Summary

There are relevant clinical overlaps between some of the painful temporomandibular disorders (TMD) and headache conditions that may hamper the diagnostic process and treatment. A non-systematic search for studies on the relationship between TMD and headaches was carried out in the following databases: PubMed, Cochrane Library and Embase. Important pain mechanisms contributing to the close association and complex relationship between TMD and headache disorders are as follows: processes of peripheral and central sensitisation which take place in similar anatomical areas, the possible impairment of the descending modulatory pain pathways and the processes of referred pain. In addition, the clinical examination does not always provide distinguishing information to differentiate between headaches and TMD. So, considering the pathophysiology and the clinical presentation of some types of headache and myofascial TMD, such overlap can be considered not only a matter of comorbid relationship, but rather a question of disorders where the distinction lines are sometimes hard to identify. These concerns are certainly reflected in the current classification systems of both TMD and headache where the clinical consequences of diagnosis such as headache attributed to or associated with TMD are uncertain. There are several similarities in terms of therapeutic strategies used to manage myofascial TMD and headaches. Considering all these possible levels of interaction, we reinforce the recommendation for multidisciplinary approaches, by a team of orofacial pain specialists and a neurologist (headache specialist), to attain the most precise differential diagnosis and initiate the best and most efficient treatment.

Keywords: temporomandibular joint disorders, myofascial pain syndromes, headache disorders, tension-type headache, pain management, physiopathology

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Introduction

Headaches and facial pain are frequently associated in the same individuals. This association has been reported in several recent papers, reflecting an attempt by the scientific community to clarify a common clinical observation. Among the various conditions that can cause facial pain, temporomandibular disorders (TMD) are highly prevalent with symptoms present in around 33% of the population (1, 2). It is the second most common musculoskeletal condition (after chronic low back pain) resulting in pain and disability, with an annual management cost in USA estimated at $4 billion (3). TMD can cause
recurrent or chronic pain, dysfunction in the jaw joint, its associated muscles, and supporting tissues as well as limitations in range of motion (1). Pain in masticatory muscles is the most frequent condition found in painful patients with TMD (1, 4).

Headaches are also a frequent complaint (5) and rank third in terms of cost among neurological disorders (6). According to the International Classification of Headache Disorders – 3rd Edition (ICHD-3), headache may be a symptom of a wide variety of diseases (secondary headaches), or it can be the disease itself (primary headaches) (7). The ICHD-3 define headache as the pain located above the orbitomeatal line, while facial pain are those located below the orbitomeatal line, above the neck and anterior to the pinnae (7) (Fig. 1). However, the patients’ reports are in terms of exact localisation often not that clear. The complexity increases by the frequent association observed in both clinical and population settings in addition to the anatomical overlaps.

Indeed, there are some relevant overlaps between TMD and HA that hamper the diagnostic process and treatment such as (a) the high prevalence and epidemiological association; (b) the diagnostic criteria; and (c) the peripheral and central nervous structures involved with both. Headache and TMD are highly prevalent painful conditions. The TMD annual incidence rate is estimated to be around 6-0% (8–10). The prevalence varies widely from 16% to 45% (1, 4), depending on the sample and diagnostic methods. For headaches in general, the 1-year rates vary from 46% to 70-6% (11, 12). Tension-type headache (TTH) is the most prevalent among the primary headaches (29.5%-42%), followed by migraine (11%-15-8%) and chronic daily headaches (CDH) (3 – 6-1%) (11, 12).

Because headache and TMD are so common, they may present integrated or as separate entities. In face of the co-occurrence of a headache and TMD, an important aspect to be considered is the diagnostic criteria of both. Besides, patients presenting primary headaches frequently report pain in an oro-facial area associated with the headache episodes (5–7). In migraineurs, the facial pain can either be related to the involvement of V2 and V3 during an attack, or with the presence of cutaneous allodynia (13, 14) and central sensitisation (15, 16). Regarding the TTH, the increased pericranial tenderness (even interictally) is part of the diagnostic criteria (7). As the criteria embrace the frontal, temporal, masseter, pterygoid, sternocleidomastoid, splenius and trapezius muscles, herein there is a distinct anatomical overlap with the TMD diagnostic criteria (7, 17). Additionally, TMD is comorbid with some types of primary headaches, as migraine and TTH. In these cases, the final phenotype of patients with the comorbidity may represent the aggregated contribution of both conditions (8–10). Besides, it has been demonstrated that TMD is a risk factor for primary headache chronification (13, 18, 19).

Finally, there is an overlap between the peripheral and central nervous structures involved with TMD and headache pathophysiology. The trigeminal nerve innervates the face and head and is obviously involved in the nociceptive transmission and processing of TMD pain and headache (20, 21). Indeed, the stimulation and activation of the trigeminal system components is thought to play a major role in the underlying mechanisms of headache and facial pain disorders (16, 21, 22). Moreover, peripheral and central sensitisation can take place and contribute to the comorbidity and with the difficulties to differentiate both conditions separated or in an association. Herein, we will discuss relevant topics regarding myofascial TMD and headaches.

**Pain mechanisms**

This section briefly presents and discusses the possible underlying mechanisms driving the relationship

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**Fig. 1.** Anatomical representation of headache and facial pain. Dashed line = orbitomeatal line. Darker grey = headache area. Lighter grey = facial pain area. Light upward diagonal black stripes background = temporalis muscle representation.
between TMD and headaches. Basic science has provided the theoretical basis to interpret the clinical presentation of various pain disorders. A comprehensive review of pain mechanisms can be found elsewhere (15, 16, 23). In particular, the studies involving the trigeminal ganglion and brainstem neuronal activity have contributed to the understanding of the pathophysiology of both TMD and headaches (24–26).

Temporomandibular disorders and headache disorders may share similar (or even identical) pain pathways. Among these common neuronal structures, one region is fundamental for the relationship between these disorders, that is the spinal trigeminal nucleus, in particular the subnucleus caudalis (24–26). This region is mainly, although not exclusively, responsible for the nociceptive inputs from the face and head and, therefore, could be considered the first ‘converging site’ between TMD and headache disorders.

The umbrella term grouping all the neuronal changes, which can affect the nociceptive responses within the subnucleus caudalis in TMD and headache patients, especially the chronic cases, is called central sensitisation. Briefly, this phenomenon could refer to a series of changes in the disposition and quantity of membrane channels and neurotransmitters that ultimately lead to a decrease of the neuron threshold activation, an increase in the firing rate and an expansion of the receptive fields (15, 16).

There are various possible mechanisms presumably involved in the central sensitisation, but at least two important processes, that is sensitisation mediated by N-methyl-D-aspartate receptor (NMDA) activation and loss of inhibitory mechanisms mediated by gamma-aminobutyric acid (GABA) and glycine receptors, are believed to be present in chronic myofascial TMD and headache disorders (15, 16, 24–26). Furthermore, other neurotransmitters such as substance P and calcitonin gene-related peptide (CGRP), both released by small fibre neurons, contribute to the long-lasting membrane depolarisation and temporal summation of nociceptive neurons. Besides these mechanisms of inducing hyperexcitability states within the central nervous system (CNS), there are mechanisms that decrease the normal inhibitory activity and ultimately enhance the facilitation of nociceptive transmission and generation. Some possible mechanisms for decreasing the inhibitory influences are the inhibition of the GABAAergic and glycinergic interneurons activity (23, 27). This loss of inhibitory signals increases the depolarisation and excitation of second-order neurons. All these central changes are amplified with the participation of nitric oxide (NO), which is liberated by the second-order neuron back to the synaptic cleft, interacts with the first-order neuron, and stimulates the release of more and more excitatory neurotransmitters, such as substance P, CGRP and glutamate, which enhance the excitation of the second-order wide dynamic range (WDR) neurons (15, 16, 23). This hyperexcitability state could also produce a gradual, frequency-dependent facilitation of the nociceptive input (wind-up phenomena) that contribute to the pain signal amplification and seems to be of great importance for the self-maintenance of chronic pain states (28).

The clinical manifestation of all these cellular and molecular processes could be: allodynia, secondary hyperalgesia, temporal summation, sensory after effects and the development of widespread and generalised hypersensitivity, where the pain spreads out from localised and well-defined to a more diffuse and larger areas (29, 30). This clinical presentation of central sensitisation has been found in chronic TMD and headache patients (28, 30) although there is no direct evidence in humans for central sensitisation of the nociceptive trigeminal pathways.

Painful TMD and TTH also share many other features, such as a history of disturbing life events and high sensitivity to stress, higher prevalence in females, highly comorbid with sleep disorders and humour disturbances and evidence of cerebral/cortical abnormalities (31–35). Another important finding is that most of these patients respond well to centrally acting pharmacotherapy, and most notably tricyclic antidepressive medication. A broader discussion of this topic, however, is not within the scope of this review and can be find elsewhere (36–38).

Additionally to central neuronal plasticity, there are peripheral sensitisation processes that are also important in myofascial TMD and headache pain. In particular, the antidromic release of neurotransmitters such as substance P and CGRP are responsible for the inflammatory response of cephalic blood vessels involved in the migraine pathophysiology, which are responsible for the central modifications described above (26). Although peripheral factors related to muscle tension or prolonged and sustained concentric contractions are not regarded as the essential factors...
in chronic myofascial TMD or TTH, they are still considered important in the pathophysiology of both disorders and may be proposed to be the main drivers of central sensitisation related to myofascial structures (39). In other words, these physiological alterations within the muscle tissue can produce nociceptive inputs, which in turn would be responsible to generate the cascade of events associated with the neuronal plasticity. Furthermore, the CNS changes would lead to a more pronounced local alteration and an enhanced peripheral sensitisation, engendering a feedback circuitry.

Taking into account the mechanistic aspects of TMD and headache disorders, there is the possibility for a bidirectional influence, which means that a headache disorder could predispose to the development of TMD symptomatology, for example frequent migraine attacks that through central sensitisation processes lower the nociceptive threshold of myofascial structures causing masticatory muscle pain. Once present, and associated with other predisposing factors, the TMD could become independent from the migraine and start function as an aggravating factor for the migraine itself. In fact, signs of chronification are more pronounced in migraineurs with TMD than without (13). Similarly, as the involvement of muscle alterations could be considered important factors in the pathophysiology of TTH and myofascial TMD, it is expected that TMD could aggravate or predispose to TTH and vice versa.

Other important pain mechanisms contributing to the close relationship between TMD and headache disorders are the impairment of the descending modulatory pain pathways and the processes of referred pain (22, 27). The former is a group of neurons located at the midbrain and medullary areas mainly responsible to modulate the amount of nociceptive inputs. Under normal conditions, this system usually works as a natural analgesic, blocking the nociceptive inputs within the level subnucleus caudalis. Adrenergic, serotonergic and opioidergic neurons are responsible for these inhibitory pain effects. In cases of chronic pain, this entire system may lose its balance and, in most cases, the inhibition pathways could be impaired, hence, leading to an enhanced pain (27).

The convergence of various primary nociceptive afferents unto a single common second-order neuron is considered the basic explanatory model for referred pain (22). Because of this convergence of inputs, the pain is usually perceived in sites far from the primary source of pain. In addition, central sensitisation and release of, for example, substance P and impaired endogenous inhibitory control systems may contribute to the referral of muscle pain. This is particularly present in deep (musculoskeletal) pain disorders, such as myofascial TMD and headaches (40, 41), and certainly could contribute to the inter-relationship between the two because of the close anatomical relationships. No doubt that the awareness of these referred pain processes is essential for the clinician in the evaluation of patients with TMD and/or headache disorders.

The cumulative progress in the knowledge of the human genome has also contributed to the understanding of pain mechanisms and pain responses (42). Not only the interaction between the environment and genetics is well established, but also many candidate genes that may increase the odds for developing TMD and primary headaches have been described (43, 44). Although no single gene variation has been unambiguously acknowledged as a decisive risk factor for TMD, classical migraine or TTH, it seems clear that genetic predisposition could drive specific phenotypes, which in turn, can predict the development of TMD or headaches (43, 45). Notwithstanding such advances in the understanding of the genetic contribution to pain, recent prospective studies have also indicated the difficulty in the identification of specific candidate genes for first-onset TMD pain but rather that a number of genotypes are significantly associated with intermediate phenotypes (e.g. non-specific oro-facial symptoms, global psychological symptoms, stress and negative affectivity) that are associated with TMD pain (43). Such indirect associations may further add to the complexity to unravel the genetic component of chronic and overlapping pain conditions such as TMD and headache.

**Diagnostic methods**

Temporomandibular disorders and headache assessment are based on a detailed and structured history and an accurate physical examination. In this section, we call attention to important aspects that must be carried out during the clinical examination when evaluating patients with TMD and headache disorders. In the scenario here discussed, one of most challenging tasks is to define if the ‘head pain’ reported by the
patient is originated from a primary headache (especially the subforms of TTH), if it comes from myofascial structures (named ‘headache’ secondary to TMD, based on current criteria) (7, 17), or if there exists an overlap and comorbidity between the two conditions. This characterisation is crucial for establishing management protocols.

One important factor to take into account in the patient interview to differentiate headache attributed to TMD and primary headache is the temporal relationship between the disorders (7). The longitudinal history of the pain is a key point to discriminate primary and secondary headaches. The direction from the cause (TMD) to the effect (headache) needs to be properly established. In cases of pre-existing headaches, the ICDH-3 recommends that both diagnoses should be given (7). Of course, there is always the risk of patient recall bias and the reliability of this information has not been established; nonetheless, a careful interview can help to elucidate this question. Besides the temporal assessment, another particularly important factor to establish the distinction between myofascial pain and headache is the report of pain modified by oral/jaw function and or digital palpation, eliciting familiar pain/headache (17). This enquiry is decisive in the assessment of patients with TMD and could be considered the core of the new Diagnostic Criteria for Temporomandibular Disorders (DC/TMD), improving the specificity of the pain provocation tests. It should be noted that the pressure pain threshold (PPT) can be considered a very informative additional tool to evaluate these patients (46).

The establishment and meaning of PPT values have been long studied in the TMD and headache field (47, 48). There is clear evidence of lower PPT values of masticatory muscles in TMD patients compared with healthy participants (49, 50). These low values could corroborate the evidence suggesting local muscle factors as an important source of pain in myofascial TMD although low PPT values in jaw muscles also simply could reflect more central sensitisation and generalised hyperexcitability. On the contrary, muscle inputs in migraines may be regarded as secondary factors, considering the well-established pathophysiology model (26). However, muscle pain is also an evident clinical manifestation in this population (51). Low PPT values of masticatory muscles have been reported during a migraine attack in myofascial TMD-free women, which support basic findings of muscle pain as a consequence of central neuron hyperexcitability (52). Therefore, even though migraine and TMD are considered different entities, they can present with overlapping signs. More than that, the presence of both conditions could aggravate the clinical presentation. In fact, even lower PPT values are observed in patients having both disorders concurrently, in comparison with those having only migraine or myofascial TMD (46).

This overlap in clinical presentation is even stronger and confusing when we associate myofascial TMD and TTH (Table 1) (53–57). In spite of the progress in the understanding of the pathophysiology of TTH, especially the evidence of central pain mechanisms as the main responsible factor in the chronic cases, peripheral muscle alterations are still considered significant factors (58). Likewise, low PPT values are also found in TTH patients when compared to healthy participants (59) and, when associated with myofascial TMD pain, a high frequency of headache pain contributes to a lower PPT (60). Accordingly, considering the pathophysiology and the clinical presentation of TTH and myofascial TMD, the overlap between them can be considered not only a matter of comorbid entities, but rather a question of disorders where the distinction line is sometimes impossible to identify, and perhaps may not be important for the management of the painful condition anymore. Moreover, if we consider the ontological aspect of defining a disease, where at the same time the term needs to be capable of including everything that it is and separating everything that it is not, to consider myofascial TMD and TTH as part of a common entity rather than different ones, it may indeed be plausible (61). This is particular noticeable when the anterior temporalis muscle is the only affected area (Fig. 1). Indeed, anterior temporalis pain upon digital palpation is significantly associated with TMD, migraine and TTH using logistic regression models (62).

**Classification**

Previously available diagnostic instruments, worldwide used as gold standards [International Classification of Headache Disorders – 2nd edition (ICHD-2) and Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD)], did not adequately address the issue of the existence of a head pain related to masticatory muscles disorders (63, 64). Currently, the new DC/TMD and the ICHD-3 could be regarded as the two major reliable
One of the major changes in the new headache classification was the redefinition of the causation criteria to diagnose secondary headaches. The former ICHD-2 only presented restricted criteria and was open to interpretation. For instance, the criterion ‘headache is greatly reduced or resolves within 3 months (this may be shorter for some disorders) after successful treatment or spontaneous remission of the causative disorder’ was mandatory, which meant that the diagnosis could only be made retrospectively (64). Accordingly, the adoption of such criteria was not clinically feasible. In particular, the criteria for headache secondary to TMJ disorder specified the need for a ‘proof’ of TMD by means of imaging tests, which is now known as not crucial in terms of evidence for the presence of a painful TMD (65). All these concerns were taking into consideration in the new ICHD-3, and the criteria are clearer and more straightforward. The causation criteria were amplified and include more options to define secondary headaches. Specifically, the criteria for headache attributed to TMD involve a set of items usually easy to assess during the clinical examination, without the need for imaging evidence of TMD. Interestingly, in the criteria comments the attention is called for a possible overlap between headache attributed to TMD and TTH (7).

Table 2 presents the valid diagnostic criteria for headache attributed to TMD and points out their similarities (7, 17). One major difference between them is the absence of any specific temporal criterion in the DC/TMD in comparison with the ICHD-3 where the temporal relationship is mandatory. One possible explanation for this difference could be the recognition that jaw movement, function or parafunction could not cause or exacerbate primary headaches. So, the presence of a headache modified with mandibular movements together with an existent painful TMD can only lead to a causal association between the two disorders. Such assumption is plausible, but there is evidence of experimental jaw activity interfering with versions of the ICHD (7, 64, 66). However, because of the high co-occurrence of headache and TMD in the clinical practice of oro-facial pain specialists and the extensive research made by dentists in this particular field (4, 18, 19, 32, 46, 67–74), the new DC/TMD, which can be considered the newest ‘reference standard’ for TMD classification, also proposed criteria to define headache attributed to TMD (17). These criteria discriminate the location of secondary headache only to the temple area and the causation criteria are restricted to the report of familiar headache modified by jaw movement, function or parafunction associated with the clinical provocation of headache. A great achievement of these criteria was the establishment of sensitivity and specificity values, which made clear for the clinician how accurate they are and for the researches how they could be improved. A detailed report of the development process of these criteria can be found in the literature (75).

References #53 to #57 were used to elaborate the table.
primary headaches (76). Accordingly, relying only on this criterion for causation can be of great risk for defining a pain condition.

Another important difference is the mandatory location of the temple area in the DC/TMD whereas the ICHD-3 does not specify any headache characteristic in terms of anatomical location, but only require the presence of ipsilateral TMD disorder when the headache is unilateral (7). The DC/TMD seems to rule out the possibility of other head areas being affected by the painful TMD. For instance, it could be possible to find anterior temporalis trigger points referring pain behind the eye. Restricting the headache location could artificially reduce the complex clinical picture of headache attributed to TMD.

On the other hand, the clinical evidence for the secondary headache is similar, even though the DC/TMD criteria present more detailed information on how to gather such clinical evidence. An important difference is the non-restriction in terms of the direction of pain modification, imposed by the ICDH-3 as only towards aggravation, not acknowledging that mandibular movements could, in some case, alleviate the headache pain.

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Table 2. Comparison between the International Classification for Headache Disorders, 3rd edition (ICHD-3) and the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) criteria for headache attributed to temporomandibular disorders (TMD)

<table>
<thead>
<tr>
<th>Headache Characterisation</th>
<th>ICHD-3</th>
<th>DC/TMD</th>
<th>Item Correspondence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Presentation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Location</td>
<td>ns*†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality</td>
<td>ns</td>
<td>ns</td>
<td>Yes</td>
</tr>
<tr>
<td>Duration</td>
<td>ns</td>
<td>ns</td>
<td>Yes</td>
</tr>
<tr>
<td>Frequency</td>
<td>ns</td>
<td>ns</td>
<td>Yes</td>
</tr>
<tr>
<td>Intensity</td>
<td>ns</td>
<td>ns</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Causality Criteria</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temporal relation</td>
<td>'Headache of any type in the temple area'</td>
<td>ns</td>
<td>No</td>
</tr>
<tr>
<td>Clinical evidence</td>
<td>'Headache has developed in temporal relation to the onset of the temporomandibular disorder' or 'headache has significantly worsened in parallel with progression of the temporomandibular disorder' or 'headache has significantly improved or resolved in parallel with improvement in or resolution of the temporomandibular disorder'</td>
<td>ns</td>
<td>No</td>
</tr>
<tr>
<td>Causative disorder</td>
<td>'Clinical and/or imaging evidence of a pathological process affecting the temporomandibular joint (TMJ), muscles of mastication and/or associated structures'</td>
<td>'Headache modified with jaw movement, function or parafunction' and 'confirmation of headache location in the area of temporalis muscle(s)' and 'report of familiar headache in the temple are with at least one of the following provocation tests: palpation of temporalis muscle or maximum unassisted or assisted mouth opening, right of left lateral or protrusive movement(s)'</td>
<td>A valid diagnosis of painful TMD must be established</td>
</tr>
</tbody>
</table>

*ns = not specified. †The criterion 4 of the ICHD-3 requires an ipsilateral TMD in cases of unilateral headaches.
Finally, neither the ICHD-3 nor the DC/TMD recognise headache characteristics (expect the temple location in the DC/TMD) as part of their criteria for headache attributed to TMD. Recently, in a controlled trial, the clinical presentation of such headaches was described as follows: bilateral and frontotemporal location of long duration ($\geq4 \text{ h day}^{-1}$) and with a tightening/pressing quality (68). However, the incorporation of such items in the classification requires further investigation to determine their validity and reliability, but certainly could be helpful in the clinical examination.

The divergences between the ICHD-3 and the DC/TMD partly reflect the confusion in the field and the multiple points of view towards the problem (61, 74). The ICHD-3 criteria may seem broad and comprehensive, but it is still open to interpretation and, therefore, is not too elucidative. On the other hand, the DC/TMD may seem narrow and focused and it is not capable to discriminate other possible types of presentation of headache attributed to TMD. All in all, future investigations are required to refine both criteria in order to find out a balance point between these extremities. Perhaps we should use the term 'associated' rather than 'attributed to' to describe the complex and even bidirectionally link between myofascial TMD and HA.

The biopsychosocial profile of pain patients also needs to be addressed as it influences the clinical course of TMD and headaches (77, 78). In this regard, the former RDC/TMD (now the new DC/TMD) can be considered a milestone in pain classification, as it presents a dual-axis diagnostic appraisal: the physical domain (Axis I) and the psychosocial domain (Axis II) (17, 63). Besides the already described correspondences regarding the ‘physical diagnosis’, the psychosocial distress can also be present in TMD and headaches (79, 80), which can contribute to an even more close relationship between them. This particular aspect of the Axis II features in TMD pain and headache patients is important for clinicians to be aware of and to evaluate before management is initiated.

Implications for management

In general, the therapeutic options can target the peripheral nociceptive input (bottom-up), or the brain or central approaches (top-down approach) (36). The central therapeutic modalities have been traditionally recommended in cases of central sensitisation. However, the clinical picture of chronic pain patients is not always that clear, with some patients presenting indications of peripheral nociceptive input combined with central sensitisation (36). Previous studies have demonstrated that the peripheral approach also has some impact on the central sensitisation (81–83). Treating acute, inflammatory or local pain is usually attainable and with a good prognosis. However, chronic and centralised pain remains challenging and only partially successful, which, in part, is related to the clinical difficulty to establish differential diagnostic, and recognising the coexistence and interaction of distinct types of pain in the same patient (36, 84). In addition, the neurobiology of chronic pain may be so much more complex than the current therapeutics efficiently can manage. In such cases, to successfully and realistically manage pain, non-pharmacological as well as pharmacological modalities aimed at centralised pain must be garnished (36, 81, 84).

TMD management

The therapeutic arsenal for myofascial TMD includes both local and central approaches, as self-care procedures, physical therapy, pharmacotherapy and occlusal appliance therapy (1, 85, 86). It is well established that education and self-care instructions should be the initial approach, and part of a more extensive treatment plan. The use of a home care program has proved to be effective in the management of TMD not only by the direct effect on muscles but also by alleviating the anxiety by informing the patient regarding their condition and symptoms (86–89). A successful home care program includes resting the masticatory muscles, limiting excessive jaw movements, controlling parafunctional habits, perhaps including recommendations of a soft diet, and moist heat and/or ice therapy (88, 89). Physical therapy is beneficial in restoring the normal function of the muscles, as well as in reducing inflammation, promoting repair and strength (90). It embraces modalities as electrotherapy (i.e. transcutaneous electrical nerve stimulation – TENS), laser and exercises. Although there is a lack of evidence from well-controlled clinical trials regarding the use of physical therapy specifically for TMD management (91), the positive effect of these modalities on pain control is well acknowledged (92). TENS is an affordable non-pharmacological intervention used in the treatment of painful conditions by the activation
of a complex neural network. It stimulates large-diameter afferent fibres resulting in the likely activation of the descending inhibitory systems and reduction in the hyperalgesia. The low-level laser therapy (LLLT) has a biostimulating, analgesic effect and anti-inflammatory effect (93). Although previous studies are reporting the effectiveness of the LLLT on myofascial TMD pain relief (94–96), more randomised controlled studies are needed to a better definition of the parameters and efficacy of its application (97). Jaw exercises have been indicated to develop and maintain comfort, function and stability of both cervical and masticatory muscles. The exercises are prescribed to achieve a specific goal and should be modified according to the patient progresses (91).

Occlusal appliances (OA) have been widely used for TMD treatment (1, 86). Previous studies have reported a reduction in TMD symptoms and sufficient efficacy to justify their use for painful TMD (2, 98) although they may only be marginally, if at all, better than a placebo control. The most common and used OA is the stabilisation appliance, made of hard acrylic and cover all the upper or lower teeth, that is a full arch device. Although it is a therapeutic approach widely used for many decades, researchers have not yet found a consensus on its putative mechanism of action (2, 99). The theories regarding the OA mechanisms embrace peripheral effects such as occlusal contact improvement and vertical dimension alterations, as well as central effects mediated by changes in the afferent impulses to the central nervous system (99, 100, 101).

The pharmacotherapy for myofascial TMD also involves drugs with peripheral and central nervous system actions. Commonly used medications include analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), local anaesthetics, muscle relaxants, botulinum toxin injections and tricyclic antidepressants (25, 87). Initial pharmacotherapy for myofascial TMD often employs a skeletal muscle relaxant as diazepam or cyclobenzaprine, used alone or in combination with NSAIDs. Recently, botulinum toxin has generated particular interest in this regard, and its action seems to include peripheral and central effects, too. It has been proposed that botulinum toxin prevents neurogenic release of substances such as glutamate, CGRP and substance P from masticatory muscle nociceptors. As these are algogenic substances, the release inhibition may be able to decrease the muscle pain (102). Other substances have been also tested, especially when the myofascial pain becomes chronic with the involvement of central sensitisation. Gabapentin is a new-generation anti-epileptic agent that acts in the CNS and showed positive results on myofascial pain. This medication has been used to manage different chronic pain conditions and has also been reported effective for the management of the TMD (103). Nevertheless, a strict meta-analyses of the different therapeutic approaches strongly suggest that care should be taken in the clinic to choose the least invasive and most reversible modality because many intervention studies may contain bias and be influenced by methodological issues such as sample size, blinding, lack of operationalised outcome parameters and statistics (91).

Management of primary headaches

The treatment of TTH and migraine embrace pharmacological and non-pharmacological options, and can be classified as acute or rescue treatment, as well as preventive therapy. Relaxation techniques, cognitive–behavioural therapies, techniques for pain management, stress control strategies and physiotherapy are some of the efficient non-pharmacological modalities indicated to integrate into a treatment plan for these types of primary headaches (104). Pharmacological treatment includes different class of medications depending on the type of primary headache, its frequency and intensity.

The acute pharmacological treatment of TTH involves the use of simple analgesics and NSAID as aspirin, acetaminophen, dipyrone and ibuprofen among others (104). The prophylactic treatment should be considered in cases of chronic tension-type headache (CTTH) and frequent TTH. The main class of drugs indicated for preventive management of TTH is the tricyclic antidepressant, for example, amitriptyline. Serotonin and serotonin–norepinephrine reuptake inhibitor antidepressants are also likely to present positive results but are less effective than the tricyclic antidepressants (104). Interestingly, these drugs present similar results when used for other types of chronic pain, as musculoskeletal pain, including TMD pain (25, 86).

The acute medications for migraine include over-the-counter analgesics such as NSAIDs and acetaminophen, and prescription drugs such as triptans and
dihydroergotamine. Candidates for preventive medication use include patients with >3 days per month of headache-related disability, individuals with contraindications to preventive medications and patients presenting infrequent yet very severe or prolonged attacks. There is a wide variety of preventive drugs therapies, including beta-adrenergic blocking agents (i.e. propranolol), anticonvulsants divalproex sodium or sodium valproate and topiramate. Also, injectable botulinum neurotoxin type A or onabotulinumtoxinA is approved for the prevention of chronic migraine (CM) under specific conditions and use (105).

**Table 3.** Treatment modality, objective, description and indications for myofascial temporomandibular disorders (TMD), tension-type headache (TTH) and migraine

| Treatment Modality* | Objective | Description | Indications*
|---------------------|-----------|-------------|----------------
| Non-pharmacological | To reduce anxiety, pain and other symptoms; To rest the masticatory muscles. | Relaxation techniques, cognitive-behavioural therapies, techniques for pain management, stress control strategies. | EM, CM ETTH mTMD
| Modalities: Parafunction Control | Awareness and control of parafunctional habits. To control stress control and to improve relaxation. | Instruction to soft diet consumptions, moist heat and/or ice therapy, automassage, stretching exercises for masticatory muscles. Training a relaxed mandibular posture. | mTMD
| Education | | | |
| Self-Care | | | |
| Physical Therapy | To restore the normal function of the muscles; to reduce inflammation and pain; to promote repair and strength. | Electrotherapy Laser Masticatory muscles exercises. | mTMD
| Occlusal Appliance | To temporary alter occlusal relationships, to redistribute occlusal forces, to prevent alterations of teeth, to manage muscle pain and dysfunction. | The most used is the stabilisation appliance made with hard acrylic and cover all the upper or lower teeth. | mTMD
| Pharmacotherapy | To reduce pain, peripheral inflammation, and centrally mediated masticatory muscle. | Analgesics, NSAIDs, local anaesthetics, muscle relaxants, botulinum toxin injections, tricyclic antidepressants, anti-epileptic (i.e. gabapentin) | mTMD ETTTH CTTH EM CM
| | Acute: to reduce pain during an attack | Acute: Analgesics, NSAID Prophylactic: tricyclic antidepressant. | |
| | Prophylactic: to prevent or to reduce the frequency/intensity of attacks. | Acute: NSAIDs, triptans, dihydroergotamine Prophylactic: beta-adrenergic blocking agents (i.e. propranolol), anticonvulsants (i.e. divalproex sodium or sodium valproate) and topiramate. | |

*The description of the treatment modalities and the indications are not based on systematic analysis of the literature. They are clinical suggestions rather than evidence-based recommendations.

mTMD: myofascial temporomandibular disorder; EM: episodic migraine; CM: chronic migraine; ETTTH: episodic tension-type headache; CTTTH: chronic tension-type headache; NSAIDs: non-steroidal anti-inflammatory drugs.
Some management modalities indicated for primary headache treatment can also be effective for myofascial TMD and vice versa (Table 3). For example, the above-cited non-pharmacological approaches for primary headache management are also effective for myofascial TMD and often integrate the education and self-care programs for TMD (107, 108). Moreover, all procedures indicated for myofascial TMD that alter peripheral nociceptive input could potentially have a positive impact on a primary headache as well. Other therapeutic approaches for myofascial TMD that help to reduce muscle pain and dysfunction (i.e. occlusal splint, self-care, massage, physical therapy) may also have a positive impact on primary headache when both are present. This hypothesis is based on the reduction of nociceptive inputs from the peripheral to the central nervous system (13, 46, 70). Some medications such as tricyclic antidepressants (amitriptyline and nortriptyline), muscle relaxants (cyclobenzaprine and tizanidine) and beta-blockers (propranolol) are likely to influence both myofascial TMD and some types of primary headaches (109).

In cases of centralised pain, an efficient treatment should aim to deconstruct complex cases, identifying potential pain (nociceptive) generators, and targeting them with pharmacological and non-pharmacological modalities (84). While strategies targeting the mechanisms related to the centralised pain are essential for a rationale treatment plan, a systematic workup for peripheral and nociceptive sources of pain would be adopted (84). It has been previously demonstrated that primary headaches negatively influenced the efficacy of TMD therapy (72). On the other hand, another study showed that when migraine and TMD coexists, a significant improvement of headache was achieved when both were treated simultaneously (70). However, it seems that the headache attributed to TMD does not interfere with the TMD management in patients with myofascial TMD (67). These data reinforce the importance to differentiate between the type of comorbidity between headaches and TMD and strengthen the recommendation for multidisciplinary approaches, when necessary, focusing on and addressing both conditions, by a team of oro-facial pain specialists and a neurologist (headache specialist).

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