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## The Interrelationship between Sleep and Chronic Pain in Adolescents

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### Abstract

Over half of youth with chronic pain report sleep deficiency including difficulties falling asleep, maintaining sleep, feeling unrested, and experiencing short sleep duration. Sleep deficiency has been shown to play a causal role in the development or worsening of chronic pain, and is associated with a variety of negative consequences for youth with chronic pain. The purpose of this review is to provide a summary of the literature on the interrelationship of sleep and chronic pain in adolescents. We review the impact and prevalence of sleep disturbances, conceptual models of the interrelationship of sleep and pain, biobehavioral mechanisms and risk factors, sleep assessment, and treatment of sleep deficiency and chronic pain in adolescents. Our recommendations for future research include understanding biobehavioral mechanisms that underlie the link between chronic pain and sleep deficiency to help guide development and testing of treatments for co-occurring pain and sleep disturbance in adolescents.

### Keywords

sleep; pain; pediatric; child; adolescent

### Prevalence and impact of chronic pain and sleep deficiency in adolescents

Chronic pain is a debilitating health condition that occurs commonly in adolescents, impacting 25–40%<sup>1–4</sup> of youth. Chronic pain may present as a distinct clinical condition

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(e.g., migraine headaches) as well as within the context of an ongoing chronic disease, such as sickle cell disease, juvenile idiopathic arthritis or cancer<sup>2-4</sup>. Chronic pain is associated with disruption of physical activity, reduced school attendance, high health care utilization and costs, and poor quality of life in youth, as well as emotional distress in both adolescents and parents<sup>1-4</sup>. Risk for ongoing pain, disability, and psychiatric disorders can extend into adulthood,<sup>5</sup> making prevention and treatment of disabling pain in childhood a major public health priority.

Over half of youth with chronic pain report sleep deficiency, defined as a deficit in the quantity or quality of sleep obtained versus the amount needed for optimal health, performance and well-being<sup>3,4</sup>. Valrie and colleagues<sup>2</sup> reviewed 56 studies of youth with juvenile idiopathic arthritis, sickle cell disease, migraine/headache, functional abdominal pain, juvenile fibromyalgia syndrome, and chronic musculoskeletal pain, finding high rates of sleep deficiency across these conditions. On self-report questionnaires, youth with painful conditions report greater sleep disturbances compared to healthy populations including difficulties falling asleep, maintaining sleep, feeling unrested, daytime sleepiness, as well as sleepwalking, sleep-related anxiety, and sleep bruxism<sup>2,4,6-8</sup>.

Fewer studies have used objective assessments of sleep such as polysomnography and actigraphy, and findings are somewhat mixed. The available data generally indicate that youth with painful conditions have more disrupted sleep patterns (e.g., shorter total sleep time, lower sleep efficiency, more time asleep during the day) and greater likelihood for physiologic sleep disorders (e.g., periodic limb movement disorder, sleep disordered breathing, bruxism) than their healthy peers<sup>9-12</sup>. Although most research characterizing sleep deficiency in adolescents with painful conditions has been cross-sectional, the available longitudinal data indicates that sleep deficiency persists over time for youth with chronic pain even after pain symptoms improve<sup>2-5,11,13</sup>.

Deficits in sleep have been linked to a variety of negative consequences for youth with chronic pain, including diminished physical function, poor quality of life and impaired cognitive function<sup>11,14</sup>. Many patients with chronic pain also suffer from psychiatric comorbidities that can impact sleep patterns and sleep quality, such as depression and anxiety<sup>7,13,15,16</sup>. Sleep problems tend to be chronic in this population, persisting over a one-year period and impacting functioning and quality of life<sup>11</sup>.

## Conceptualization of the interrelationship of pain and sleep

Early conceptual models described a bidirectional relationship between pain and sleep, where pain can cause sleep disruptions, and in turn, disturbed sleep can enhance pain sensitivity<sup>6</sup>. As research has accumulated on the interrelationship of sleep and pain in pediatric and adult samples, there are now more studies that support the direction of sleep impacting pain than vice versa<sup>17</sup>. In these studies, the effect of sleep deficiency on subsequent pain is stronger than the effect of pain on subsequent sleep. Longitudinal studies have also indicated that sleep deficiency is associated with the development of new-onset chronic pain as well as worsening pain and disability in individuals with existing pain conditions<sup>2-4,11,18</sup>.

## Biobehavioral mechanisms and risk factors

The development and maintenance of sleep deficiency in chronic pain is likely determined by a number of interacting influences including disease- and pain-specific effects on sleep, shared neurobiological pathways, and behavioral patterns, as well as the effects of medications and other treatments on sleep. Earlier research suggested shared neurobiological pathways (e.g., mesolimbic dopaminergic and opioidergic signaling) as mechanisms to explain the association between pain, sleep and other common comorbidities (e.g., depression, anxiety) 15,17. More recently, Finan and Smith emphasized the effects of dopaminergic pathway disturbance or imbalance on pain sensitivity, arousal promotion and mood changes<sup>15</sup>. Additionally, opioid peptides are thought to play a major role in the regulation of descending pain modulatory systems with impaired pain inhibitory capacity, and sleep deprivation, in turn, leads to dysregulation of the endogenous opioid system as well as attenuation of the effects of  $\mu$ -opioid receptor agonists. Furthermore, opioid receptors regulate pain and sleep in several key nuclei, such as nuclei controlling sleep-wake cycles (i.e., preoptic suprachiasmatic) and those influencing the descending pain inhibition pathway (i.e., periaqueductal gray)<sup>17</sup>.

While there has been growing evidence to suggest an association between chronic pain, sleep deficiency and mood disturbance, the directionality and the temporal dynamics among these co-occurring problems remain unclear<sup>11,17,19–21</sup>. In a study examining predictors of chronic insomnia in youth with persistent pain, pain intensity did not predict chronic insomnia but rather poor sleep habits and higher depressive symptoms emerged as significant predictors of elevated insomnia symptoms over a one-year period<sup>11</sup>. Similar findings were reported in studies that included patients with back pain, facial pain and fibromyalgia<sup>19–21</sup>. Sociodemographic factors (age, sex, and race) are also important correlates of both sleep deficiency and chronic pain<sup>17</sup>. Specifically, more frequent and severe sleep disturbance and/or chronic pain were seen in patients who were of older age, females or African Americans<sup>17</sup>.

## Sleep Assessment

Sleep is a multi-dimensional construct and includes sleep patterns, sleep behaviors, and perceptions of feeling unrested, difficulty falling or staying asleep, waking too early, or experiencing daytime sleepiness. Due to the multidimensional nature of sleep, a variety of tools can be used in sleep assessment including clinical interview, objective measures, and self-report questionnaires. Objective measures of sleep are helpful for understanding sleep physiology and sleep patterns, and include polysomnography and actigraphy.

Polysomnography is typically conducted in a hospital laboratory and records physiological changes that occur during sleep (e.g., heart rate, muscle activation) in order to elucidate physiologic causes of sleep disturbance (e.g., obstructive sleep apnea, restless leg syndrome)<sup>22</sup>. Sleep patterns can also be assessed using actigraphy, which assesses sleep patterns by recording motor movement using a continuous acimetry sensor<sup>23</sup>.

Self-report questionnaires are critical for understanding behavioral causes of sleep disturbance, and can be used alone or in combination with objective measures of sleep.

Multidimensional sleep measures can be helpful to screen for a wide range of behavioral and physiologic sleep problems (e.g., Sleep Disturbance Scale for Children<sup>24</sup>), and include both parent and child self report. More targeted self-report questionnaire are also available to assess specific behavioral sleep-related concerns including daytime sleepiness (e.g., Pediatric Daytime Sleepiness Scale<sup>25</sup>), sleep habits/hygiene (e.g., Adolescent Sleep Hygiene Scale<sup>26</sup>), sleep cognitions (e.g., Presleep Arousal Survey for Children<sup>27</sup>), sleep initiation/maintenance (e.g., Adolescent Sleep Wake Scale<sup>26</sup>, and PROMIS-Sleep disturbance<sup>28,29</sup>). Prospective sleep diaries are also useful for obtaining sleep pattern data and other global daily measurements (e.g., sleep quality); diaries delivered using eHealth and mHealth technologies are becoming more widely available and provide advantages of real time monitoring.

### **Treatment of sleep deficiency in youth with painful conditions**

Very few studies have been conducted to evaluate interventions for addressing sleep deficiency in youth with painful conditions. Insomnia is a common and treatable cause of sleep deficiency and has thus received the most attention. Cognitive-behavioral therapy for insomnia (CBT-I) is recommended by the American Academy of Sleep Medicine as first-line treatment for insomnia in adults<sup>30,31</sup>; however, it can be modified for adolescents with chronic pain. CBT-I targets a range of cognitive, behavioral, and social factors that may perpetuate insomnia such as poor sleep hygiene practices (e.g., too much time in bed) and negative cognitions and attitudes about sleep (e.g., concern about daytime deficits). There is robust evidence from numerous randomized controlled trials, which have demonstrated efficacy of CBT-I for improving sleep in adults with comorbid insomnia and chronic pain<sup>32,33</sup>. However, subsequent improvements in pain after CBT-I treatment have been inconsistent<sup>34,35</sup>.

Treatment for adolescents with co-morbid chronic pain and sleep deficiency is still in initial stages of development and evaluation. In one pilot trial, Palermo and colleagues<sup>36</sup> intervened with adolescents with insomnia and comorbid physical or psychological difficulties, of which approximately 50% had chronic pain. Compared to pre-treatment outcomes, following receipt of a brief 4-session CBT-I protocol, adolescents had improved sleep hygiene and sleep quality, and reduced insomnia symptoms, and improvement in subsequent health-related quality of life and daily functioning. In another pilot trial, Law and colleagues<sup>37</sup> developed and demonstrated preliminary efficacy of a CBT-I intervention for improving sleep and reducing headache frequency in youth with chronic migraine.

Although sleep deficiency in youth can be managed with psychological interventions alone, pharmacologic interventions and combinations of psychological and pharmacologic interventions are also used in practice. A wide variety of medications are commonly prescribed or recommended to treat sleep problems in adolescents including melatonin, antihistamines, antidepressants, and benzodiazepines<sup>38,39</sup>. However, there are minimal data on safety or efficacy of any sleep-promoting medication in pediatric populations<sup>40,41</sup> and further research in this area is needed.

## Conclusions/future directions

Sleep is a critical aspect of health and well-being for children with painful conditions. Because sleep problems are common and associated with negative consequences for youth with chronic pain, clinicians should be prepared to screen for sleep disturbances in this population using available age-appropriate validated sleep measures. There are also several important directions for future research. First, longitudinal studies are needed to better understand common mechanisms underlying sleep and chronic pain in pediatric populations as well as the directionality of their interrelationship in order to develop targeted therapies. Studies that examine biobehavioral mechanisms may be particularly relevant to understanding the link between chronic pain and the most common sleep disturbances of sleep initiation and maintenance difficulties. Second, randomized controlled clinical trials are needed to definitively demonstrate efficacy and safety of interventions for youth with chronic pain and co-morbid sleep deficiency. Interventions include both non-pharmacological treatments including CBT-I as well as commonly used medications such as melatonin. Third, questions remain regarding optimal approaches for matching interventions to patient and family treatment needs. For example, some youth with chronic pain may benefit from less intensive behavioral sleep interventions (e.g., sleep hygiene education), while others may require more intensive approaches such as CBT-I. Still others may benefit most from sleep-promoting medications alone or in combination with psychological treatment. Future work that aims to prospectively identify patient and family treatment needs for sleep and pain management is needed to address questions related to what treatment type and dose will be most effective for which patients.

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