

Sleep disturbances in tension-type headache and migraine

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Abstract: Current research into the pathogenesis of tension-type headache (TTH) and migraine is focused on altered nociceptive pain processing. Among the potential factors that influence sensitization mechanisms, emotional stress, depression, or sleep disorders all have an essential role: they increase the excitability of nociceptive firing and trigger hyperalgesic responses. Sleep disturbances and headache disorders share common brain structures and pathogenic mechanisms and TTH, migraine, and sleep disturbances often occur together; for example, 50% of individuals who have either TTH or migraine have insomnia. Moreover, insomnia and poor sleep quality have been associated with a higher frequency and intensity of headache attacks, supporting the notion that severity and prevalence of sleep problems correlate with headache burden. It should be noted that the association between headaches and sleep problems is bidirectional: headache can promote sleep disturbances, and sleep disturbances can also precede or trigger a headache attack. Therefore, a better understanding of the factors that affect sleep quality in TTH and migraine can assist clinicians in determining better and adequate therapeutic programs. In this review, the role of sleep disturbances in headaches, and the association with depression, emotional stress, and pain sensitivity in individuals with TTH or migraine are discussed.

Keywords: headache, insomnia, migraine, sleep, tension-type headache

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Introduction

Tension-type headache (TTH) and migraine are the most common headache disorders, and both have an important socio-economic impact and burden for society.¹ For example, the general costs of headache in Europe, mostly attributed to migraine and TTH, were €13.8 billion in 2010.² The global prevalence of TTH has been estimated to be around 42%,³ and that of migraine to be almost 12%.⁴ In the Global Burden of Disease Study, headache was the second most prevalent disorder in the world, leading to a high economic burden, estimated to be around 1.6 billion dollars.⁵ In fact, most of the costs from the Global Burden of Disease Study derived from TTH and migraine headaches.⁵

Current research into the pathogenesis of TTH⁶ and migraine⁷ is focused on altered nociceptive pain processing and its role on chronification. Although both primary headaches can exhibit

similar pathogenic mechanisms, some differences can be observed. In TTH, sensitization of the pain pathways seems to result in facilitation of nociceptive gain due to sensitization of the trigeminocervical nucleus caudalis, leading to typical clinical manifestations of TTH,⁶ whereas in migraine, it has been established that the pain is associated with abnormal neuronal excitability leading to cortical spreading depression and to central sensitization of the trigeminovascular pain pathways.⁷

Several factors, including physical, neurophysiologic, or emotional, can increase the excitability of nociceptive firing to the central nervous system. For example, stress can precipitate a headache attack in patients with TTH by reducing the thresholds to noxious input from pericranial sensitized structures.⁸ In individuals with chronic headaches, defined in the International Classification of

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Headache Disorders 3rd edition (beta version) as persistent headache for 15 days or more per month on average for more than 3 months, stress and sleep disturbances are the most common headache triggers⁹ and, when combined, have an additive effect.¹⁰ For example, two consecutive days of decreased sleep have been associated with an increased risk for headache, and in individuals with chronic headaches, shorter sleep duration has been associated with more severe pain.¹⁰ Moreover, 48–74% of patients with migraine and 26–72% of patients with TTH identified “lack of sleep” as a factor triggering a headache attack.^{11,12} Interestingly, although stress is considered to precipitate headaches, its role has been proposed to be less robust than previously suggested, at least in migraine.¹³

In this review, we discuss the role of sleep disturbances in TTH and migraine, as well as potential interactions between emotional and psychological factors with sleep quality. We conducted a search in PubMed for English-language papers published between 1990 and July 2017. The following search terms were used: ‘tension-type headache’, ‘migraine’, ‘sleep disturbances’, ‘sleep deprivation’, ‘sleep quality’, ‘depression’, ‘anxiety’, ‘pressure pain sensitivity’, and ‘insomnia’. Reference lists of included articles were searched for additional articles, and articles introducing general concepts were included. Papers were selected by reading the method section of the full papers. Articles on other headache conditions were excluded.

Sleep disturbances in TTH and migraine

Prevalence and comorbidities

The term ‘sleep disturbances’ includes sleep disorders, such as insomnia or obstructive sleep apnea, as well as other sleep perturbations, such as poor sleep quality.¹⁴ Sleep deprivation has been proposed to have severe effects on human health: it is a risk factor for the presence of neurologic diseases in general, and particularly, headaches.¹⁵ Indeed, headache disorders and sleep disorders have a well-established comorbid association.^{16,17}

In patients with chronic headache, insomnia seems to be the most common sleep disorder. Kelman and Rains found that approximately half of individuals with migraine reported at least occasional symptoms of insomnia, 38% reported sleeping for less than 6 h per night, and 50% reported that sleep disturbances triggered their

migraines.¹⁸ Uhlig and colleagues observed that the prevalence of insomnia was 1.8 times higher in subjects with TTH compared with those without headache.¹⁹ The same study also found migraine to be linked with an increased risk of insomnia (odds ratio [OR] 1.4–2.6).¹⁹ In another study, insomnia was found to be even more common in individuals with TTH than in those with migraine.²⁰ De Luca Canto and colleagues reported that TTH and migraine were also associated with sleep bruxism with respective ORs of 3.12 (95% confidence interval [CI] 1.25–7.7) and 3.8 (95% CI 1.8–7.8).²¹

It is important to note that the sleep problems increase in line with the frequency of headaches; indeed, the majority (68–84%) of individuals with chronic migraine suffer from insomnia on a near-daily basis.²² In fact, insomnia is considered a risk factor for higher headache frequency, particularly in TTH and migraine.²³

Besides loss of sleep, poor sleep quality may also be a risk factor for progression from episodic to chronic TTH.²⁴ Moreover, worse sleep quality has been associated with a higher intensity of headache in patients with TTH.²⁵ Chronic headaches have been linked with daytime sleepiness and snoring.²⁶ Poor sleep quality has several components such as sleep disruption, early morning awakening, and difficulty in falling asleep, which may explain some of the inconsistency in studies evaluating its role in headache. Although Caspersen and colleagues found worse self-perceived sleep quality in patients with TTH, they also reported that the hours of sleep per night were not significantly different between headache patients and healthy controls.²⁷

According to a recent study, subjects with migraine experience more insufficient sleep than those with nonmigraine headache.²⁸ Discrepancies between studies are related to the fact that sleep disturbances can have different manifestations depending on each particular headache. Supporting this hypothesis, Verma and colleagues observed that subjects with chronic TTH showed better slow-wave sleep but significantly increased daytime sleepiness compared with those with chronic migraine.²⁹

Bidirectional relationship

Finally, clinicians should be aware that association between headaches and sleep disorders is

bidirectional: headache promotes sleep disturbances, but sleep disturbances can also precede and trigger headaches. For example, a large population-based cohort study reported a higher risk (adjusted hazard ratio 3.52, 95% CI 3.28–3.79) of developing a subsequent migraine in subjects with non-apnea sleep disorders.³⁰ Further, patients with headaches are at significantly higher risk of developing sleep problems (OR 2.5, 95% CI 2.0–3.1) than headache-free subjects, regardless of specific headache type.³¹ In this study, adults with headache reported more difficulty in initiating sleep (OR 2.0, 95% CI 1.6–2.5), difficulty staying asleep (OR 2.5, 95% CI 2.1–3.0), early morning awakening (OR 2.0, 95% CI 1.7–2.5), and more daytime fatigue (OR 2.6, 95% CI 2.2–3.2).³¹ This bidirectional relationship can be related to the fact that sleep and headaches share common brain structures, such as the thalamus, hypothalamus, and brainstem nuclei, including the locus coeruleus and raphe nuclei.³²

Poor sleep quality is an umbrella term including symptoms that can interact with several other variables. Sleep quality is usually self-defined by the patient on the basis of several characteristics such as total sleep time, sleep onset latency, total wake time, sleep fragmentation, sleep efficiency, and the presence of sleep-disruptive events.³³ An individual will describe their sleep quality based on several aspects, including tiredness on waking and throughout the day, feeling rested and restored on waking, and the number of awakenings that they experienced in the night. A better understanding of the potential relationships between these variables potentially associated with sleep quality in patients with TTH and migraine could assist clinicians in determining better therapeutic programs.

Clinical and emotional variables associated with sleep quality

Sleep and depression

A recent systematic review found moderate evidence indicating that depression, anxiety, poor sleep, medication overuse, stress, and poor self-efficacy for managing headaches were potential factors associated with poor prognosis and unfavorable outcomes from preventive drug treatment in chronic headaches.³⁴ It is possible that these variables interact at the same time, but at different levels, in patients with headache. Among these variables, particular attention has been

given to mood disorders, i.e. depression and anxiety, because they are commonly associated with sleep disturbances.³⁵

In the general population, prevalence of depression is 4.4–5.0%³⁶ and that of anxiety 4.8–11%,³⁷ respectively. TTH is often associated with comorbid anxiety and depression.³⁸ For example, a recent study has reported anxiety to feature in 9.5% of individuals with TTH and depression in 14.2%.³⁹ Individuals with chronic TTH were particularly likely to experience anxiety (21.4%, OR 4.0).³⁹ Another study reported the prevalence of depression to be increased (64%) in patients with chronic headaches.⁴⁰

Sleep, depression, and pain sensitivity

Chronic pain,⁴¹ including headache,⁴² has been reported to be associated with impaired sleep quality and depression, and poor sleep quality has been linked to higher levels of depression and pain.⁴³ Moreover, poor sleep quality is associated with lower daily life activities⁴⁴ in patients with chronic pain, including those with migraine.⁴⁵ This association may be mediated by the capability of depression and sleep disorders to trigger hyperalgesic responses within the central nervous system by increasing excitability of nociceptive firing.⁴⁶ An example of this hyperexcitability, allodynia, is a clinical sign of central sensitization strongly related to sleep quality in individuals with migraine.⁴⁷ Moreover, patients with TTH who exhibit sleep disturbances also show lower pressure pain thresholds.⁴⁸ Bezov and colleagues suggested that unfulfilled need for sleep enhances central sensitization, probably underlying the observed pressure sensitivity to pain in patients with TTH.⁴⁹ Others have reported sleep disturbances and depression to be independently associated with sensitivity to pressure, supporting an independent role for each factor.⁵⁰ Although it is possible that a bilateral relationship exists, it is more likely that depression leads to a lowered pain threshold than *vice versa*, particularly given that the relationship persisted after adjustment for pain group.⁵⁰ These findings have led to the hypothesis that underlying etiology of depression, sleep, and headaches can share common brain mechanisms,²⁴ that is, hypothalamic alterations and serotonin and melatonin dysregulation.⁵¹ Another mechanism may be an emotional modulation of pain by depression *via* supraspinal mechanisms.⁵² It is more plausible that depression and poor sleep quality enhance central

sensitization leading to decreased pain thresholds, rather than the opposite.

Sleep and headache frequency

Poor sleep may contribute to this increased pain sensitivity by also increasing the frequency of headache attacks, given the finding that severity and frequency of sleep problems increase in line with the frequency of headaches.¹⁰ In fact, it has been found recently that depression and sleep quality mediated the relationship between headache frequency and the emotional burden of headache and pain experience in a sample of patients with chronic TTH.⁵³ To summarize, a complex interplay of sleep quality, depression, and headache seems to underlie the increased excitability of the central nervous system.

Clinical applications

Despite the uncertainty over the biological mechanisms of the interactions described above, they have several implications for clinical practice. Given that poor sleep quality is a common trigger of TTH and migraine, management of sleep perturbations seems crucial. In this review, we have described factors associated with poor sleep quality, including depression, emotional stress, and pain hypersensitivity. Some of these factors, namely, emotional stress and depression, are also modifiable risk factors of chronic pain.⁵⁴

Pain alleviation *per se* may not be the most effective strategy to improve sleep quality in patients with headache. Rather, sleep quality may be best restored by reducing emotional stress and pain sensitivity, potentially combined with proper management of depressive symptoms. Therefore, current findings suggest that therapeutic management of patients with TTH and migraine should include approaches targeting depression (i.e. psychological approaches), the emotional burden of the headache (i.e. cognitive behavioral techniques), quality of sleep (i.e. coping strategies, a conscious effort from the patient to solve a personal problem), and pain (i.e. pharmacologic drugs and physical interventions). This multimodal therapeutic proposal agrees with current literature showing that longer sleep periods is a common self-management coping strategy used by subjects with TTH⁵⁵ and that cognitive behavioral treatment of insomnia produced large reductions in the frequency of headache.⁵⁶ This multimodal approach, comprising pharmacologic

treatment, education, and lifestyle modification including sleep hygiene, has been also proposed as a therapeutic strategy in children suffering from headaches.⁵⁷

Conclusion

Research findings support an association between TTH, migraine, and sleep disturbances. This association is bidirectional: headache can promote sleep disturbances but sleep problems can also trigger headache. The bidirectional association can be explained by the fact that sleep and headache share common brain structures and pathogenic mechanisms. The interactions between sleep quality, depression, headache, and pain sensitivity provide an opportunity for multimodal therapeutic intervention.

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Conflict of interest statement

The authors declare no conflicts of interest in preparing this article.

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