Chapter 76

Synthesis of Tension-Type Headache Mechanisms

Lars Bendtsen and Jean Schoenen

The mechanisms leading to tension-type headache have been investigated in a number of good studies over the recent years, and it has become clear that this disorder is not caused by either peripheral (mainly muscular) factors or central factors as previously suggested. The pathophysiology is multifactorial and varies between subjects, and in most patients with frequent tension-type headaches both peripheral and central mechanisms are probably involved.

BACKGROUND

Chronic muscle pain is a very prevalent disorder, which affects some regions of the body more often than others. Andersson et al. (1) found that the most common location of chronic muscle pain was the shoulder and neck regions in which chronic muscle pain was reported by 30% of the general population, followed by low back pain affecting 23% of the population. Muscle pain from the shoulder and neck as well as from chewing and facial muscles probably plays an important role in tension-type headache, which may be the most common form of myofascial pain (6,10). Myofascial tissues are constructed to move; muscles need exercise, whereas change of position is necessary for joints and fasciae. Long-term immobilization or static posture affects these tissues and causes them to hurt. During normal functioning, there is a constant cross-talk between myofascial tissues and the central nervous system, eliciting the necessary changes in position and rest. In this way, the normal person is kept free of myofascial pain. Every time slight discomfort is felt from myofascial tissues there are afferent impulses in small-diameter myelinated Aδ- and unmyelinated C-fibers (*nociception*). This physiologically important afferent input, however, may be a latent source of pain, depending on the central modulation of nociception, which may explain why myofascial pain is so common.

But why is shoulder and neck pain and tension-type headache more common than myofascial pain from other areas in the body? One reason could be that pain thresholds to pressure are lower (increased sensitivity) in the cranium than in the extremities (19). Moreover, it was recently demonstrated that muscle pain sensitivity is higher in the trapezius than in the anterior tibial muscle, and that temporal summation of pain is higher in muscle than in skin in the trapezius, but not in the anterior tibial, region (3). Chewing and neck muscles are involved in emotional behavior, such as facial expression, aggression, and gnashing of teeth, as well as in stabilization of the head, and the head and face have a particular large cortical sensory representation. Pain perception is not a simple reflection of afferent noxious input, but a dynamic process that is highly influenced multiple factors, for example, past experience and emotional status. Liability to central sensitization in response to repetitive noxious input as well as the degree of descending inhibition may differ between input from extracranial and pericranial myofascial tissues (3). Thus, there are a multitude of factors that may explain the high prevalence of tension-type headache.

GENETIC PREDISPOSITION

Because of the enormous prevalence and variability in frequency and severity of tension-type headache, any inheritance is almost certain to be polygenic. Sufferers of tension-type headache must by chance have many affected first-degree relatives. The population relative risk in relatives compared with normal controls has been calculated in a single study. In chronic tension-type headache, the risk was increased threefold, indicating a genetic predisposition (18). The transmission suggested complex inheritance. At present, we adopt the view that the great majority of the population, perhaps all, have the potential to develop

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tension-type headache if exposed to sufficiently strong environmental factors.

ENVIRONMENTAL AND PSYCHOLOGICAL FACTORS

Headaches are generally reported to occur in relation to emotional conflict and psychosocial stress, but the cause–effect relationship is not clear. Stress and mental tension are the most frequently reported precipitating factors, but they occur with similar frequency in tension-type headache and migraine (22). These findings are in correspondence with the findings of widely normal personality profiles in subjects with episodic tension-type headache, whereas studies of subjects with the chronic form often reveal higher frequency of depression and anxiety (9,16). As in other chronic pain disorders, psychological abnormalities in tension-type headache may be viewed as secondary rather than primary (9) and anxiety and depression are probably comorbid with chronic tension-type headache.

MUSCULAR FACTORS

The origin of pain in tension-type headache has traditionally been attributed to increased contraction and ischemia of head and neck muscles. However, it has been demonstrated that muscle activity is normal or only slightly increased in tension-type headache (10), and that muscle lactate levels are normal during static muscle exercise in patients with chronic tension-type headache, ruling out muscle ischemia as cause of the pain (2). A large number of studies have consistently shown that the pericranial myofascial tissues are considerably more tender in patients with tension-type headache than in healthy subjects, and that the tenderness is positively associated with both the intensity and the frequency of tension-type headache. These findings are valid both for patients with episodic and for patients with chronic tension-type headache and both during and outside of headache (10,13). It has also been demonstrated that the consistency of pericranial muscles is increased (2).

The increased myofascial pain sensitivity in tension-type headache could be caused by release of inflammatory mediators resulting in excitation and sensitization of peripheral sensory afferents (6). This hypothesis was challenged in a recent study investigating in vivo interstitial concentrations of inflammatory mediators and metabolites in a tender point of patients with chronic tension-type headache (5). Ashina et al. (5) found no difference in these substances between patients and healthy controls during rest or in response to static exercise. The authors suggested that tender points are not sites of ongoing inflammation. Mork et al. infused a combination of endogenous substances into the trapezius muscle and reported that patients with frequent episodic tension-type headache developed more pain than healthy controls (17). Concomitant psychophysical measures indicated that a peripheral sensitization of myofascial sensory afferents was responsible for the muscular hypersensitivity in these patients.

To summarize, pericranial myofascial pain sensitivity is increased in patients with tension-type headache. Peripheral sensitization of myofascial nociceptors could play a role in the increased pain sensitivity, but firm evidence is lacking.

CENTRAL PAIN MECHANISMS

The stimulus–response function for pressure versus pain in pericranial muscles is not only quantitatively but also qualitatively altered in patients with chronic tension-type headache (7). This is most likely explained by central sensitization at the level of the spinal dorsal horn/trigeminal nucleus. The pain sensitivity in general has been found normal in patients with episodic tension-type headache (10). In contrast, pressure–pain detection and tolerance thresholds are reduced in patients with chronic tension-type headache (6,21). These patients are also hypersensitive to electrical and thermal stimuli and the sensitivity to the various stimulus modalities (pressure, thermal, and electrical) is increased both at cephalic and extracephalic locations (6,12,21). The fact that chronic tension-type headache patients are hypersensitive to several types of stimuli applied both at cephalic and extracephalic locations strongly indicates that the pain sensitivity is affected at the supraspinal level.

Sensitization of pain pathways is associated with activation of nitric oxide synthase (NOS), and NOS inhibitors reduce central sensitization in animal models of persistent pain. The analgesic effect of a NOS inhibitor was therefore examined in patients with chronic tension-type headache, and it was found that the drug significantly reduced headache (4) as well as pericranial myofascial tenderness and hardness (2). In addition, infusion of a nitric oxide donor induces tension-type headache in these patients (2). Sarchielli et al. reported increased platelet NOS activity in patients with chronic tension-type headache, possibly reflecting central upregulation of NOS (20). These pharmacologic data strongly support the idea that central sensitization is involved in the pathophysiology of chronic tension-type headache.

To summarize, the central nervous system is sensitized both at the level of the spinal dorsal horn/trigeminal nucleus and supraspinally in patients with chronic tension-type headache; central pain processing may be normal in patients with episodic tension-type headache.

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BIOCHEMICAL ABNORMALITIES

The role of neurotransmitters and neuromodulators has been extensively examined in plasma, cerebrospinal fluid, and muscle, but no consistent abnormalities have been detected (2,5,6,11). It is possible that the applied techniques have not been sufficiently sensitive, or that the most relevant compartments, for example, specific neuronal pathways, have not been examined. The latter has not been possible for ethical reasons in humans, but might be feasible if a reliable animal model is developed.

A MODEL OF TENSION-TYPE HEADACHE

Individual Episode

In healthy subjects, the processing of pain from myofascial tissues is finely regulated, such that the degree of perceived pain is appropriate for the actual situation. The nociceptive system allows the detection of potential harmful events and enables the individual to react appropriately to these, for example, to avoid unphysiologic working positions that cause painful pericranial muscles and headache. The painful stimulus from the periphery is usually eliminated by actions from the individual and, if necessary, by local reparative mechanisms in the myofascial tissues, and the properties of the nociceptive system are normally not altered after a short-lasting painful episode. This may be representative for the nociceptive system in subjects with rare episodes of tension-type headache.

Under some conditions, the painful stimulus from the pericranial myofascial tissues may be more prolonged or more intense than normal. The mechanisms behind this are unknown, but may include increased muscle activity or the release of various chemical mediators secondary to local pathologic conditions. Increased muscle activity secondary to psychogenic stress is likely to be of relevance in this respect, because the psychogenic stress condition may cause a prolonged increase of muscle tone via the limbic system and at the same time potentiate pain facilitation from the brain stem to the spinal dorsal horn (14). In most subjects, these conditions are self-limiting because of central pain modulatory mechanisms and local reparative processes and are experienced

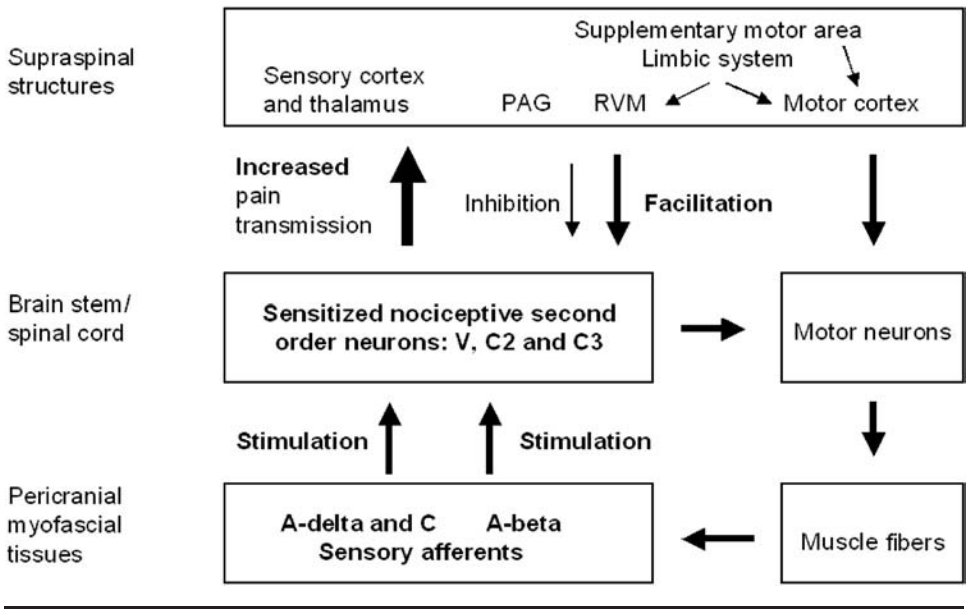

FIGURE 76-1. A model of chronic tension-type headache. The model states that the main problem in chronic tension-type headache is sensitization of dorsal horn neurons owing to increased nociceptive inputs from pericranial myofascial tissues. Important alterations from the normal pain state are presented in bold: The nociceptive input from myofascial Aδ- and C-fibers is increased for unknown reasons, resulting in plastic changes in the spinal dorsal horn/trigeminal nucleus. The increased nociceptive stimulation of supraspinal structures may result in increased facilitation and decreased inhibition of pain transmission at the level of the spinal dorsal horn/trigeminal nucleus and in increased pericranial muscle activity. Together these mechanisms may induce and maintain the chronic pain condition. *Abbreviations:* V, trigeminal nerve; C2 and C3, second and third cervical segment of the spinal cord; PAG, periaqueductal grey; RVM, rostral ventromedial medulla. (Reproduced from Bendtsen L. Central sensitization in tension-type headache—possible pathophysiological mechanisms. *Cephalalgia.* 2000;20:486–508, with permission.)

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as frequent headache episodes for a limited period of time.

How Chronicity May Develop

In predisposed individuals, the prolonged nociceptive input from the pericranial myofascial tissues may lead to sensitization of nociceptive second-order neurons at the level of the spinal dorsal/trigeminal nucleus (Fig. 76-1). The pathophysiologic basis for the increased susceptibility to central sensitization is unknown. Possible mechanisms include an impaired supraspinal inhibition of nociceptive transmission in the spinal dorsal horn. In the sensitized state, the afferent Aβ-fibers that normally inhibit Aδ- and C-fibers by presynaptic mechanisms in the dorsal horn, on the contrary stimulate the nociceptive second-order neurons. In addition, the effect of Aδ- and C-fiber stimulation of the nociceptive dorsal horn neurons is potentiated, and the receptive fields of the dorsal horn neurons are expanded (8). The nociceptive input to supraspinal structures is therefore considerably increased, which may result in increased excitability of supraspinal neurons as well as decreased inhibition or increased facilitation of nociceptive transmission in the spinal dorsal horn, that is, in generalized pain hypersensitivity. The central neuroplastic changes may also increase the drive to motor neurons both at the supraspinal and at the segmental level, resulting in slightly increased muscle activity and in increased muscle hardness. It is possible that low-grade tension that normally does not result in pain does so in the presence of central sensitization. By these mechanisms, the central sensitization may be maintained even after the initial eliciting factors have been normalized, and the individual then experiences daily headaches. This hypothesis (6) may account for the majority, but not all, cases of chronic tension-type headache. In some patients the central dysfunction, for example, deficient supraspinal descending inhibition, may be the primary abnormality making the individual more susceptible to a normal level of nociceptive input, and in other patients the disorder may be purely central with no interaction with the periphery.

To summarize, pericranial myofascial mechanisms are probably of importance in episodic tension-type headache, whereas sensitization of pain pathways in the central nervous system owing to prolonged nociceptive stimuli from pericranial myofascial tissues seem to be responsible for the conversion of episodic to chronic tension-type headache (Fig. 76-2). This hypothesis delineates two major targets for future treatment strategies: (a) to identify the source of peripheral nociception in order to prevent the development of central sensitization and thereby the conversion of episodic into chronic tension-type headache, and (b) to reduce established central sensitization (2,6,10,15).

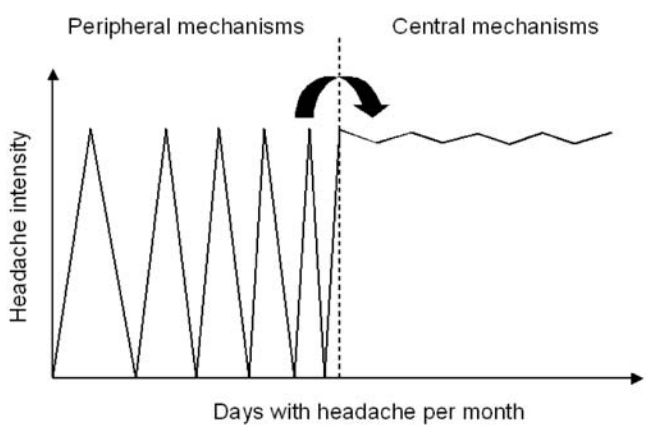

FIGURE 76-2. Prolonged nociceptive stimuli from pericranial myofascial tissues may lead to sensitization of pain pathways in the central nervous system and thereby be responsible for the conversion of episodic to chronic tension-type headache. This hypothesis delineates two major aims for future research: (a) to identify the source of peripheral nociception to prevent the development of central sensitization in patients with episodic tension-type headache, and (b) to reduce established central sensitization in patients with chronic tension-type headache. (Modified from a slide by R. Jensen with permission.)

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