Temporomandibular Disorders and Migraine Chronification

Debora Bevilaqua Grossi, PT, PhD, Richard B. Lipton, MD, and Marcelo E. Bigal, MD, PhD

Corresponding author
Debora Bevilaqua Grossi, PT, PhD
Department of Biomechanics Medicine and Rehabilitation of the Locomotor Apparatus, University of Sao Paulo, Avenida Bandeirantes, 3900 CEP 14.049-900 Ribeirao Preto, Sao Paulo, Brazil.
E-mail: deborabg@fmrp.usp.br

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Among the established and potential comorbidities of migraine, the temporomandibular disorders (TMD) are rarely discussed, although they are of importance for several reasons. TMD may cause headaches per se, worsen existent primary headaches, and add to the burden of headache disorders. This article explores the potential comorbidity between migraine and TMD and the role of TMD as a potential factor to induce chronic migraine. We discuss the similarities between both conditions, review evidence to support the idea that both disorders are comorbid, and highlight the limited evidence suggesting that TMD influence migraine progression. Finally, we discuss the importance of cutaneous allodynia mediating the TMD/frequent headache relationship.

Introduction

Among the conditions associated with migraine, temporomandibular disorders (TMD) are rarely mentioned [1•]. Nonetheless, TMD are of importance for several reasons. First, TMD may be a cause of headaches (headaches attributed to TMD), a secondary disorder identified in the International Classification of Headache Disorders, 2nd Edition (ICHD-II) [2]. Second, TMD may exacerbate existing primary headache disorders. Finally, individuals with TMD and primary headaches (eg, migraine) may experience an added burden because more than one disorder is present (migraine, headache from TMD, other symptoms of TMD).

This article focuses on the importance of TMD in the context of migraine chronification (from episodic into chronic migraine). To do so, we first discuss the similarities and differences in the clinical approach to diagnosing primary headache disorders and TMD. We then consider the relationship between primary headache disorders and TMD. Finally, we consider the possible mechanism that may link these disorders and discuss areas for future research.

Primary Headache Disorders and Temporomandibular Disorders: Issues in Classification and Diagnosis

Migraine and TMD are characterized by intermittent head and face pain. They both have internationally accepted criteria for diagnosis. Migraine is diagnosed according to the ICHD-II [2]. The gold standard for diagnosing TMD is based on the Research Diagnostic Criteria for TMD (RDC/TMD). The RDC/TMD criteria, intended for both clinical practice and research, subdivide TMD into three main groups: group I, muscular disorders; group II, disk displacements; and group III, arthralgia, osteoarthritis, or osteoarthrosis (Table 1) [3]. The RDC/TMD, as with the ICHD-II, provided an agreed-upon definition for TMD [4]. For primary headaches, the physical examination serves primarily to exclude other disorders. For TMD, the physical examination provides positive evidence to support the diagnosis [5]. Both migraine and TMD are diagnoses of inclusion, in which specific features are required to make the diagnosis, and diagnoses of exclusion, in which other disorders must be excluded before diagnosis is firmly established.

TMD are characterized by pain in the muscles of mastication, the temporomandibular joint (TMJ), or both. In addition, signs include tenderness at the TMJ area, joint sounds (clicks or crepitation), limitations or deviation upon mandibular opening, and "distance symptoms" such as pain in the neck or headache [6•]. The headaches associated with TMD are typically temporal, periorbital, or frontal and may irradiate into the ears and frequently to the posterior neck [7•]. The discomfort may be unilateral, but is usually bilateral. Some patients experience an ongoing sense of ear fullness that may be mistaken for a recurrent pain in the ear. Deep retro-orbital pain also can be felt when the lateral pterygoid muscle is in spasm [8].

The dysfunctions associated with TMD (microtraumas or recurrent mechanical stimuli due to bruxism and clenching of the teeth, along with myogenic pain from the

Table 1. Classification of temporomandibular disorders according to Research Diagnostic Criteria

Axis	Diagnosis	Subtypes
I	Muscle diagnosis	Myofascial pain
		Myofascial pain with limited opening
II	Disk displacements	Disk displacement with reduction
		Disk displacement without reduction, with limited opening
		Disk displacement without reduction, without limited opening
III	Arthralgia, osteoarthritis, osteoarthrosis	Arthralgia
		Osteoarthritis of the temporomandibular joint
		Osteoarthrosis of the temporomandibular joint

(*Data from* Dworkin and LeResche [3].)

masticatory muscles) induce the release of serotonin and norepinephrine from the dorsal raphe and locus ceruleus of the brain, therefore causing a cascade of events. As we discuss below, these events may worsen preexisting headaches such as migraine and contribute to overall muscle tension [9]. Accordingly, TMD may be a source of headaches per se (in addition to pain in the joint), but may also worsen preexisting headaches.

Are Temporomandibular Disorders and Migraine Comorbid?

The epidemiology of migraine is well described. In occidental countries, migraine affects 10% to 15% of adults [10,11••]. Chronic daily headache (CDH), defined as a headache occurring 15 or more days per month, occurs in about 4% of the general population [12,13]. Chronic migraine (CM), a subtype of the CDHs, is the consequence of migraine progression (defined herein as evolution from an episodic into a chronic form). The prevalence of CM is around 2% (nearly half of the CDHs).

TMD are also common in the population. The annual incidence rate of TMD in the population is 6.5% [14•] and in adolescents 2.9%, being higher in girls (4.5%) than boys (1.3%) [15]. In a dental student population, the annual incidence of TMD is 12% [16].

Pain in the TMJ is relatively uncommon in children ages 7 to 17 (2%–4%). Like migraine, TMD are more prevalent in young and middle-aged adults and decline in frequency among the elderly and women in postmenopausal years. The prevalence rates peak in adults ages 25 to 44 (10% of men and 18% of women) [17]. As for migraine, hormonal factors seem to be of importance in TMD [17], and the intensity of musculoskeletal pain associated with TMD varies across the menstrual cycle. The highest pain level occurs at times of low estrogen (during the menstrual flow) and at times of rapid estrogen change (late luteal and midcycle) [18].

Beyond being prevalent and disabling disorders, limited evidence also suggests that specific headache disorders (eg, migraine) and TMD are comorbid. Population data show that TMD symptoms are more prevalent in individuals with headache than in those without headache. Among headache sufferers, TMD symptoms are more common among individuals with migraine and CDH relative to episodic tension-type headache (ETTH), supporting the idea that TMD and migraine are comorbid [19•]. A population study found that 27.4% of subjects who reported headache also reported temporomandibular pain, whereas only 15.2% of subjects without headache experienced temporomandibular pain [20]; in the same way, it was observed that headache prevalence was markedly higher for the TMD group (72.7%) than the control group (31.9%) ($P < 0.001$) [21].

Do Temporomandibular Disorders Influence Migraine Progression?

A subgroup of migraine sufferers worsens over time and some develop chronic migraine [22••]. However, the progression of TMD or the process of TMD chronification has not been studied. A longitudinal study showed that progression to severe pain and dysfunction of the masticatory system was rare [23], but it is possible that some variables such as gender, myofascial pain, and physical–psychological interface could affect the development of TMD chronicity [24].

The influence of TMD on migraine progression has not been formally studied. However, available epidemiological data suggest the importance of TMD in the process. In a study conducted in Sweden, frequent symptoms of TMD and frequent headache were strongly associated (OR, 4.1; 95% CI, 2.4–6.9; $P < 0.0001$) [25••].

Similarly, in a large epidemiological study conducted in Brazil, all forms of headache were significantly more common in individuals with TMD compared to individuals without TMD [19•]. The prevalence ratio (PR) of TMD symptoms was significantly higher in individuals with ETTH (PR, 1.48; 95% CI, 1.20–1.79), migraine (PR, 2.10; 95% CI, 1.80–2.47), and CDH (PR, 2.41; 95% CI, 1.84–3.17). The prevalence of TMD symptoms was very similar in individuals with migraine and CDH and significantly increased in both groups relative to individuals with ETTH. However, a higher number of TMD symptoms (as a metric of TMD severity) was associated with CDH, suggesting that the severity of both TMD and primary headaches are correlated. Although causal relationship cannot be addressed by cross-sectional studies, the link between TMD and frequent headaches was established.

Table 2. Presence and severity of headache-related allodynia, as measured by the ASC-12

Allodynia categories	No TMD, *n*	Myofascial TMD, *n*	Mixed TMD, *n*	Myofascial vs no TMD, *P* value	Mixed vs no TMD, *P* value	Myofascial vs mixed TMD, *P* value
No allodynia	8 (53.3%)	3 (13.04%)	3 (17.64%)	0.042	0.028	0.4048
Mild allodynia	2 (13.3%)	5 (21.73%)	2 (11.76%)	–	–	–
Moderate allodynia	0	8 (34.78%)	2 (11.76%)	–	–	–
Severe allodynia	5 (33.3%)	7 (30.43%)	10 (58.82%)	–	–	–
Any allodynia	6 (46.6%)	20 (86.95%)	14 (82.35%)	RR, 3.2; 95% CI, 1.5–7.0; $P = 0.041$	RR, 2.5; 95% CI, 1.2–5.3; $P = 0.02$	RR, 0.85; 95% CI, 0.4–1.9; $P = 1.0$

ASC-12—12-item Allodynia Symptom Checklist; TMD—temporomandibular disorders.
(*Data from* Bevilaqua-Grossi et al. [42••].)

Studies conducted in adolescents pointed to the same direction [21,26–30,31•]. TMD are more common in individuals with headaches versus not, and with high frequency headaches versus low frequency headaches [1•,32,33•,34]. Furthermore, the severity of headache is greater and is related to musculoskeletal problems like myalgia or myofascial pain.

These studies suggest a relationship between TMD and headache overall, a stronger relationship between TMD and migraine, and an even stronger association between TMD and CDH.

Because this relationship has been suggested, but putative mechanisms to explain the relationship have not been demonstrated, we conducted a study to investigate whether central sensitization (and its clinical surrogate, cutaneous allodynia [CA]) influences the TMD/migraine relationship [22••]. CA is a risk factor for migraine progression.

TMD and migraine patients exhibit lower nociceptive thresholds in multiple body areas that implicate a generalized dysfunction of the nociceptive system, suggesting a generalized upregulation of nociceptive processing [35]. Central sensitization has been studied in TMD using different methodologies, including ischemic stimuli, pressure stimuli, heat stimuli, infusion of hipertonic saline [35–37], or the Quantitative Sensory Test (QST) [38•].

In our study, we used QST and the 12-item Allodynia Symptom Checklist (ASC-12) to assess CA in migraineurs with and without TMD [39••,40,41]. Our sample consisted of 55 individuals with migraine; 40 (73%) had TMD (23 with myofascial TMD and 17 with the mixed type [myofascial plus artrogenic problem]). CA of any severity (as assessed by ASC-12) occurred in 40% of those without TMD (reference group), 86.9% of those with myofascial TMD (RR, 3.2; 95% CI, 1.5–7.0; $P = 0.041$), and in 82.3% of those with mixed TMD (RR, 2.5; 95% CI, 1.2–5.3; $P = 0.02$) (Table 2). Individuals with migraine plus TMD were more likely to have moderate or severe CA associated with their headaches. Interictally (QST), thresholds for heat and mechanical nociception were significantly lower in individuals with migraine plus TMD. Cold nociceptive thresholds were not significantly different in migraine patients with and without TMD. The presence of TMD was also associated with change in extracephalic pain thresholds. In logistical regression, TMD remained associated with CA after adjusting for aura, gender, and age [42••].

Accordingly, we concluded that both ictal and interictal central sensitization are more common in migraineurs with TMD compared with those without TMD. This offers a biologically plausible mechanism to understand the TMD/frequent headache relationship. Indeed, TMD and migraine may be linked through the phenomenon of central sensitization in the trigeminal distribution. It is well established that neurons in the nucleus caudalis integrate nociceptive input from both intracranial and extracranial tissues and receive supraspinal facilitatory as well as inhibitory inputs. They sum all these inputs and project the net results to the thalamus and onto the cortex [43]. It can be hypothesized that nociceptive inputs from the masticatory muscles or the TMJ could lead to the aforementioned activation. Futhermore, the presence of proinflammatory factors at the TMJ could be another form of sensitization. High levels of prostaglandin E2, cytokines such as interleukin (IL)-1β and IL-6, and tumor necrosis factor (TNF)-α have been detected in synovial fluid of inflamed joints and demonstrated a strong correlation with pain [44]. Calcitonin gene–related peptide, the most potent vasodilatory peptide known and a major contributor to neurogenic inflammation and nociception substance P [44], and serotonin have been detected in the TMJ [45,46]. Thus, TMD symptoms may cause an excitatory impact on migraine, especially in patients presenting severe and frequent migraine attacks, which are more susceptible to central sensitization [21,47•]. Our findings do not exclude the possibility that other mechanisms influence the TMD/frequent headache relationship. For example, depression is comorbid to both conditions and a risk factor for migraine progression. Additionally, shared genetic factors may predispose to both disorders. For example, a functional polymorphism in the cathechol-O-methyl transferase gene has been associated with TMD and pain in general.

Conclusions

Migraine and TMD seem to be associated, and some evidence shows that TMD may be involved with CM. Despite an obvious lack of a well-designed longitudinal study that irrefutably confirms the relationship between headache progression and TMD, a clinical correlation can be seen. Accordingly, a multidisciplinary approach to these patients is necessary to improve diagnosis and treatment.

Disclosure

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Dr. Marcelo E. Bigal is a full-time employee of Merck Research Laboratories, and he owns stock and stock options from Merck.

No other potential conflicts of interest relevant to this article were reported.

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