Trigger point evaluation in migraine patients: an indication of peripheral sensitization linked to migraine predisposition?

E. P. Calandre, J. Hidalgo, J. M. García-Leiva and F. Rico-Villademoros
Instituto de Neurociencias, Universidad de Granada, Granada, Spain

Keywords: central sensitization, migraine, peripheral sensitization, referred pain, trigger points

Although migraine is a neurovascular disorder, both scalp tenderness and referred pain have been observed in migraine patients. The present study was carried out to investigate the presence of trigger points eliciting referred pain in 98 migraine patients and in 32 healthy subjects. Trigger points were found in 92 (93.9%) migraineurs and in nine (29%) controls ($P < 0.0001$). The number of individual migraine trigger points varied from zero to 14 (modal number: 4), and was found to be related to both the frequency of migraine attacks ($P < 0.0001$), and the duration of the disease ($P = 0.017$). About 74% of the total detected trigger points were found in temporal and/or suboccipital areas; other locations were mainly found in patients showing more than four trigger points. Trigger point palpation provoked a migraine attack in 30 (30.6%) patients. Pericraneal allodynia was found in 15 (15.3%) patients. These data indicate that nociceptive peripheral sensitization is a usual finding in migraine, and that central sensitization can develop in patients with frequent attacks and long-lasting disease. Trigger points’ detection in migraine patients could be useful when applying therapies like acupuncture, needling or botulinum toxin injections directed to reduce peripheral sensitization.

Introduction

Migraine is essentially a neurovascular disorder. However, both pericranial muscle tenderness and referred pain have been described during attacks as well as during attack-free periods [1–4], and nociceptive inputs of myofascial origin have been postulated to play a role in migraine pathogenesis [1,5,6]. When dealing with patients with frequent migraine attacks with partial or no response to prophylactic drug therapy, in whom local anaesthetic injections contribute to provide significant amelioration, we observed that the presence of trigger points causing migraine-like pain was a common finding [7]. As most of our patients suffered disabling and long-lasting migraine, we thought that the presence of these trigger points could be the consequence of repetitive migraine attacks leading to persistent sensitization, but the possibility that they reflected a primary hyperexcitability associated to migraine condition could not be ignored without examining people experiencing less severe migraine. Moreover, it seemed important to evaluate whether the prevalence of trigger points eliciting referred pain in subjects with migraine was similar or higher than in healthy subjects.

In view of the above-mentioned statements, the present study was carried out with the following objectives:

1. To compare the frequency of referred pain in migraine patients with that of healthy subjects;
2. To explore and characterize the presence of trigger points in the scalp and neck of migraine patients;
3. To investigate whether the number of trigger points in patients was related with the frequency of the attacks and/or with the duration of the illness.

Subjects and methods

Patients with frequent migraine attacks ($\geq 3$ per month) were recruited amongst those attending our headache clinic for prophylactic drug treatment or trigger points’ infiltrations. Patients with less frequent migraine attacks and controls were found amongst relatives and friends of our patients, as well as amongst employees and students of the school of medicine. Patients were diagnosed by an experienced interviewing physician according to the current criteria of the IHS [8] and had at least 1 year of headache history. The control group was composed of healthy people not suffering from any chronic disease or painful condition, specifically stating that they had never suffered any headache with migraine-like characteristics; however, the inclusion of subjects experiencing infrequent tension-type headache ($<1$ attack per month) was allowed since, as acknowledged by the IHS, this headache subtype has little impact on the individual and does not require medical attention [8]. Both, patients and controls, gave informed consent.
Manual palpation of the scalp was performed by a trained expert in this field to assess the presence of trigger points in absence of a headache attack. Palpation, always bilateral, was carried out with the second and third fingers of each hand by exerting a pressure not more than 4 kg, which is the standard technique to explore the presence of tender and trigger points [9]. The palpation was always carried out in interictal conditions to avoid eventual detection of painful areas due to the sensitization provoked by the acute attack. The explored areas were the following (see Fig. 1 for areas’ location):

1. Medial border of the supraciliar arch, close to the insertion of the medial fibres of the frontal muscle;
2. Medial part of the proximal/anterior fibres of temporal muscle;
3. Medial part of the medium fibres of temporal muscle, close to its insertion surrounding the sagittal suture;
4. Suboccipital area, at the level of the insertion of the thick muscles of the neck;
5. Occipital area, surrounding the emergence of the Arnold’s nerve;
6. Medial area of the superior trapezius in the neck.

The presence of referred pain amongst patients was established taking into consideration the location of those trigger points whose pressure elicited pain with migraineous features which the patient recognized as characteristic of his attacks, i.e. unilateral location, throbbing quality, accompanied with photophobia or phonophobia, etc. The number and location of trigger points in each patient were recorded. The presence of tenderness was not taken into account as this is a very unspecific symptom which can be found in a wide array of musculoskeletal disorders, as well as in healthy people just as a consequence of inadequate postures, bruxism or various noxious stimuli.

Statistical tests employed to analyse the data included the Fisher’s exact test when comparing controls with migraineurs, linear regression to correlate the number of trigger points with the frequency of migraine attacks and the duration of the illness, and the chi-square test, when evaluating the number and location of trigger points. Statistical analysis was performed using GraphPad Prism version 4.00 (GraphPad Software, San Diego, CA, USA: http://www.graphpad.com) for Windows (2004).

Results
The sample was composed by 32 healthy subjects, 18 (56%) of them reporting infrequent tension type headache, and 98 patients with migraine. Demographic data of both groups are shown in Table 1. Migraine sample included eight patients with aura and 90 without aura. Thirty-five patients (35.7%) were diagnosed with chronic migraine according to the current IHS classification. Concomitant diagnoses included fibromyalgia (15 cases, 15.3% of the sample) and temporomandibular dysfunction (10 cases, 10.2% of the sample).

Nine (29%) of the controls reported referred pain of myofascial characteristics, whereas 92 (93.9%) of the migraine patients reported referred pain of migraine-like quality ($P < 0.0001$, Fisher’s exact test). The rest of the six patients without trigger points appertained to the group of infrequent migraine, i.e. those experiencing two or less attacks per month. Thirty-five (40.7%) of the 92 patients reporting migraine-like referred pain experienced also referred pain of myofascial characteristics. In 30 (29.6%) patients, the palpation elicited a full-blown migraine attack which required abortive treatment. Amongst those controls exhibiting referred pain, one showed only one trigger point, two showed two trigger points, one showed three trigger points, three showed four trigger points, and one showed five trigger points. Six of them reported infrequent tension type headache and one temporomandibular dysfunction. The number of trigger points in migraine patients varied markedly, ranging from 0 to 14, with a modal number of 4 which was found in 36 (36.7%) of the patients. As it can be seen in Figs 2 and 3, there was a

<table>
<thead>
<tr>
<th></th>
<th>CRL ($n = 32$)</th>
<th>Migraine ($n = 98$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (female/male)</td>
<td>19/13</td>
<td>79/19</td>
</tr>
<tr>
<td>Age (years)</td>
<td>21–83</td>
<td>15–75*</td>
</tr>
<tr>
<td></td>
<td>41.4 ± 16.8</td>
<td>38.5 ± 13.5</td>
</tr>
<tr>
<td>Illness duration (years)</td>
<td>–</td>
<td>1–55</td>
</tr>
<tr>
<td></td>
<td></td>
<td>21.6 ± 12.9</td>
</tr>
</tbody>
</table>

*: not significant differences between controls and patients. CRL, Control group.
positive relationship between the number of trigger points and the frequency of migraine attacks as well as the duration of the illness.

The location of the trigger points was highly consistent: from a total number of 425 trigger points, 118 (42.6%) were found in temporal areas, 142 (33.4%) were found in suboccipital areas, and 102 (24%) in other areas; the latter included the medial part of the temporal muscle, trapezius, the cervical muscles at C2/C3 levels, frontalis, parietalis, masseter, ptérygoïdeus lateralis, digastricus, occipitalis at the level of the emergence of the Arnold’s nerve, and the gábbellal muscles (corrugator cili ii and procerus). Fifty-two (53.1%) of the patients had from 1 to 4 trigger points located in the proximal area of the temporal muscles and/or in the suboccipital area, and 40 (40.8%) patients exhibited alternate or – much more frequent – additional trigger points located in other areas. Thus, we considered trigger points located in anterior temporal and suboccipital areas as typical, as they seemed to be characteristic of migraine, and those trigger points located in other areas of atypical. As it can be seen in Fig. 4, atypical trigger points were mainly found in patients with multiple trigger areas, whereas they were infrequently found in patients with four or fewer trigger points. It is worthy to mention that patients with five or more trigger points showed at least one of them located in typical areas. Fifteen (15.3%) patients also presented an allodynic pain pattern of hyperalgesic areas: all of them experienced chronic migraine, with nine of them suffering also from fibromyalgia, and, with only two exceptions, all of them had their migraine started 20 or more years ago.

Discussion

The percentage of migraine with aura in our sample is lower than usual. This is probably due to the fact that 35 of our patients experienced chronic migraine which, according to the IHS diagnostic criteria, is a complication of migraine without aura. Amongst the remaining 63 patients the percentage of migraine with aura is 12.7, which is much closer to the commonly observed proportion.

Our data show that trigger points are a common finding in patients with migraine and that, in most of the cases, pain exhibits typical migraine features. Referred pain in migraine has been described by several authors. Tfelt-Hansen et al., [10] evaluated 50 migraine patients whilst experiencing an attack and found re-
ferred pain in 75% of the patients, with the major pathways observed from the sternocleidomastoid to temporofrontal area and occiput, and from occiput to temporofrontal area and vertex. Lous and Olesen [1] described referred pain in 29 of 38 (76%) patients experiencing migraine, tension-type headache or both, the most common pathway being from sternocleidomastoid to temporofrontal area and occiput, and from anterior temporal muscle to brow. Hesse et al. [11], investigating the efficacy of dry needling in the prophylactic management of migraine, reported that they needed trigger and tender points, but they did not specify any criteria for distinguishing between both. Referred pain in primary headaches has also been described as associated to muscles temporalis, trapezius, splenius capitis and sternocleidomastoid, although not specifically linked with migraine diagnosis [12]. None of these authors, however, specified the quality of referred pain. It is frequently assumed that the characteristics of referred pain are always of myofascial type, but this is not necessarily the case. In fact, it has been recently described that pressure on the active trigger points located in the psoas muscle exacerbated the pain of renal colic and their inactivation abolished the pain in most of the patients [13]. Likewise, pain in chronic prostatitis has been postulated to have a myofascial origin [14]. Our results show that, in most of the cases, referred pain in migraine exhibits typical migraine characteristics and in a noticeable percentage of patients, trigger points’ palpation provokes a migraine attack. Given that migraine trigger points as well as migraine attacks after exploration were found both in patients with very frequent attacks as well as in those experiencing sporadic attacks, we think that these data strongly suggest that peripheral sensitization is associated with migraineous condition.

The predominance of the location of trigger points in temporal anterior and suboccipital areas seems coherent, as these – especially the temporal territories – are also the most typical locations of migraine pain as well as amongst the most common areas of referred pain in headache patients [12,15].

Except for the limited data from the above-mentioned authors, referred pain in migraine has been scarcely investigated, whereas tenderness and, more recently, allodynia, have received considerable attention, perhaps because trigger points have almost always been exclusively related with myofascial pain. However, in our opinion, the assessment of migraine trigger points is more important than evaluating just tenderness. Head and neck tender points are unspecific and can be found either in subjects with migraine, or tension-type headache, or in the general population [3,4,16,17].

Based on data obtained from animal models with migraine, Malick and Burstein [18] proposed that both peripheral and central sensitization are involved in migraine pain generation. Migraine trigger points which, in our sample, were frequently found even in patients who experienced only sporadic migraine attacks, can be representative of spontaneously hyperactive peripheral nociceptors – or blunt-pressure hyperalgesia – linked to migraine predisposition. Central sensitization in migraine has been related to the development of cutaneous allodynia during attacks [19]. Allodynic patients in the latter study were found to be older and the duration of their illness longer than those of non-allodynic patients. These data agree with our finding that allodynic patients suffered chronic migraine, and had a long-lasting evolution in most of the cases. Interictal multiple trigger points and allodynia seem indicative that a recruitment process both of peripheral and central nociceptors can take place through the years in patients with frequent migraine attacks. The fact that the first locations of trigger points are almost always temporal and suboccipital and spread progressively to other areas in relation to the chronicity of the disease, suggests the existence of a hierarchy in the recruitment of previously silent nociceptors. Both the increase in the number of trigger points and the allodynia observed in patients with more frequent and long-lasting migraine concurs with the expansion in the receptive fields, i.e. the cutaneous area innervated by a single spinal neuron, which has been described in pain modulation, and attributed both to peripheral and central sensitization [20].

The presence of trigger points in migraine patients during headache-free periods can be related to the improvement of migraine observed after dry needling [11], or acupuncture [21]. The latter found that acupuncture especially benefited patients with migraine as compared with patients with other idiopathic headaches, particularly tension-type headache. One explanation for this observation is that inactivation of myofascial migraine trigger points by acupuncture would reduce the excitability of myofascial nociceptors and, as a consequence, contribute to the amelioration of migraine. One of the most recent additions to migraine prophylactic therapies is botulinum toxin type A (BoNT-A). Initially this drug was thought to act by the primary mechanism of action of the toxin, i.e. the inhibition of acetylcholine liberation at the neuromuscular junction. However it has been recently shown that BoNT-A exerts an analgesic effect independent of its action upon acetylcholine, related to the inhibition of peripheral sensitization in nociceptive fibres, and it has been suggested that this last mechanism would be the primary mechanism of action of botulinum toxin in
migraine and other primary headaches [22,23]. Until now, toxinum botulinum injections in migraine have been performed either in fixed sites or in a ‘follow the pain’ manner on tender spots [24,25]. An alternate way of administration would be to identify specific individual trigger points and select them as targets for injection in each patient.

The limitations of our study arise essentially from its observational design. The fact that we worked initially with patients attending a headache clinic implies that a selection bias could not be avoided; to lessen this bias, new patients from the general population, i.e. with less severe migraine, were recruited; but this means that our sample was not randomly collected. However, it must be remembered that we could not, in any case, know a priori if a subject would have detectable trigger points or not. In addition, and most significantly, our study was not blinded. Blinding was difficult, if not impossible, given that one of our primary endpoints was to characterize the quality of referred pain experienced by the patients. Nevertheless, we thought that this lack of blinding would not probably have a major impact on the results, as the key issue was to know whether the pain experienced by patients had migraine features or not, for migraine sufferers easily recognize migraine attacks. In fact, as stated in the Results, almost 41% of our patients reported both migraine pain and pain of myofascial characteristics arising from different trigger points and were able to discriminate them easily.

In conclusion, our data show that temporal and suboccipital trigger points eliciting referred migraine-like pain is a common feature in patients with migraine, suggesting that peripheral nociceptive sensitization is associated with migraine susceptibility. The fact that both the number of trigger points and pericranial cutaneous allodynia are frequently observed in patients with chronic migraine seems indicative that frequent and long-lasting migraine attacks can lead to persistent central sensitization. Trigger points’ detection in patients with migraine could be useful when applying therapeutic measures directed to reduce peripheral sensitization like acupuncture, needling or botulinum toxin injections; this deserves further investigation. As this is the first study which details the presence of trigger points in migraine and relates it with the chronicity of the illness, it would be worthwhile to perform additional studies in order to replicate our data and to investigate more thoroughly referred pain and allodynia in patients suffering from chronic migraine.

Funding

This research has not received any funding.

References


