general, with 11 % experiencing migraine, 42 % tension-type headache and 3 % chronic daily headache [1]. Scientific interest in the pathogenesis and aetiology of headache has increased in the last decades. The current review article provides an overview of the role of muscle pain and how referred pain from myofascial trigger points in the posterior cervical, head and shoulder muscles can be the source of head pain by contributing to the development and/or maintenance of sensitization mechanisms in some headaches such as tension-type or migraine.

Muscle Referred Pain to the Head

Muscle Pain: Sensitization Mechanisms

Muscle pain is caused by the excitation of muscle nociceptors, i.e. free nerve endings responding to mechanical, thermal or chemical stimuli, as well as to direct stimulation by algogenic substances. Particularly, effective stimulants for muscle nociceptors are substance P, glutamate, bradykinin or serotonin [2, 3]. Other endogenous algogenic substances which are released with nociceptors excitation are serotonin, histamine or prostaglandins. The release of these substances causes antidromic release of other neuropeptides, i.e. calcitonin gene-

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related peptide, or neurokinin A from nerve endings [4]. Under normal circumstances, the threshold for triggering nociceptive signals is high, so that a pain response is triggered by stimuli that are potentially or actually damaging to body tissues. However, the algogenic substances mentioned earlier acts as sensitizing agents that increase the excitability of muscle nociceptors. As a result, low-intensity stimuli that are normally not perceived as painful can trigger an electrical signal resulting in muscle deep and aching pain.

If the input from muscle nociceptors is long lasting, this can lead to changes in the central nervous system. It seems that sensitization of the central nervous system is induced by prolonged nociceptive inputs from the peripheral structures. In fact, nociceptive inputs from deep tissues, i.e. muscles or joints, are more effective in inducing prolonged changes in the behaviour of dorsal horn neurons than nociceptive inputs from superficial tissues, i.e. skin [5]. During this sensitization process, dorsal horn neurons become hyper-excitable in response to noxious stimulation. Nociceptive stimuli will arrive to specific receptive field generating new receptive fields at a distance from the original within minutes, and therefore, referred pain will be developed.

Referred Pain to the Head: Sensitization of the Trigemino-Cervical Nucleus Caudalis

One of the most relevant phenomenons that are thought to have an important role in the development of head pain is the referral of muscle pain. In fact, referred muscle pain can be perceived in any region of the body, but the size of the pain area is highly variable and is influenced by pain-induced changes in central somatosensory maps [6]. Several theories have been proposed for explaining muscle referred pain [7, 8]. The most recent theories suggest that referred pain occurs at the dorsal horn level resulting from activation of otherwise quiescent axonal connections between affective nerve fibres and dorsal horn neurons activated by different mechanisms of sensitization [7, 8]. In fact, muscle referred pain appears in seconds following stimulation of the affected tissue suggesting that the induction of neuroplastic changes related to referred pain is a rapid process.

In the context of headache, it is important to note that second dorsal horn neurons are integrated into the trigemino-cervical nucleus caudalis, i.e. the convergence of trigeminal and cervical afferents onto neurons in the brainstem [9]. There is clinical and scientific evidence on cervical to trigeminal and trigeminal to cervical sensitization. A study provided evidence for a bi-directional effects reflecting convergence of muscle afferents from the trigeminal and upper cervical neural systems supporting this hypothesis [10]. Therefore, referred pain from any structure receiving nociceptive information on the trigemino-cervical nucleus caudalis can refer pain to the head.

Myofascial Trigger Points

Definition

Muscle referred pain is clinically expressed as myofascial trigger points (TrPs). The most commonly accepted definition states that a TrP is a hypersensitive spot within a taut band of a skeletal muscle that is painful on mechanical stimulation and causes a referred pain that is perceived distant from the spot [11]. From a clinical point of view, we distinguish active and latent TrPs. Active TrPs are those in which local and referred pain reproduce sensory or motor symptoms reported by the patient, and the pain is recognized by the patient as a usual or familiar pain. Latent TrPs are those in which local and referred pain do not reproduce any symptom familiar or usual for the individual [11]. For instance, in a patient with headache, the referred pain evoked by active TrPs should reproduce, at least, part of the pain pattern that they experience during their headache attacks. Both types of TrPs exhibit similar physical findings on examination. The difference is that latent TrPs do not reproduce spontaneous sensory symptoms. Nevertheless, both active and latent TrPs provoke motor dysfunctions, e.g. weakness, inhibition, increased motor irritability, muscle imbalance and altered motor recruitment [12•, 13•].

TrP diagnosis is mainly based on clinical manual examination and requires adequate manual skills, training and clinical practice to develop a high degree of reliability. There are some signs and symptoms that may be used for TrP diagnosis: (a) presence of a palpable taut band in a skeletal muscle when accessible to palpation; (b) presence of a hypersensitive spot in the taut band; (c) palpable local twitch response on snapping palpation (or needling) of the spot and (d) referred pain elicited by stimulation or palpation of the hyperirritable spot [11].

Trigger Points and Sensitization of Central Pathways

One question that has increased the interesting in the etiologic role of muscle tissues in headaches is as follows: assuming that the liberation of endogenous algogenic substances provokes the sensitization of nociceptors and the resulting processes that lead to central sensitization, which mechanisms cause the liberation of the algogenic substances? The current section will briefly discuss current evidence suggesting a relationship between TrP and these sensitization mechanisms.

At the molecular and biomechanical levels, microdialysis studies have shown that the concentrations of bradykinin, substance P, tumour necrosis factor-α, interleukin-1β, serotonin and norepinephrine were significantly higher near the active TrP [14] and in distant regions [15]. As outlined in the beginning of this article, bradykinin is a potent stimulator of prostaglandin synthesis, and the release of these substances contributes to a decrease in the pain thresholds, promoting the

cycle of peripheral sensitization. A more recent animal rabbit study confirmed the presence of increased concentrations of β-endorphin, substance P, tumour necrosis factor-α, cyclooxygenase-2, hypoxia-inducible factor 1-alpha, inducible nitric oxide synthase and vascular endothelial growth factor in the TrP [16••]. The higher release of algogenic substances and chemical mediators at active TrPs supports the presence of nociceptive hypersensitivity in TrP areas [14, 15, 16••]. There is additional evidence supporting that active TrPs represent focus of peripheral sensitization since they are able to sensitize both nociceptive (C) and non-nociceptive (Aδ) nerve endings [17] and also non-nociceptive myelinated fibres [18].

More importantly, emerging research suggests a physiological link between TrPs and the phenomenon of central sensitization, although the causal relationship and mechanisms are still unclear. It has been found that spinal cord connections of TrPs are more effective in inducing neuroplastic changes in the dorsal horn neuron than non-TrPs [19] and that mechanical stimulation of TrPs provoke pressure hypersensitivity in both segmental-related muscles [20] and extra-segmental [21] tissues by inducing central sensitization. Further, imaging studies have demonstrated that active TrP pain is, at least partially, processed at supra-spinal levels since TrP hyperalgesia is processed in various brain areas as enhanced somatosensory activity was observed in the primary and secondary somatosensory cortex, inferior parietal, mid-insula and limbic system [22].

All these factors could play a relevant role in developing chronification in headaches. For instance, the presence of multiple TrPs (spatial summation) or the presence of active TrP during prolonged periods of time (temporal summation) may sensitize spinal cord and supra-spinal structures by continued nociceptive afferent barrage into the central nervous system.

Trigger Points in Tension-Type Headache

Epidemiological Studies

Current research into the pathogenesis of tension-type headache (TTH) focused on the role of muscles and pain processing impairments [23]. It is becoming increasingly clear that this headache has a muscular origin and that peripheral as well as central nervous system factors play a crucial role in its development and chronification [24•].

There is scarce evidence before 2000 about the association between TrPs and TTH. Marcus et al. reported that patients with TTH had a greater number of either active or latent TrPs than healthy controls; however, this study did not specify in which muscles TrPs were most frequently found [25]. A series of blinded-controlled clinical studies had demonstrated that active TrPs are extremely prevalent in subjects with episodic or chronic TTH. These studies observed that the referred pain elicited by TrPs in the neck/shoulder and head musculature including suboccipital [26], upper trapezius [27], sternocleidomastoid [28] and temporalis [29] muscles and extra-ocular muscles such as the superior oblique [30] and lateral rectus [31] reproduced the headache pattern (i.e. active TrPs) in patients with chronic TTH. In these studies, the referred pain elicited by these muscles was recognized by the patients as their usually headache pain pattern. In fact, in most of the patients, the referred pain elicited by these active TrPs was able to completely reproduce the headache pattern, similarly what has been found in women with fibromyalgia syndrome [32, 33] In addition, the presence of active TrPs in these muscles was associated with headaches of greater intensity, frequency and duration of the headache [26–29] and also to greater pressure hypersensitivity [34]. Given that temporal summation of pain is centrally mediated, a temporal integration of nociceptive signals from active TrPs by central neurons can contribute to sensitization of central pathways seen in chronic TTH.

Additionally, active TrPs in the same musculature have been also reported in episodic TTH as well [35, 36] but less frequently than in the chronic form. This finding was confirmed in another study where active TrPs were more prevalent in patients with chronic TTH than in those with episodic TTH [37]. The presence of active TrPs in patients with episodic TTH would not support the hypothesis that active TrPs are always consequence of central sensitization, since sensitization of the central nervous system is not as common in episodic TTH as it is in chronic TTH [38••].

It is interesting to note that active TrPs are also present in children with TTH. A case series of nine 13-year-old girls with TTH suggested that TrPs play an important role in at least a subgroup of children with TTH [39]. In a posterior blinded-controlled study, we observed that children with chronic TTH exhibited active TrPs in the same muscles than adults such as suboccipital, temporalis, upper trapezius and sternocleidomastoid [40]. In fact, Alonso-Blanco et al. showed that the referred pain elicited from active TrPs shared similar pain patterns as spontaneous headache in adults and children, but slightly differences in TrP prevalence and location of the referred pain areas could be observed between adults and children [41].

Current evidence would suggest a relevant role of TrPs in the pathogenesis of TTH and the relevance of early treatment of active TrPs in this population. In fact, a recent review concluded that TrPs, in combination with other musculoskeletal impairments, inform about TTH pathophysiology, diagnosis and interdisciplinary patient care [42••]. Nevertheless, we should recognize that all these studies have a cross-sectional design, so cause and effect relationships cannot be inferred. Unfortunately, no longitudinal study has currently determined the role of active TrPs in the development or chronification of TTH. Future studies should longitudinally investigate the

development of active TrP during time to further confirm their participation in the aetiology of TTH.

TrPs as Cause of Headache: a Pain Model for Tension-Type Headache

Combining clinical and basic scientific evidence on TTH, a pain model for this headache was formulated [43]. This pain model combined the theoretical peripheral sensitization by active TrPs and central sensitization mechanisms. Accordingly to this model, active TrPs located in muscles innervated by the upper cervical segments (C1–C3) and the trigeminal nerve can be responsible for peripheral nociception. This nociception, if prolonged in time, will represent a continuous afferent barrage to the trigeminal nucleus caudalis, which will sensitize the central nervous system. In predisposed subjects, nociception induced by active TrPs, if prolonged, may lead to sensitization of the central nervous system, which may in turn contribute to the persistence, amplification and spreading pain and the conversion from episodic to chronic TTH. Accordingly to the model proposed by our research group, the referred pain elicited by TrPs would be one of the main causes (but not the only one) of the headache experienced by patients with TTH [43]. Nevertheless, this updated model needs future studies for further confirmation and verification.

Interventional Studies

To determine the potential role of TrPs in the aetiology of TTH, treatment studies should offer an effective treatment of this condition; however, few studies have explored the effects of TrP management in TTH. A pilot study found that a massage programme targeted at inactivating TrPs was effective for reducing headache pain and disability in TTH; however, this study did not include a control group [44]. The same authors have recently conducted the only randomized controlled trial related to TrP management in patients with TTH. This study observed that the application of TrP release massage focused on the cervical musculature was effective for reducing headache frequency; however, these authors also observed a placebo effect [45••]. Another controlled study found that application of positional release manual therapy on active TrPs was effective for reducing the frequency and duration of the headache and medication intake [46]. Nevertheless, it has been proposed that not all patients will respond positively to the same therapy. Two clinical prediction rules tried to identify those women with TTH who most likely would experience short-term favourable outcomes after active TrP manual therapy; however, no control group was again included [47, 48]. The preliminary results for these studies suggest that the presence of active TrP in the neck and shoulder muscles and a lower degree of central sensitization are clinical features of those patients who responded more quickly to manual therapy targeted at inactivating TrPs [47, 48].

Other therapeutic options such as injections or dry needling have been also used for inactivating TrPs in patients with headache. Venâncio et al. found that TrP dry needling was equally effective for decreasing headache and for the use of rescue medication than lidocaine or corticoid injections [49]. These results are similar to those also observed after the application of botulinum toxin A injections over active TrP in individuals with TTH [50, 51]. Nevertheless, a recent systematic review concluded that although the literature suggests that TrP dry needling may be a useful addition to conventional physiotherapy in headaches, further research with a stronger methodological design is required [52••].

Trigger Points in Migraine

Epidemiological Studies

It is clear that migraine headache is related to dysfunctional changes in the brainstem; however, peripheral nociceptive inputs from active TrP may act as a migraine trigger in many patients. A link between pain generators of neck, head and shoulder muscles and migraine may be the activation of the trigeminal nerve nucleus caudalis and hence the activation of the trigemino-vascular system. In such instance, TrPs located in any muscle innervated by the trigeminal nerve or the upper cervical nerves may be considered as “irritative thorns” that can precipitate, perpetuate or aggravate migraine attacks. Obviously, other triggers also exist for migraine.

TrPs have been also found in individuals with migraine. Again, some studies showed that patients with migraine exhibited active TrPs in the same musculature than TTH including the upper trapezius, sternocleidomastoid, temporalis and ocular superior oblique muscles [53, 54]. In fact, active TrPs were located only ipsi-lateral to migraine attacks as compared to the non-symptomatic side. Another study of 92 individual with bilateral migraine showed that 94 % exhibited TrPs in the temporalis and suboccipital muscles [55]. Further, the number of TrPs was related to the frequency of migraine and the duration of the disease [55]. An important topic is that the referred pain from active TrPs reproduced the pain features of migraine attacks, although patients were headache free when examined, supporting that neck muscles can be a potential trigger factor. A more recent study confirmed the presence of active TrPs in patients with episodic migraine in the upper trapezius and sternocleidomastoid muscles [56].

Nevertheless, unlike in TTH, it is more conceivable that active TrPs are a potential trigger factor precipitating migraine attacks in some patients, rather than a causative factor of the headache.

Interventional Studies

Similarly than with TTH, evidence supporting a potential role of TrPs in migraine comes from the resolution of migraine by treating TrPs with lidocaine injections [57, 58]. In addition, inactivation of active TrPs in migraine patients not only reduced the electrical pain thresholds in the head but also reduced the number of migraine attacks [59]. Finally, the same group also reported that TrP injection with ropivacaine (10 mg) was effective for reducing the frequency and intensity of migraine [60].

Trigger Points in Other Headaches

Although TTH and migraine represent the headaches where active TrPs probably are more prevalent, TrPs have been also observed in cervicogenic and cluster headaches. An old study found in a small cohort of 11 patients with cervicogenic headache that all patients showed at least three TrPs on the symptomatic side, especially in the sternocleidomastoid and temporalis muscles [61]. Further, patients who were treated exhibited significant decreases in their headache frequency and intensity, which supports the role of TrPs in pain perception in this headache. Roth et al. described a case report where TrPs from the sternocleidomastoid muscle mimicked this headache [62]. A recent study has shown that manual treatment of active TrPs is effective for the management of cervicogenic headache [63•]. However, it is possible that not all patients with this headache exhibit TrPs, and they may represent a specific subgroup.

Finally, only one study reported the presence of active TrPs in patients with cluster headache [64]. All patients showed active TrPs reproducing their headache. In this case series, TrP injections were effective in approximately 80 % of the individuals. The authors suggested that, in some patients, TrPs may also trigger cluster headaches [64].

Conclusion

Current evidence clearly shows that muscle referred pain elicited by TrPs can play a relevant role in headaches, particularly TTH and migraine. Most of the studies have a transversal design, so cause and effect relationships should not be inferred. Therapeutic strategies targeting active TrPs have reported promising results in the management of these headaches, but high quality trials are now required to clarify the etiologic role of muscle referred pain in head pain.

Compliance with Ethics Guidelines

Conflict of Interest César Fernández-de-las-Peñas declares no potential conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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