Research Reviews
Sleep Disturbance and Pain

Introduction: Sleep is crucial for both musculoskeletal and neurological repair and restoration.[1-5] Despite the importance of sleep, sleep disturbance – manifesting as deficient sleep duration, quality, or a combination thereof – is all too common. In fact, over one-half of Americans experience intermittent sleep disturbance and nearly one-quarter suffer from a chronic sleep disorder.[6] In individuals with pain, sleep disturbance is highly prevalent.[7-9] In fact, in one study, 88% of patients with chronic pain reported sleep complaints[10] and in another, 53% had sleep scores suggestive of clinical insomnia.[8] A growing body of literature is providing insight into the relationship between disturbed sleep and pain.[11-13]

Literature Overview: Research suggests that the relationship between sleep and pain is bidirectional – disrupted sleep may influence pain and pain may influence sleep.[11,13] In a recent review, Cohen et al.[14] suggest that disturbed sleep may be a common consequence of pain, particularly chronic pain. Pain may prolong sleep latency or promote irregular waking. Indeed, pain does appear to be associated with subsequently disturbed sleep.[15,16] Interestingly, Finan et al.[11] suggest the converse relationship – sleep disturbance may more reliably predict pain than pain predicts sleep. Despite being made ten years ago, this assertion is still supported. In fact, research suggests that sleep disturbance predicts increased pain intensity,[17,18] increased pain frequency,[19] and hyperalgesia.[17,20] Sleep disturbance also notably predicts new onset of pain[21,22] and worse prognosis.[11] And, when sleep improves, pain improves.[23-25] Evidence continues to emerge about the link between disturbed sleep and pain. Given the high prevalence of sleep disturbance in both clinical and non-clinical populations,[6-8] as well as the apparent influence of sleep on pain, new considerations for pain management may need to be made, particularly with regard for screening, diagnosis, and treatment.

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Articles

Afolalu EF, Ramlee F, Tang NKY. Effects of sleep changes on pain-related health outcomes in the general population: A systematic review of longitudinal studies with exploratory meta-analysis. Sleep Med Rev. 2018;39:82-97. doi:10.1016/j.smrv.2017.08.001

Abstract

Emerging longitudinal research has highlighted poor sleep as a risk factor of a range of adverse health outcomes, including disabling pain conditions. In establishing the causal role of sleep in pain, it remains to be clarified whether sleep deterioration over time is a driver of pain and whether sleep improvement can mitigate pain-related outcomes. A systematic literature search was performed using PubMed MEDLINE, Ovid EMBASE, and Proquest PsycINFO, to identify 16 longitudinal studies involving 61,000 participants. The studies evaluated the effect of sleep changes (simulating sleep deterioration, sleep stability, and sleep improvement) on subsequent pain-related outcomes in the general population. A decline in sleep quality and sleep quantity was associated with a two- to three-fold increase in risk of developing a pain condition, small elevations in levels of inflammatory markers, and a decline in self-reported physical health status. An exploratory meta-analysis further revealed that deterioration in sleep was associated with worse self-reported physical functioning (medium effect size), whilst improvement in sleep was associated with better physical functioning (small effect size). The review consolidates evidence that changes in sleep are prospectively associated with pain-related outcomes and highlights the need for further longitudinal investigations on the long-term impact of sleep improvements.

Finan PH, Goodin BR, Smith MT. The association of sleep and pain: an update and a path forward. J Pain. 2013;14(12):1539-1552. doi:10.1016/j.jpain.2013.08.007

Abstract

Ample evidence suggests that sleep and pain are related. However, many questions remain about the direction of causality in their association, as well as mechanisms that may account for their association. The prevailing view has generally been that they are reciprocally related. The present review critically examines the recent prospective and experimental literature (2005-present) in an attempt to update the field on emergent themes pertaining to the directionality and mechanisms of the association of sleep and pain. A key trend emerging from population-based longitudinal studies is that sleep impairments reliably predict new incidents and exacerbations of chronic pain. Microlongitudinal studies employing deep subjective and objective assessments of pain and sleep support the notion that sleep impairments are a stronger, more reliable predictor of pain than pain is of sleep impairments. Recent experimental studies suggest that sleep disturbance may impair key processes that contribute to the development and maintenance of chronic pain, including

endogenous pain inhibition and joint pain. Several biopsychosocial targets for future mechanistic research on sleep and pain are discussed, including dopamine and opioid systems, positive and negative affect, and sociodemographic factors.

Haack M, Simpson N, Sethna N, Kaur S, Mullington J. Sleep deficiency and chronic pain: potential underlying mechanisms and clinical implications. Neuropsychopharmacology. 2020;45(1):205-216. doi:10.1038/s41386-019-0439-z

Abstract

Pain can be both a cause and a consequence of sleep deficiency. This bidirectional relationship between sleep and pain has important implications for clinical management of patients, but also for chronic pain prevention and public health more broadly. The review that follows will provide an overview of the neurobiological evidence of mechanisms thought to be involved in the modulation of pain by sleep deficiency, including the opioid, monoaminergic, orexinergic, immune, melatonin, and endocannabinoid systems; the hypothalamus-pituitary-adrenal axis; and adenosine and nitric oxide signaling. In addition, it will provide a broad overview of pharmacological and non-pharmacological approaches for the management of chronic pain comorbid with sleep disturbances and for the management of postoperative pain, as well as discuss the effects of sleep-disturbing medications on pain amplification.

Krause AJ, Prather AA, Wager TD, Lindquist MA, Walker MP. The Pain of Sleep Loss: A Brain Characterization in Humans. J Neurosci. 2019;39(12):2291-2300. doi:10.1523/JNEUROSCI.2408-18.2018

Abstract

Sleep loss increases the experience of pain. However, the brain mechanisms underlying altered pain processing following sleep deprivation are unknown. Moreover, it remains unclear whether ecologically modest night-to-night changes in sleep, within an individual, confer consequential day-to-day changes in experienced pain. Here, we demonstrate that acute sleep deprivation amplifies pain reactivity within human (male and female) primary somatosensory cortex yet blunts pain reactivity in higher-order valuation and decision-making regions of the striatum and insula cortex. Consistent with this altered neural signature, we further show that sleep deprivation expands the temperature range for classifying a stimulus as painful, specifically through a lowering of pain thresholds. Moreover, the degree of amplified reactivity within somatosensory cortex following sleep deprivation significantly predicts this expansion of experienced pain across individuals. Finally, outside of the laboratory setting, we similarly show that even modest nightly changes in sleep quality (increases and decreases) within an individual determine consequential day-to-day changes in experienced pain (decreases and increases, respectively). Together, these data provide a novel framework underlying the impact of sleep loss on pain and, furthermore, establish that the association between sleep and pain is expressed in a night-to-day, bidirectional relationship within a sample of the general population. More broadly, our findings highlight sleep as a novel therapeutic target for pain management within and outside the clinic, including circumstances where sleep is frequently short yet pain is abundant (e.g., the hospital setting).

Whibley D, AlKandari N, Kristensen K, et al. Sleep and Pain: A Systematic Review of Studies of Mediation. Clin J Pain. 2019;35(6):544-558. doi:10.1097/AJP.0000000000000697

Abstract

Objectives: A relationship between sleep and pain is well established. A better understanding of the mechanisms that link sleep and pain intensity is urgently needed to optimize pain

management interventions. The objective of this systematic review was to identify, synthesize, and critically appraise studies that have investigated putative mediators on the path between sleep and pain intensity. Methods: A systematic search of 5 electronic bibliographic databases (EMBASE, MEDLINE, CINAHL, PsycINFO, and the Cochrane Central Register of Controlled Trials) was conducted. Eligible studies had to apply a formal test of mediation to variables on the path between a sleep variable and pain intensity or vice versa. All searches, data extraction and quality assessment were conducted by at least 2 independent reviewers. Results: The search yielded 2839 unique articles, 9 of which were eligible. Of 13 mediation analyses, 11 investigated pathways from a sleep variable to pain intensity. Putative mediators included affect/mood, depression and/or anxiety, attention to pain, pain helplessness, stress, fatigue, and physical activity. Two analyses investigated pathways from pain intensity to a sleep variable, examining the potentially mediating role of depressive symptoms and mood. Although evidence supported a mediating role for psychological and physiological aspects of emotional experiences and attentional processes, methodological limitations were common, including use of cross-sectional data and minimal adjustment for potential confounders. Discussion: A growing body of research is applying mediation analysis to elucidate mechanistic pathways between sleep and pain intensity. Currently sparse evidence would be illuminated by more intensively collected longitudinal data and improvements in analysis.

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