CLINICAL REVIEW

Sleep and pain
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KEYWORDS
sleep, pain, headache, migraine, rheumatoid arthritis, osteoarthritis, fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome

Summary Noxious stimuli and painful disorders interfere with sleep, but disturbances in sleep also contribute to the experience of pain.

Chronic paroxysmal hemicrania and possibly cluster headaches are related to REM sleep. Whereas headache is associated with snoring and sleep apnea, morning headaches are not specific for any primary sleep disorder. Nevertheless, the management of the sleep disorder ameliorates both morning headache and migraine.

Noxious stimuli administered into muscles during slow-wave sleep (SWS) result in decreases in delta and sigma but an increase in alpha and beta EEG frequencies during sleep. Noise stimuli that disrupt SWS result in unrefreshing sleep, diffuse musculoskeletal pain, tenderness, and fatigue in normal healthy subjects. Such symptoms accompany alpha EEG sleep patterns that often occur in patients with fibromyalgia. The alpha EEG patterns include phasic and tonic alpha EEG sleep as well as periodic K alpha EEG sleep or frequent periodic cyclical alternating pattern. Moreover, alpha EEG sleep, as well as sleep-related breathing disorder and periodic limb movement disorder, occur in some patients with fibromyalgia, rheumatoid arthritis and osteoarthritis. Depression and not alpha EEG sleep are features of somatoform pain disorder. Disturbances in sleep, pain behaviour and psychological distress influence return to work in workers who have suffered a soft tissue injury, e.g., low back pain. Patients with irritable bowel disorder have disturbed sleep and have increased REM sleep. In conclusion, there is a reciprocal relationship between sleep quality and pain. The recognition of disturbed or unrefreshing sleep influences the management of painful medical disorders.

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INTRODUCTION

Both sleep disorders and pain problems are among the most common complaints in society so that it is not surprising that the two conditions frequently coincide. Indeed, common experience reveals that any painful condition will disturb sleep and impact on mood, energy and behaviour. As shown by the recent Gallop Poll, 56 million Americans complain that night-time pain interferes with their falling asleep, promotes awakenings during the night or early morning awakenings [1]. The 1991 General Social Survey by Statistics Canada shows that 44% of people with pain suffer difficulties in initiating and maintaining sleep whereas 19% who have such problems have no pain [2]. The odds ratio for relative risk for the association of insomnia or unrefreshing sleep and pain increases with severity of pain. These pain and sleep problems are especially
prevalent among the elderly [3]. In a survey of 10,216 elderly Swedes, the disturbances in sleep from a variety of painful chronic diseases (including cardiovascular, kidney, arthritis, and metabolic conditions) contribute to subjective daytime sleepiness that is not related to the use of hypnotics [4].

Experimental studies of persistent nociception produced by formalin injection into the tibialis anterior of freely moving cats showed, not only behavioral manifestations of pain, but also increased wakefulness, reduced light and deep slow-wave sleep (SWS). With abatement of the formalin pain stimulation and decline of behavioral manifestation of pain, light sleep appeared, but SWS and REM sleep were greatly decreased. This study suggests that sleep stages are differentially affected by acute painful stimulation [5]. However, sleep disturbance is not simply the result of noxious stimuli or painful medical disease. A Japanese survey of 192 pregnant women shows that during the third trimester backache, aching in the hips, and fetal movements interfere with sleep and reduce daytime alertness [6].

Furthermore, disturbances in sleep affect pain. Experimental studies show that REM deprivation of rats reduces pain threshold as long as 96-h after termination of the REM deprivation [7]. Human studies show that intrinsic disturbances to sleep physiology that accompanies unrefreshing nocturnal sleep influence daytime musculoskeletal pain and fatigue. This paper will review the literature on this interrelationship of sleep and pain in headache, arthritic, nonarticular musculoskeletal disorders, somatoform disorders, and gastrointestinal painful medical conditions.

**HEADACHE AND SLEEP**

Until recently, there have been no epidemiological studies on the relationship of various categories of headaches to sleep and to primary sleep disorders. Paiva et al.'s [8] initial study of 25 patients who complained of nocturnal or morning headaches revealed that relationship of sleep to headaches is complex. Polysomnography resulted in a change of clinical diagnosis in 13 of these patients to include periodic involuntary movement disorder, fibromyalgia and obstructive sleep apnea. Only cluster headaches and paroxysmal hemicrania were related to electroencephalographic (EEG) sleep physiology. In half those patients with tension or migraine headaches there was evidence of a connection to sleep. Subsequently, Paiva et al. [9] extended these observations of nocturnal or early morning (before final awakening) headache symptoms, which represented 17% of their patients in their headache clinic. They found that there was a significant impact of sleep disorders on headache and daytime function. Polysomnography showed that 55% of their subjects had specific sleep disorders. The treatment of the sleep disorder resulted in an improvement or elimination of the headache. However, those subjects who were treated for sleep-related periodic limb movements continued to require additional headache treatment, despite improvement in their sleep. These observations raise the question of the nature of the interaction and association of sleep-related headache and periodic limb movement syndrome (PLMS).

Rather than studying the prevalence of sleep disorders in patients with headache, the correlative studies of the specificity of headache for sleep laboratory evidence for sleep disorders show that headache is not specific to any primary sleep disorder [10,11]. However, Jennum et al. [12] found that self reports of snoring were correlated with complaints of headache in their study of more than 3300 middle aged and elderly Danes. Furthermore, in a large regional Swedish epidemiological study, Ulfberg et al. [13] showed that morning headache among both men and women was three times more prevalent among heavy snorers and patients with obstructive sleep apnea syndrome compared with the general population. In a retrospective study of 80 patients with obstructive sleep apnea, Loh et al. [14] showed that 23 patients who complained of awakening with morning headaches of less than 30 min in duration were likely to be associated with obstructive sleep apnea. Their occurrence and severity were related to the severity of the apnea disorder. As with Kiely et al. [15], who found improvement in headache as well as other symptoms in their controlled prospective clinical trial of sleep apnea with nasal continuous positive airway pressure (CPAP), Loh et al. showed that treatment of obstructive sleep apnea with nasal CPAP or uvulopalatopharyngoplasty reduced headaches [14].

Clinical observations have noted a link between sleep and migraine. Migraine attacks may be precipitated by sleep deprivation or excessive sleep, and sleep may be associated with relief of migraine attacks. In a retrospective study of 121 of 159 migraine patients who described an effect of sleep...
on symptoms, Inamorato et al. [16] showed that in about half the patients who described a relationship of improvement of their migraine with sleep, 30% reported that their attacks were precipitated by sleep, 24% by deprivation and 6% by sleep excess. Earlier studies of patients with migraine who awoke from sleep showed a temporal but not exclusive relationship to REM sleep. Hsu et al. [17] showed that waking with migraine often occurred from REM sleep, and that plasma total catecholamines, and in particular, plasma noradrenaline were higher during sleep disturbance may serve as an indicator of response to pharmacological or surgical treatment of osteoarthritis. Recently, reports have appeared on the beneficial effects of analgesic treatment of osteoarthritic pain and improvement of sleep with either immediate release oxycodone-acetaminophen that was given four times daily or controlled release of oxycodone given at 12-h intervals [27]. These findings are important, especially considering the observation that patients with osteoarthritis of the fingers and morning pain and stiffness had sleep-related PLMS. Patients who had similar joint pathology, but did not have the morning symptoms did not have primary disturbances to their sleep [28]. While we can assume that proper management of osteoarthritic joint pain with analgesics or anti-inflammatory drugs would reduce the nocturnal disturbances, there is the possibility that sleep disturbances may contribute to un-refreshing sleep, pain and fatigue symptoms. Therefore, large-scale sleep laboratory studies are required for patients with osteoarthritis to determine the frequency of primary sleep disorders and the effect of treatment for those sleep disorders on symptoms. In particular, studies are needed on the role of narcotic analgesics, e.g. oxycodone, that are known to favourably influence PLMS versus other non-narcotic medications, e.g. NSAIDs, or glucosamine and chondroitin supplements, on patients with osteoarthritis who may or may not have a primary sleep disorder.

**ARTHRITIC DISEASE AND SLEEP**

Sleep disturbances are troublesome in people with painful rheumatic disease. Seventy-five percent of 688 patients with various rheumatic diseases reported sleep problems [23]. Fatigue, which was present in 88–98% of 1488 patients with rheumatic disorders, was largely explained by pain, sleep disturbance, and depression [24].

**Osteoarthritis and sleep**

Since the late 1980s, several small-scale studies have documented sleep disturbances in patients with osteoarthritis or ankylosing spondylitis. Polysomnographic studies of 14 patients with osteoarthritis show tendencies to light sleep with increased stage one and less stage two sleep than in an age and sex-matched group of healthy subjects [25]. A subsequent study by these researchers showed that osteoarthritic patients are restless during sleep as determined by a motility bed-measuring device [26]. These authors suggest that the sleep disturbance may serve as an indicator of assessing response to pharmacological or surgical treatment of osteoarthritis. 

**Rheumatoid arthritis and sleep**

A number of studies show that sleep disturbance is an important feature of patients with rheumatoid arthritis. Their fatigue is associated with poor sleep, functional disability, greater joint pain, more depression and lower hematocrit than a comparison group of healthy controls [29]. Along with increased weakness and diminished energy Moldofsky et al.
H. MOLDOFSKY, showed an alpha (7.5–11.0 Hz) electroencephalogram (EEG) arousal disturbance during the sleep of patients experiencing an acute flare in their rheumatoid arthritis. Their sleep disturbance was associated with an overnight increase in tenderness in the peripheral joints and in the non-articular tender points typically found in fibromyalgia. Similarly, Landis et al. [31] showed sleep fragmentation and arousal disturbance within the sleep of rats with artificially induced arthritis. While Mahowald et al. [32] described alpha EEG sleep in 13 of 16 patients and fragmented sleep disturbances, they also reported other sleep problems, including periodic limb movements, restless legs syndrome and sleep apnea. The importance of recognizing sleep apnea is highlighted in those patients with instability of the cervical spine, a potential lethal complication of the disease [33]. Lavie et al. [34] confirmed the sleep fragmentation and the excessive alpha EEG activity during non-rapid eye movement (NREM) sleep in the patients with active classic or definite rheumatoid disease. Eight of the thirteen patients also showed either periodic limb movements, or sleep apnea or both [34]. In a subsequent study, Lavie et al. [35] reported on actigraphy monitoring of sleep–wake behaviour over several nights in patients with rheumatoid arthritis, low back pain and healthy controls. They confirmed that rheumatoid arthritic patients tend to have periodic limb movements, more sleep disturbance than controls and those with low back pain, and that their sleep disturbance is related to their symptoms. Similarly, Drewes et al. [36] showed that in comparison to normals, rheumatoid patients had increased alpha EEG sleep and PLMS. Moreover, their statistical model demonstrated a complex but independent relationship of morning stiffness, pain and joint tenderness with awakenings from sleep, stages 2 to 4 and REM sleep. The sleep fragmentation and increased alpha EEG sleep also associated with a tendency to sleepiness as determined by the multiple sleep latency test and increased time for afternoon naps in children with juvenile rheumatoid arthritis [37]. These studies indicate that EEG physiological arousal disturbances during sleep are associated with the painful, stiff joints. In some cases, primary sleep disturbances such as sleep apnea or periodic limb movements may contribute to the morning symptoms. Furthermore, there is the possibility that in the absence of active inflammatory disease the morning symptoms of diffuse myalgia and fatigue may persist along with primary sleep pathologies. Indeed, as indicated above, such was the case in the study of patients with osteoarthritis of the peripheral joints and morning symptoms versus those with similar joint pathology and no morning symptoms [28].

The biochemical mechanisms that result in the morning stiffness and pain of rheumatoid arthritis are not known. Recently, serum hyaluronan and antigenic keratan sulfate activity from blood samples taken 1 h after arising in the morning were shown to be directly related to the severity of disease. Moreover, in comparison to normals and a matched group of rheumatoids who remained in bed, hyaluronan remained elevated 3 h later in comparison to measures taken 1 h before morning awakening. This substance as well as antigenic keratan sulfate and matrix metalloproteinase-3 did not change in the rheumatoids who remained at rest [38]. Such chronobiological metabolic studies are important in illuminating diurnal symptom changes that occur in this disease.

Ankylosing spondylitis

The quality of life in ankylosing spondylitis is adversely affected by a combination of pain, stiffness, fatigue and sleep problems but not commonly by mood problems or social relationships [39]. A study of the inter-relationships of sleep with these troublesome symptoms shows that patients with ankylosing spondylitis who experience daytime fatigue have more sleep disturbance, more functional disability, pain and stiffness than those who do not claim fatigue [40].

NON-ARTICULAR MUSCULOSKELETAL PAIN AND SLEEP

Back pain and sleep

Low back pain is the most common of all musculoskeletal disorders in young adults, but most back strain injuries resolve within 3 months. The only reported EEG sleep study in back pain subjects was carried out by Hartman and Pivik [41]. They found that chronic low back pain subjects had less restful sleep and more alpha EEG sleep compared to controls. The alpha EEG sleep anomaly in such patients might reflect pain stimuli from injured muscles that intrude into sleep. In Drewes et al.


[42] study where different types of pain stimuli were applied during SWS, muscle pain stimuli resulted in a decrease in delta (0.5–3.5 Hz) and sigma (12–14 Hz) and an increase in alpha (8–10 Hz) and beta (14.5–25 Hz) frequencies. They showed that different types of pain stimulation (i.e. resulting in joint pain or cutaneous pain) produce different EEG sleep responses.

As indicated above, Lavie et al. [35] showed that actigraphic measures of sleep–wake behavior of low back pain patients were not significantly different from the patients with rheumatoid arthritis and differed from controls only in the number of sleep wake transitions. A subsequent prospective study by Cesta et al. [43] using similar actigraphic methodology found that measures of sleep, musculoskeletal tenderness and behavior but not pain severity were related to return to work in workers who had low back pain. Low back pain subjects reported more disturbed and unrefreshing sleep, and had longer awakenings on the actigraph recordings, compared to controls. 80% of low back pain workers returned to work by 15 weeks post-injury, at which time the subjects reported improvement in non-restorative sleep, and in somatic depressive symptoms. The 20% of subjects who did not return to work slept somewhat longer, reported greater functional disability, had more generalized tenderness, but showed no differences in pain severity or mood compared to those who returned to work. Similarly, Crook and Moldofsky’s [44] longitudinal, prospective behavioral study of 148 workers who suffered a soft tissue strain or sprain injury showed that those subjects who had not returned to work at 21 months post-injury were more likely to describe an increase in sleep complaints, diffuse pain, fatigue and psychological distress compared with subjects who had returned to work. Those subjects with the greatest number of pain sites, highest functional disability scores and the highest pain behavior, showed an improvement in pain and functional disability over time but sleep disturbances, fatigue, psychological distress, interference in social relations and recreation and consequent handicaps worsened over time [45].

**Chronic illnesses with diffuse pain, fatigue and sleep**

In a variety of chronic diffuse painful musculoskeletal conditions where there is no evidence for structural pathology, sleep disturbances, and daytime fatigue are common. Diffuse musculoskeletal pain, fatigue, unrefreshing sleep and psychological distress are not confined to patients with a diagnosis of fibromyalgia. Such symptoms along with a hypersensitivity to various environmental, food and tactile noxious stimuli are also found in patients with chronic fatigue syndrome (CFS), irritable bowel syndrome and temporomandibular joint disorder. More than 90% of patients with fibromyalgia and chronic fatigue syndrome describe disturbed sleep [46]. In a study of patients with recurrent abdominal cramps and functional disturbances in bowel, i.e. irritable bowel syndrome (IBS), 74% reported poor sleep [47]. These authors found a significant correlation between morning IBS symptoms and the quality of the prior night’s sleep. Sleep disturbances, in particular, nocturnal bruxism have been thought to play an etiological role in some patients with temporomandibular joint dysfunction (TMD) [48]. The non-restorative sleep is not only common in patients with primary fibromyalgia, but such sleep disturbances are common in patients with primary Sjogren’s syndrome who also have co-morbid fibromyalgia [49] and in patients with unexplained chronic fatigue in systemic lupus erythematosus [50].

**Fibromyalgia and sleep**

Clinical studies of patients with fibromyalgia show that the sleep disturbances are intimately related to the somatic symptoms and not to personality. Kolar et al. [51] found that the myalgia and tender points in specific anatomic regions, that are characteristic of fibromyalgia, are related to unrefreshing sleep. Jacobsen and Danneskiold-Samsoe [52] showed that sleep quality was associated with musculoskeletal tenderness. Therefore, the poorer the sleep, the greater the number of tender points in patients with fibromyalgia. The number of tender points and painful regions, and the frequency of poor sleep and fatigue were not related to psychological status [53].

In 1975, Moldofsky et al. [54] described an alpha (7.5–11 Hz) EEG NREM sleep anomaly in patients with fibrositis (fibromyalgia). They proposed that the alpha EEG sleep is related to the unrefreshing sleep, diffuse myalgia, numerous localized areas of tenderness in specific anatomic areas and mood symptoms [54]. Such symptoms were experimentally produced by noise-disruption of stage...
4 NREM (delta, SWS) or deep sleep in normal sedentary people [55]. Subsequently, Older et al. confirmed that noise-induced disruption of SWS was followed by generalized aching and fatigue in healthy subjects, but their modified protocol did not demonstrate changes in tenderness [56]. Recent research by Lentz et al. [57] confirmed the induction of increased tenderness, diffuse myalgia and fatigue over 3 nights of noise-induced disruption of SWS in normal middle-aged women. However, Lentz et al. [57] reported that the disruption of SWS did not lead to alpha-delta sleep or increased alpha activity in the sleep EEG. A possible explanation for Lentz et al.’s claim that there were no increased alpha and delta waves lies in their methodology. They relied upon an automated computerized system that delivered a 2000 Hz tone whenever delta Hz occurred for more than 3 s. The sound was turned off if delta power dropped, or if “high frequency power” increased (i.e. 8 to 11.5 Hz and 14.5 to 35 Hz). The authors acknowledge that the method was not satisfactory in eliminating the delta frequency so that the subjects were aroused by having their names called or by gentle shaking on the third or final night of disrupted sleep. Their results showed that the method abolished stages 3 and 4 sleep on the first 2 nights and permitted negligible amounts of SWS on the final or third night of disrupted sleep. Therefore, their automated computerized method likely excluded from their analyses the presence of noise induced phasic alpha delta sleep. In contrast, the study of Moldofsky et al. disrupted stage 4 sleep with noise, which did not eliminate stage 3 sleep. This method permitted the artificial phasic induction of alpha delta sleep, which was seen visually and shown by EEG frequency analyses [54].

Moreover, as shown in Roizenblatt et al. [72] report on frequency analyses of the sleep EEG of patients with fibromyalgia, a similar method that Lentz et al. employed (the Oxford Sleep Acquisition Computer System for measuring zero crossing combined with period amplitude and pattern recognition) proved to be less effective in detecting phasic alpha, and alpha/delta time in stage 2 sleep in patients with fibromyalgia than the Fourier frequency transformation method. In the Lentz et al. paper, 11 of 12 subjects had increase in their low arousal scale (worn out, tired, sluggish, sleepy, exhausted and fatigue) as the result of the disruption of SWS. Clearly, the Lentz et al. experiment supports the notion that disruption of their healthy women’s sleep artificially induces unrefreshing sleep as well as musculoskeletal pain and fatigue. Such arousal disturbance in sleep, pain, and fatigue symptoms that are artificially induced in healthy people, and also observed in patients with fibromyalgia and CFS may reflect a vigilant state during sleep with daytime symptoms of non-restorative sleep [58]. This sleep over 3 nights of noise-induced disruption of SWS physiological disturbance and the coincident perception of light, unrefreshing sleep results in not only a daytime hyperalgesic state, but the pervasive fatigue and cognitive impairment observed in patients with fibromyalgia and CFS [59]. However, the symptoms were not induced by the disruption of SWS in a small group of physically fit long distance runners [55]. This observation suggests that physical fitness plays a significant role in fibromyalgia. Subsequently, cardiovascular fitness programme was shown to reduce tenderness [60], and increase muscle strength [61].

A number of investigators have reported on the alpha EEG sleep disorder in patients with fibromyalgia [58, 62–73]. Most of these studies comprise small numbers of subjects. Carette et al. [72] reported that only eight of 22 patients in their drug trial of amitriptyline showed the alpha EEG sleep. This paper stands in contrast to several other authors who have used systematic computerized EEG analyses and have found a much higher likelihood of the presence of alpha EEG sleep pattern in fibromyalgia patients who have been specifically assessed for this disorder [68–72]. Furthermore, until recently the characteristics of the alpha EEG sleep pattern have not been clarified. The computerized analyses of the sleep EEG by Roizenblatt et al. [72] demonstrated three alpha EEG sleep patterns: phasic (50% of patients vs 7% of normals), tonic (20% of patients vs 9% of normals) and low alpha (30% of patients vs 84% of normals). Those with the phasic pattern of the alpha intrusion in SWS (or alpha-delta sleep) were more likely to have increased post-sleep tenderness and subjective pain, longer duration of pain, poor sleep efficiency and less SWS than the other groups. Such differences in sleep physiology suggest differing pathogenesis and possible differences in management of the fibromyalgia syndrome.

Recent findings of increased overnight sympathetic activity using electrocardiographic methodology is consistent with the notion of an arousal
disturbance during the sleep of patients with fibromyalgia [74,75]. The possibility of a familial or genetic influence in the pathogenesis of the disorder is evidenced by the finding of the alpha EEG sleep pattern in children and their mothers [71]. Furthermore, some patients with fibromyalgia have fragmented sleep as a result of sleep-related periodic, involuntary, arousal disturbances that occur over the course of the night. These periodic sleep-related disturbances include: restless legs or periodic involuntary movement disorder [76,77], sleep-related periodic K-alpha EEG sleep, a variety of frequent cyclic alternating pattern [78], and sleep apnea, especially in men [63,79,80]. Recent studies that have documented disruptions of sleep associated with disturbances in respiration and oxygen desaturation have led to exploration of whether there might be a fundamental disturbance in respiratory function. While fibromyalgia is uncommon in male sleep apnea patients [81], greater nocturnal sleep-related reduction in arterial oxygen saturation was reported in sleepy fibromyalgia female patients versus control subjects [82]. Moreover, Sergi et al. [83] reported that such patients have a lower transfer factor for carbon monoxide from the lungs, and that periodic breathing correlated with the transfer factor for carbon monoxide, number of oxygen desaturations and carbon dioxide tension in arterial blood. Those who complained of daytime sleepiness had more tender points, about twice as many arousals per hour of sleep and lower sleep efficiency than those patients who did not report sleepiness. Moreover, in this sleepy subgroup of fibromyalgia, the transfer factor for carbon monoxide from the lungs was more impaired and they had more periodic breathing.

Although alpha EEG sleep may be found in non-complaining people [84], and is not specific for patients with fibromyalgia [85], the phasic alpha EEG sleep pattern may be a sensitive indicator for the subjective complaints of unrefreshing sleep and daytime symptoms [72,86]. In fact, patients with CFS show similar sleep physiologic disturbances [78,87–89]. In both fibromyalgia and CFS the physiologic arousal disturbances during nocturnal sleep are thought to be related to the daytime symptoms of these illnesses. Whereas normal subjects have least pain sensitivity in the morning [90], patients with fibromyalgia have increased tenderness in the morning, or no overnight improvement in pain [55]. Furthermore, as with CFS [91–93], and in patients with TMD [94], patients with fibromyalgia have cognitive impairment that relates to the chronic disturbance in sleep [59]. Indeed, such patients are more likely than controls to meet lifetime symptom and diagnostic criteria for CFS, fibromyalgia, irritable bowel syndrome, multiple chemical sensitivities and headache [95].

**PAIN IN PSYCHIATRIC DISORDER**

**Somatoform disorder**

The problem of chronic pain in somatoform disorder is perplexing, especially in terms of the connection to fibromyalgia. In order to determine whether those patients with somatoform pain disorder differed from those with fibromyalgia we studied sleep physiology and symptoms. Our research showed that sleep physiology and measures of psychological distress differentiate those patients who show features of “somatoform” disorder from those with fibromyalgia. That is, those patients who described psychological distress associated with the onset or perpetuation of their generalized pain symptoms and had no objective evidence for any disease, showed no specific EEG sleep abnormality versus those with fibromyalgia who showed the alpha EEG sleep disorder, and were more depressed than those with fibromyalgia [96].

**PAIN IN FUNCTIONAL GASTROINTESTINAL DISORDERS AND SLEEP**

**Irritable bowel disorder**

Patients with irritable bowel syndrome (IBS) typically complain of unpredictable bouts of abdominal cramps, bloating, gas, diarrhoea and/or constipation and incomplete evacuation of their bowels. Approximately 57% of such people report that their abdominal pain awakens them from their sleep. Whereas Fass et al. [97] report that sleep disturbance is not related to symptoms of IBS, but is related to the subjective rating of severity of gastrointestinal symptoms in patients with functional dyspepsia. Jarrett et al. [98] suggest that poor sleep leads to more gastrointestinal symptoms on the following day among women with IBS.

Lifetime rates of irritable bowel syndrome are especially common in CFS (92%), fibromyalgia (77%),
TMD (64%) compared with controls (18%) [94]. However, as yet, no comparative sleep studies have been carried out in patients with fibromyalgia, CFS, IBS and TMD to determine whether there is sleep physiological differences among such patients who suffer these poorly understood somatic pain disorders where there is no objective evidence for disease.

There are some reports of alterations of sleep physiology in patients with IBS. Greater amounts of REM sleep were observed in a small group of IBS patients, compared with controls [99,100]. In addition, Orr et al. [100] showed that normally there is a decrease in the amplitude of the dominant electrogastrographic frequency from waking to non-REM sleep, and an increase in the amplitude from non-REM to REM sleep. No such changes were noted in the patients with IBS. However, a subsequent study by this group of investigators revealed that although perception of poor sleep quality was more common in IBS patients than in healthy controls, no differences were observed in sleep efficiency, sleep latency, number of arousals and percentage of SWS [101]. Heitkamper et al. [102] reported greater numbers of awakenings during sleep and a longer latency to REM sleep in IBS versus controls. They also reported on the role of psychological distress on sleep and symptoms. They found that the greater the psychological distress, the less alert and rested women with IBS felt in the morning. The greater the distress, the more time the women spent in SWS and less time in stage 2 and REM sleep. Therefore, the role of psychological distress on sleep physiology and symptoms require further study in functional bowel disorders where pain and fatigue are disabling features of the disorder.

RESEARCH IMPLICATIONS

Moldofsky theorizes that the diffuse myalgia, fatigue, and psychological distress are not only related to a disorder of their sleep-wake system, but also to circadian alterations of associated biologic systems of the body. These include: neurotransmitters (e.g. serotonin, substance P), neuroimmune (e.g. interleukin-1, natural killer cell activities), neuroendocrine (e.g. hypothalamic–pituitary–adrenal/thyroid axes), and the autonomic nervous systems that are altered in patients with fibromyalgia and CFS [103–106]. Future research studies should aim to assess the physiological and behavioural aspects of the sleep and chronobiology of these systems. Such knowledge may provide further insights into the etiology and management of the chronic musculoskeletal pain, fatigue, non-restorative sleep and psychological distress that afflict a substantial proportion of the population. Furthermore, there are age and gender differences in patients who complain of persistent pain and insomnia with females more prevalent than males in both conditions, yet little is known about the physiological and behavioural mechanisms that are involved. Therefore, research is required on the contribution of age, gender, and psychological distress to sleep and pain problems.

The notion that nonrestorative sleep is inextricably linked to bodily pain, fatigue, and psychological distress has been known for more than 4000 years. In the Sumerian epic of Gilgamesh, the hero complains, “my face was not sated with sweet sleep, I fretted myself with wakefulness, I filled my joints with misery” [107].

Practice Points

1. Chronic paroxysmal hemicrania and possibly cluster headaches are associated with REM sleep.
2. Management of disordered sleep often benefits morning headache and migraine.
3. Primary sleep disorders are frequent in patients with rheumatic illness and may contribute to morning musculoskeletal pain and fatigue.
4. Alpha EEG sleep disorder commonly occurs in patients with fibromyalgia. Phasic alpha EEG sleep (alpha-delta sleep) is associated with increased post-sleep pain and tenderness in this disorder.

Research Agenda

1. An understanding is required of the pathological mechanisms that underlay the experimental production of musculoskeletal pain and fatigue in healthy subjects as the result of disruption of their slow-wave sleep.
2. Furthermore, in order to determine how unRefreshing sleep contributes to the pain and fatigue of patients with fibromyalgia and chronic fatigue syndrome, knowledge is
required on the mechanisms that contribute to the sleep/wake-related dis regulation of neurotransmitters involved in pain (e.g. serotonin, substance P), neuroimmune (e.g. interleukin-1, natural killer cell activities), neuroendocrine (e.g. hypothalamic–pituitary–adrenal/thyroid axes) endocrine and autonomic nervous functions. Such knowledge should lead to better methods of management of fibromyalgia and chronic fatigue syndromes and to preventative measures when these disorders occur following muscle sprain or strain injuries.

3. As persistent pain and insomnia is more prevalent in females, research is required on the contribution of age, gender, and psychological distress to the pain and sleep problems in rheumatic disease, e.g. rheumatoid arthritis.

4. Large-scale clinical and laboratory studies are required to advance the understanding of the role of sleep and its significance in the management of various painful disorders including headache, migraine, rheumatic disease and irritable bowel syndrome.

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