

Sleep and pain: relationship, mechanisms, and managing sleep disturbance in the chronic pain population

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Sleep is a vital and ubiquitous process that is essential for optimal bodily functioning and overall health.¹ Despite the need for good-quality sleep, nonrestorative or reduced sleep has become an increasingly global issue.² Several observational and experimental studies have shown the impact of sleep disturbance on pain processing and perception.^{3,4} Long-term dysregulation of the “pain system” could lead to chronic pain, which is characterized by pain persisting for three months or longer.⁵ Previous studies on the prevalence of insomnia in the chronic pain population showed a range from 25% to 73%.^{6,7} These differences in point estimates among studies may be attributable to methodological heterogeneity such as differences in study samples, participant criteria, and various insomnia assessments. The prevalence of sleep disturbance may be higher in chronic pain samples than other chronic illnesses (e.g., asthma or diabetes),⁸ and patients with chronic pain report more sleep problems (49%) than people without chronic pain (17%).⁹ Further, the prevalence of chronic pain may be as high as 50% in individuals with chronic insomnia versus 18% in those without insomnia.⁹

It is widely established that sleep and pain are reciprocally associated, such that pain could lead to sleep disturbance and sleep loss could exacerbate pain.³ Although previous reviews have summarized the literature on the bidirectionality of this relationship,^{3,4,10–12} there is some inconsistency in the included studies. Recent studies have begun to investigate the mechanisms underlying the sleep-pain association and treatment options for sleep disturbance in the context of pain. The objectives of the present review are to (1) discuss the current literature on the sleep-pain interaction and its bidirectionality; (2) summarize findings on the mechanisms contributing to the relationship between sleep and pain; and (3) describe the use of hybrid interventions to target sleep disturbance and pain in patients with chronic pain.

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Relationship between sleep and pain

Observational and experimental research

It is widely established that the relationship between sleep and pain is bidirectional, such that pain negatively impacts sleep and sleep disruption can exacerbate pain. Table 1 shows the micro-longitudinal and longitudinal studies investigating the sleep-pain relationship. In a 1-year longitudinal population study, pain symptoms increase the risk of developing insomnia, and conversely, insomnia was a significant predictor of persistent pain.²¹ Similarly, a population-based cohort study found that total sleep time (< 6 or ≥ 9 h) was predictive of pain frequency and more pain the next day, and pain predicted subsequent sleep duration.¹⁸ In patients with major burn injury, having insomnia at discharge was associated with more pain two years later, and greater levels of pain were predictive of sleep-onset insomnia.³³

The relationship between sleep and pain appears to be dose dependent.^{25,28,29,35,38} An 11-year cohort study of older adults found a dose-dependent and reciprocal relationship between sleep disturbance and persistent pain severity and number of pain sites.²⁹ Similarly, an 11-year study of 19,271 adults found an increased risk of insomnia in those with headaches lasting ≥ 7 days per month (odds ratio = 2.2) versus those with headaches of lower frequency.²⁸ Another cohort study of 6676 older adults found that the risk of insomnia three years later was greatest in individuals reporting widespread pain (odds ratio = 2.31) versus those having some (odds ratio = 1.57) or no pain at baseline.³⁵

A growing body of literature suggests that sleep disturbance may predict pain to a greater extent than pain predicts sleep disturbance (Table 1). Sleep disturbance may increase the likelihood of the development, exacerbation, or spreading of chronic pain or painful conditions.^{13,14,16–22,24–32,35,36,38} At a 1-year follow-up visit, patients with fibromyalgia reported that poorer sleep quality predicted more pain, whereas pain was not related to sleep.¹⁵ In veterans with musculoskeletal pain, change in sleep at three months was a stronger predictor of change in pain at 12 months, than vice versa.²³ In older patients with osteoarthritis and insomnia, short-term improvements in sleep after treatment of insomnia and pain were more predictive of pain improvements at an 18-month follow-up, than vice versa.³⁷ In patients with chronic noncancer pain, sleep quality significantly predicted pain levels the next day, whereas pain did not reliably predict sleep.³⁴ Better patient-reported sleep quality predicted less pain in the first half of the next day, which is consistent with greater physical activity and physical functioning after sleep with better quality.^{39,40} Overall, these studies demonstrate that sleep disturbance significantly and strongly predicts the onset or

Table 1**Micro longitudinal and longitudinal studies investigating the sleep-pain relationship.**

References	Participants	Design	Assessments	Pain → Sleep	Sleep → Pain
Agmon and Armon ¹³	General population N = 3421	Baseline; 3.7 y follow-up	Self-report insomnia and back pain onset	No	Yes*
Aili et al ¹⁴	General population N = 1249	Baseline; 5-y follow-up; 18-y follow-up	Self-report sleep problems and chronic widespread pain onset	NA	Yes* (stronger for 5-y follow-up vs. 18-y follow-up)
Bigatti et al ¹⁵	Fibromyalgia N = 492	Baseline; 1-y follow-up	Self-report sleep quality and pain	No	Yes*
Boardman et al ¹⁶	General population N = 1589	Baseline; 1-y follow-up	Self-report sleep problems and headache onset	NA	Yes
Dzierzerski et al ¹⁷	Insomnia N = 50	Daily for 14 d	Actigraphy; self-report sleep diary and pain	NA	Yes*
Edwards et al ¹⁸	General population N = 971	Daily for 8 d	Self-report sleep and pain onset	Yes (weaker)**	Yes***
Generaal et al ¹⁹	General population N = 1860	Baseline; 6-y follow-up	Self-report insomnia and chronic multisite musculoskeletal pain onset	NA	Yes***
Gupta et al ²⁰	General population N = 3171	Baseline; 15-mo follow-up	Self-report sleep problems and chronic widespread pain onset	NA	Yes
Jansson-Fröjmark and Boersma ²¹	General population N = 1746	Baseline; 1-y follow-up	Self-report insomnia and pain persistence	Yes**	Yes**
Jones et al ²²	General population N = 1881	Baseline; 4-y follow-up	Self-report sleep problems and musculoskeletal pain onset	NA	Yes (good-quality sleep was predictive of good musculoskeletal health)
Koffel et al ²³	Chronic musculoskeletal pain N = 250	Baseline; 1-y follow-up	Self-report insomnia and pain severity	Yes* (weaker)	Yes***
Lin et al ²⁴	Insomnia N = 1579	Baseline; 10-y follow-up	Clinician-diagnosed myofascial pain syndrome	NA	Yes***
Mork and Nilsen ²⁵	Women N = 12,350	Baseline; 10-year follow-up	Self-report sleep problems and fibromyalgia onset	NA	Yes***
Nitter et al ²⁶	Women N = 1338	Baseline; 17-y follow-up	Self-report sleep problems and chronic pain onset	NA	Yes (disrupted sleep was a risk factor for chronic pain onset)
O'Brien et al ²⁷	Women N = 22	Daily for 14 d	Actigraphy; self-report sleep diary and daytime pain ratings	Yes***	Yes***
Ødegård et al ²⁸	General population N = 19,271	Baseline; 11-y follow-up	Self-report insomnia and headache and chronic musculoskeletal complaints	Yes (stronger for headache pain vs. chronic musculoskeletal pain)	NA
Pan et al ²⁹	General population N = 1099	Baseline; 10.7-y follow-up	Self-report sleep and pain; knee radiography	Yes (stronger for knee pain vs. multisite pain)	Yes (stronger for multisite pain vs. knee pain)
Quartana et al ³⁰	Temporomandibular joint disorder N = 53	Baseline; 3-mo follow-up	Self-report insomnia and pain	No	Yes*
Salwen et al ³¹	Knee osteoarthritis and insomnia N = 74	Baseline; 6-mo follow-up	Actigraphy; self-report sleep diary and CBT-I-related reductions in pain	NA	Yes* (sleep duration was predictive of pain reduction during CBT-I)
Skarpsno et al ³²	General population N = 6033	Baseline; 10-y follow-up; 20-y follow-up	Self-report sleep quality and chronic pain onset	NA	Yes (change from good to poor sleep between baseline and 10-y follow-up was predictive of chronic pain onset at 20-y follow-up)
Smith et al ³³	Insomnia and major burn injury N = 333	Baseline; 24-mo follow-up	Self-report insomnia and pain	Yes**	Yes**
Tang et al ³⁴	Chronic pain and insomnia N = 119	Daily for 7 d	Actigraphy; self-report sleep and pain	No	Yes*** (sleep quality was predictive of pain the next day)
Tang et al ³⁵	General population N = 6676	Baseline; 3-y follow-up	Self-report insomnia onset and musculoskeletal pain based on American College of Rheumatology criteria	Yes (stronger for widespread pain vs. some pain)	NA

Table 1
(Continued)

References	Participants	Design	Assessments	Pain → Sleep	Sleep → Pain
Uhlig et al ³⁶	General population N = 13,429	Baseline; 11-y follow-up	Self-report insomnia and chronic musculoskeletal complaints	No	Yes
Vitiello et al ³⁷	Osteoarthritis and insomnia N = 367	Baseline; 18-mo follow-up	Self-report insomnia and pain severity	No	Yes***
Wiklund et al ³⁸	Localized pain N = 959	Baseline; 24-mo follow-up	Self-report insomnia and spreading of pain	NA	Yes

NA indicates not applicable.
*P < 0.05.
**P < 0.01.
***P < 0.001.

maintenance of chronic pain conditions, whereas pain does not reliably predict the risk of sleep problems. Given that demographic characteristics, such as physical or psychological comorbidities, may influence the strength of the sleep-pain relationship, future studies should account for the confounding effects of these variables.^{41,42}

In healthy participants, experimental sleep restriction (ie, one night sleep time reduced by 50%) can increase sensitivity to pain and spontaneous pain levels.⁴³ In patients with rheumatoid arthritis versus healthy control participants, four hours of continuous sleep restriction during one night led to increased patient-reported pain, fatigue, depression, and anxiety.⁴⁴ In pain-free participants, partial sleep deprivation through forced awakenings each hour increased spontaneous pain and reduced pain inhibition the next day.⁴⁵ Hence, the causal effects of sleep disturbance on subsequent pain may be attributed to disruptions in sleep continuity, and treatment of sleep fragmentation could act as a viable target for managing chronic pain.

Mechanisms underlying the sleep-pain relationship

Although the relationship between sleep and pain is well known, the mechanisms contributing to this association are not fully understood. The current literature suggests the potential roles of dopaminergic signaling, opioidergic signaling, central pain modulation, inflammation, negative affect, and pain-related beliefs and coping behaviors (Fig. 1). The following section will describe these factors in more detail.

Dopaminergic signaling

Dopamine is a neurotransmitter involved in regulating sleep, arousal, and responses to rewards.⁴⁶ Although dopamine signaling is increased during wakefulness, reduction of dopamine neurotransmission promotes sleepiness.⁴⁶ Moreover, sleep disturbance may lead to alterations in dopamine signaling, such that dopamine receptor (D2/D3) availability is reduced after acute sleep loss.^{47,48} Although a previous study by Volkow et al⁴⁸

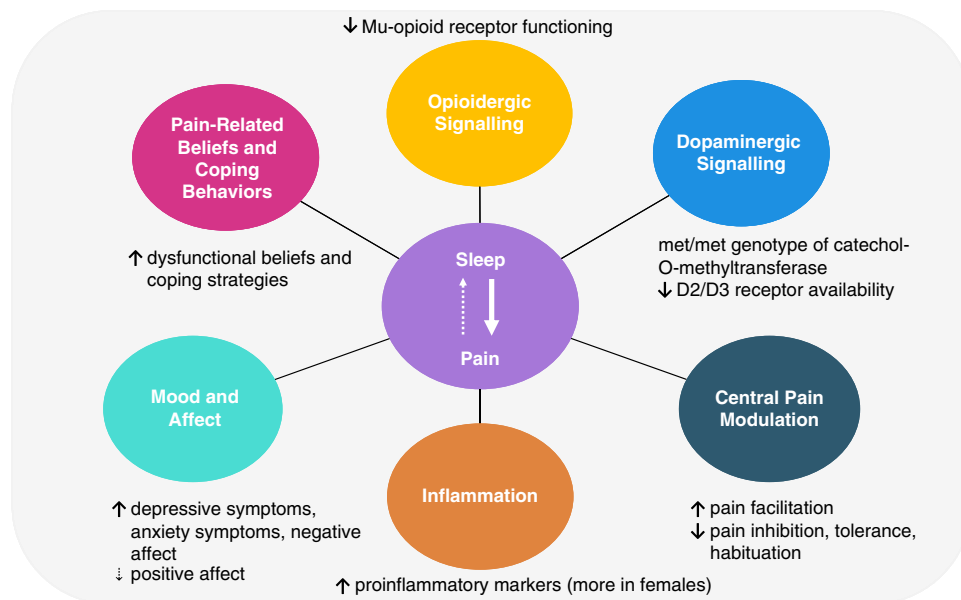


Figure 1. Possible mechanisms underlying the relationship between sleep and pain. [full color online](#)

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attributed this diminished availability to increased dopamine neurotransmission, subsequent research by the group found that a downregulation of D2/D3 receptors led to lower receptor availability. Nonetheless, changes in dopamine signaling caused by sleep disturbance may affect responses to rewards and chronic pain. For instance, imaging studies of patients with fibromyalgia have shown reduced dopamine metabolism,⁴⁹ which is associated with reduced gray matter density.⁵⁰ In a rodent model, the administration of modafinil (a dopamine reuptake inhibitor) reversed sleep loss-induced elevations in pain sensitivity.⁵¹ Hyperalgesia caused by rapid eye movement sleep loss was associated with diminished activity of dopamine D2 receptors located in the nucleus accumbens, whereas injection of a D2 agonist prevented this hyperalgesia.⁵² In addition, certain genotypes of chemicals involved in dopamine neurotransmission, such as the enzyme catechol-*O*-methyltransferase, could be associated with lower positive affect in the presence of greater pain in patients with fibromyalgia.⁵³ Women with fibromyalgia and the met/met genotype of catechol-*O*-methyltransferase reported more pain during days when pain attention or catastrophizing was greater than in participants with other genotypes of the enzyme.⁵⁴ These findings suggest that altered dopamine signaling as a result of sleep disturbance may influence pain processes. More research is needed to understand the roles of dopamine signaling and the reward system in the sleep-pain relationship, and whether they act as mediators or moderators for this association. These findings could help develop interventions to regulate dopamine neurotransmission or reward system functioning, thereby mitigating the deleterious effects of sleep disturbance on pain and responses to pain flare-ups.

Opioidergic signaling

Opioids exert their analgesic effects by activating mu-opioid receptors of the endogenous opioid system.⁵⁵ Patients with chronic pain have shown diminished mu-opioid activation during a painful experience in comparison with a neutral environment.⁵⁶ Although opioids may be prescribed for noncancer pain management, a recent meta-analysis of 96 randomized-controlled trials (RCT) found significant but small associations between opioid use and improvements in chronic noncancer pain and physical functioning versus placebo, and similar effects to non-opioid interventions.⁵⁷ However, chronic opioid use may have adverse effects, including nausea, excessive daytime sleepiness, sleep-disordered breathing, and hyperalgesia.^{57–59}

Rodent models suggest that sleep deprivation reduces the analgesic effects of mu-opioid receptor agonists.⁶⁰ Experimentally induced partial (50%) or total sleep deprivation in healthy participants has been shown to induce hyperalgesia and dysregulate endogenous pain inhibition processes, which are mediated by endogenous opioid peptides.^{61,62} Although experimental administration of 0.1 mg/kg of morphine may decrease rapid eye movement and slow wave sleep in pain-free individuals,⁶³ a recent meta-analysis reported that opioid therapy may lead to improvements in self-reported sleep quality in patients with chronic pain.⁵⁸ In addition, the immediate negative impact of opioid therapy on sleep may not be observed by patients without adequate access to sleep monitoring instruments. Future experimental studies should increase understanding of the potential mediating role of endogenous opioid systems in the sleep-pain association, and observational studies should investigate whether opioid therapy moderates

the effects of sleep disturbance on pain outcomes in patients with chronic pain.

Central pain modulation

Another mechanism underlying the sleep-pain relationship involves changes in central pain modulation processes. Central pain modulation is characterized by processes in the central nervous system that affect pain signal processing.⁶⁴ Impaired central pain modulation can result in enhanced pain facilitation (defined by temporal summation or enhanced pain perception in response to repeated exposure to painful stimuli) or decreased pain inhibition (defined as suppressed pain perception in response to repeated exposure to painful stimuli).⁶⁴ Experimental studies have shown that sleep loss or disruption may elevate pain signals by increasing pain facilitation and reducing pain inhibition, tolerance, and habituation.^{62,65–68} Alterations in these central pain modulatory circuits have been found to increase the risk of chronic pain,^{69–71} suggesting that sleep disturbance in the form of sleep fragmentation or reduced sleep duration may contribute to the development of chronic pain through central pain pathways. Females may be more vulnerable to impairments in central pain modulation induced by total sleep deprivation than males.⁶⁶ Further, the central pain modulatory processes underlying the relationship between sleep disturbance (in the form of forced awakenings) and central sensitization (defined as more pain caused by an increased gain of nociceptive pathways) may differ between the sexes, whereby sleep disturbance causes hyperalgesia in males versus enhanced temporal summation in females.⁶⁸ Lower self-reported sleep quality and sleep efficiency have also been associated with impaired central pain modulatory processes in chronic pain samples.^{65,72} Patients with insomnia have also demonstrated decreased pain inhibition, which may indicate a “ceiling effect” on pain-inhibitory processes caused by prolonged subthreshold pain.⁷³ Interestingly, changes in certain central pain modulation processes, specifically pain habituation, may only occur after chronic sleep deprivation, and prolonged sleep recovery may be needed to reverse these changes.⁶⁷ Further research is needed to increase understanding on the role of central pain modulatory circuits in the sleep-pain relationship. Future studies should also determine the extent to which changes in central pain processes recover upon sleep restoration.

Inflammation

Inflammatory mechanisms may play a role in elevating the pain response after sleep deprivation. Experimental sleep loss has been shown to increase levels of proinflammatory markers, such as the tumor necrosis factor alpha, C-reactive protein, and interleukins.^{74–76} Indeed, a recent meta-analysis of 72 studies found that sleep disturbance, shorter sleep duration <7 hours, and longer sleep duration >8 hours were associated with enhanced concentration of interleukin-6 and C-reactive protein.⁷⁷ Elevations in these markers appear to be more exacerbated in females after partial sleep deprivation of 4 hours,⁷⁸ which may contribute to the increased risk of chronic pain in females versus males.⁷⁹ Moreover, previous research has shown significant correlations between higher levels of interleukin-6 and sleep deprivation-induced increases in pain.⁷⁵ Longitudinal research has also shown that every 1-hour reduction in sleep duration is related to increased levels of C-reactive protein and interleukin-6 5 years later.⁸⁰ These findings indicate the need for experimental

trials and longitudinal studies to determine the causality of these associations and whether restoring sleep could reduce the activation of proinflammatory markers.

Depressive symptoms, anxiety symptoms, and negative affect

Both the chronic pain and insomnia populations commonly report comorbid depressive^{81,82} and anxiety symptoms.^{83,84} Conversely, previous research has investigated whether sleep influences pain indirectly through psychosocial factors. For instance, depressive symptoms,^{19,27,85–87} negative affect,^{88,89} and anxiety symptoms^{21,90} may contribute to sleep disturbance reported by patients with chronic pain, and have been shown to mediate the relationship between sleep disturbance and pain outcomes (eg, pain severity, pain interference, disability, development of chronic pain). In turn, sleep may influence the relationship between pain and depressive symptoms,^{91,92} and sleep disturbance may predict the onset of depression in patients with chronic pain.⁹³ Further, pain may mediate the sleep-depression association⁹⁴ and depressive symptoms may also mediate the association between insomnia or short sleep duration (≤ 6 h) and chronic pain development.¹⁹ Further, depressive symptoms have shown to be greatest in patients with poorer sleep and pain, suggesting that sleep disturbance may increase the risk of depression in patients with severe chronic pain.⁸⁷ Although it is postulated that poorer sleep could result in decreased positive affect, there are mixed findings on whether positive affect mediates the relationship between sleep and pain.^{89,95,96} Further studies are needed to enhance knowledge on the interrelationships between sleep, pain, and mood outcomes in adults with chronic pain. Findings from this research could aid the development of interventions that identify and target sleep disturbance and negative affect in the context of chronic pain.

Pain-related beliefs and coping behaviors

Several cognitive processes may contribute to the severity of sleep disturbance, including pain-related dysfunctional beliefs and attitudes about sleep,⁹⁷ the belief that sleep is an “escape” from pain,⁹⁸ worries about sleep,⁹⁹ and presleep arousal.¹⁰⁰ Pain catastrophizing is the tendency to exaggerate the threat level of a painful stimulus, feel helpless, and show an inability to reduce pain-related thoughts during a painful experience.¹⁰¹ Pain catastrophizing has shown to be a risk factor for sleep disturbance in patients with chronic pain, and indirectly influences pain severity and interference through sleep disturbance.¹⁰² In patients with knee osteoarthritis, pain catastrophizing moderated the association between sleep efficiency and central sensitization, such that patients with lower sleep efficiency and greater catastrophizing had increased central sensitization.¹⁰³ Pain catastrophizing is increased in patients with both chronic pain and insomnia.¹⁰⁴ Moreover, having comorbid chronic pain and insomnia is associated with increased avoidance of cognitive tasks that were perceived to worsen symptoms or exceed the participant’s mental capacity.¹⁰⁴

Behavioral mechanisms may also play a role in sleep disturbance among patients with chronic pain. Due to their pain, patients are often underactive and report low levels of physical activity.¹⁰⁵ It is well established that engaging in physical activity throughout the day will elevate levels of adenosine, a sleep-promoting neurochemical, thereby increasing the pressure to fall

asleep (ie, sleep drive) and facilitating slow-wave sleep at night.¹⁰⁶ Anticipating pain or avoiding activity can also worsen pain intensity¹⁰⁷ and lower physical functioning.¹⁰⁸ In addition, patients may spend a significant portion of their day in a lying position to cope with their pain or fatigue, perform their daily tasks in the bedroom environment, or take naps in an attempt to “catch up on their sleep.”^{109,110} However, these behaviors may exacerbate sleep disturbance, reduce sleep drive, and strengthen the bedroom environment as a conditioned stimulus for arousal instead of sleepiness.¹¹¹ Indeed, patients with chronic pain and insomnia engage in more safety-seeking behaviors than those with pain or insomnia alone.¹⁰⁴ Due to their sleep-interfering effects, these behaviors are often identified and challenged during treatment for insomnia.

Other factors influencing the sleep-pain relationship

Other potential mediators of the sleep-pain association include fatigue,¹¹² cortisol reactivity,¹¹³ and pain helplessness.⁹⁴ Although diet and physical activity are not indicated as mediators, both factors have been related to sleep^{114,115} or pain.^{116,117} Future studies should conclusively determine whether these factors play mediating roles in the impact of sleep disturbance on pain.

Managing sleep disturbance in patients with chronic pain

Hybrid interventions for managing sleep disturbance and chronic pain

Given the prominent co-occurrence of chronic pain and sleep disturbance, an emerging trend in research is the development of hybrid programs involving cognitive behavioral therapy for insomnia (CBT-I) and chronic pain (CBT-P).¹¹⁸ CBT-I is the first-line recommended treatment for insomnia,^{119,120} and involves a multicomponent approach to targeting cognitive and behavioral processes that contribute to persistent sleep disturbance.¹¹¹ Common CBT-I components include psychoeducation on sleep, relaxation training, stimulus control (instructions to strengthen the bed/bedroom as a cue for sleepiness, such as avoiding wakeful activities in the bed), sleep restriction (increase the proportion of time spent in bed asleep vs. awake), cognitive restructuring, and strategies to prevent relapses.¹¹¹ Several RCTs have investigated the effectiveness of CBT-I in patients with comorbid insomnia and chronic noncancer pain. In a meta-analysis of 12 RCT, Selvanathan et al¹²¹ reported significant treatment effects on self-reported sleep questionnaires (eg, Insomnia Severity Index, Pittsburgh Sleep Quality Index), sleep diary variables (sleep onset latency, wake after sleep onset, and sleep efficiency), pain, and depressive symptoms at posttreatment.

Common CBT-P components include psychoeducation on pain, relaxation/mindfulness exercises, activity pacing, training to improve pain-related communication, cognitive restructuring, and coping strategies for pain flare-ups.¹²² Although their long-term efficacy remains unclear, CBT-P could lead to small to moderate improvements in pain interference and intensity.¹²³ Our recent meta-analysis demonstrated that combining CBT-I with CBT-P can lead to significant effects on pain intensity and interference at posttreatment versus control (i.e., no or passive

intervention), but not at follow-up.¹²¹ However, these effects on pain were similar to trials utilizing CBT-I alone.¹²¹

Evidently, future studies incorporating robust and randomized-controlled designs are warranted to further investigate the effectiveness of hybrid treatments in patients with chronic pain and sleep disturbance. Future studies should utilize longer follow-up periods and compare the effects of hybrid treatments in patients with different levels of pain. Research on hybrid treatments could provide valuable insight into providing patient care through a more holistic and efficient approach, whereby multiple comorbidities can be simultaneously treated through one program.¹¹⁸ In turn, these programs can increase the accessibility of sleep and pain care by reducing wait-times and the need to obtain referrals to separate sleep or pain management services, which can ultimately lead to enhanced, comprehensive, and coordinated patient care.

Conclusions

Sleep disturbance is a common complaint in patients with chronic pain. The relationship between sleep and pain is bidirectional, with evidence suggesting that sleep is a stronger predictor of pain than vice versa. Experimental and observational research has elucidated the potential direct (dopaminergic and opioidergic neurotransmission, central pain modulation, inflammation) or indirect (mood, pain-related beliefs and coping behaviors) mechanisms underlying the relationship between sleep and pain. In patients with chronic pain, CBT-I is an established therapy for sleep disturbance improving health outcomes beyond sleep and pain, including depressive and anxiety symptoms. Despite the growing body of literature on this topic, further research is warranted on the following areas: (1) examine longitudinal data to conclusively determine whether sleep disturbance predicts the onset and persistence of chronic pain, (2) utilize preclinical models, imaging methods, and epidemiological studies to investigate the mechanisms underlying the sleep-pain association, and (3) conduct experimental trials to assess the feasibility and efficacy of delivering CBT-I in a hybrid (eg, CBT-I/CBT-P) format in individuals with chronic pain and sleep disturbance. Given the significant variability in sleep and pain assessments in the reviewed studies, future studies should consider the suitability of an assessment based on the aspect of sleep or pain it measures, along with the need to include self-reported and objective instruments. As both chronic pain and sleep disturbance have been shown to impair overall health and increase burden on the individual and society, developing methods to prevent and manage sleep disturbance and pain would be an important step toward addressing these global health issues.

Conflict of interest disclosure

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