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REVIEW ARTICLES

Pediatric sleep and pain: etiologies, consequences, and clinical considerations

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Study Objectives: To examine current evidence of the relationship between sleep and pain from the neonatal period through adolescence. This review serves as a critical review of the literature and of the needs for future research on pediatric sleep and pain.

Methods: The PubMed online database was queried from January 1, 1960, to March 1, 2020, producing 149 articles applicable to pain and sleep in the pediatric population. Of those, 97 articles were cited in this review with the key articles including over 3800 participants.

Results: The pediatric literature supports the relationship between poor sleep (both sleep efficiency and nighttime awakenings) and subsequent risk for pain, especially among children with chronic disease. The reverse effect of pain on sleep is not yet well delineated. The key moderating factors explored in the literature are pharmacologic and nonpharmacologic therapies, psychologic health, and the etiology of pain. There is evidence that both altered sleep and pain early in life impact neurodevelopment, as seen by changes in sleep structure in clinical studies and alterations in brain development in animal models.

Conclusions: The complicated relationship between sleep and pain is critically important during pediatric development when alterations to a normal sleep structure can have a lifelong impact. It is becoming clear that sleep deprivation and poor sleep quality exacerbate pain. Further research is needed into the complex alterations of sleep in chronic pain conditions as well as treatments to improve sleep in pediatric care.

Keywords: pediatric, neonatal, sleep, pain, neurodevelopment

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INTRODUCTION

Disordered sleep is common among pediatric populations, with one study reporting that 74% of children are affected by sleep problems and, separately, up to 30% of children live with chronic pain.[1] There is overlap in the prevalence of the 2 disorders and increasing evidence that poor sleep quality and frequent night wakening may be a precursor to the development of chronic pain later in life.[2–4] While the clinical consensus has been that the sleep and pain relationship is equally bidirectional, recent evidence suggests that sleep may have a stronger influence on the development of chronic pain than pain's influence on the development of chronic sleep disorders.[2,5] Additionally, pharmacologic treatments, like opioids, for pain negatively impact the structure and quality of sleep.[6,7] An understanding of how providers can optimize sleep quality is of critical importance in the neonatal and pediatric populations due to the lifelong impact of poor sleep on development.

We aim to provide an updated review of the current literature in pediatric sleep and pain. Currently, a 2013 systematic review by Valrie et al[8] investigates the sleep and pain relationship in pediatric literature and highlights the presence of sleep impairment in children and adolescents with persistent pain. A second systematic review,[9] published in 2017, focuses on sleep and its impact on the developing brain, and finds consistent evidence supporting the importance of sleep but emphasized the critical need for more high-quality prospective studies. Existing reviews in pediatric sleep and pain[10–12] have either focused on specific populations or exclude the emerging literature base in animal research describing the potential impact of these disorders on neurodevelopment.

This review seeks to explore the relationship between sleep and pain from the neonatal period through adolescence and specifically to answer 3 questions incompletely understood in pediatrics:

1) Is there sufficient evidence to support a bidirectional relationship between sleep and pain in the pediatric population?
2) What are the key moderating factors to consider in pediatric sleep and pain?
3) What is the impact of sleep and pain disorders on neurodevelopment?

We performed this review of the recent literature and seek to identify future research needs and directions.

METHODS

The PubMed online database was searched from January 1, 1960, to April 1, 2019, using a language filter for English articles. The query "pediatric OR neonatal" and "sleep" and "pain" yielded 929 articles. Changing "pain" to "chronic pain"

yielded 199 articles. Adding "opioid OR opiate OR narcotic" to the first query yielded 104 articles (**Figure 1**).

Additionally, searching the PubMed online database with the query "PICU OR NICU OR pediatric intensive care unit OR neonatal intensive care unit" and "sleep" yielded 662 articles. Adding "pain" yielded 62 articles. The query "PICU OR NICU OR pediatric intensive care unit OR neonatal intensive care unit" and "opioid OR opiate OR narcotic" yielded 820 articles. Adding "sleep" yielded 22 articles.

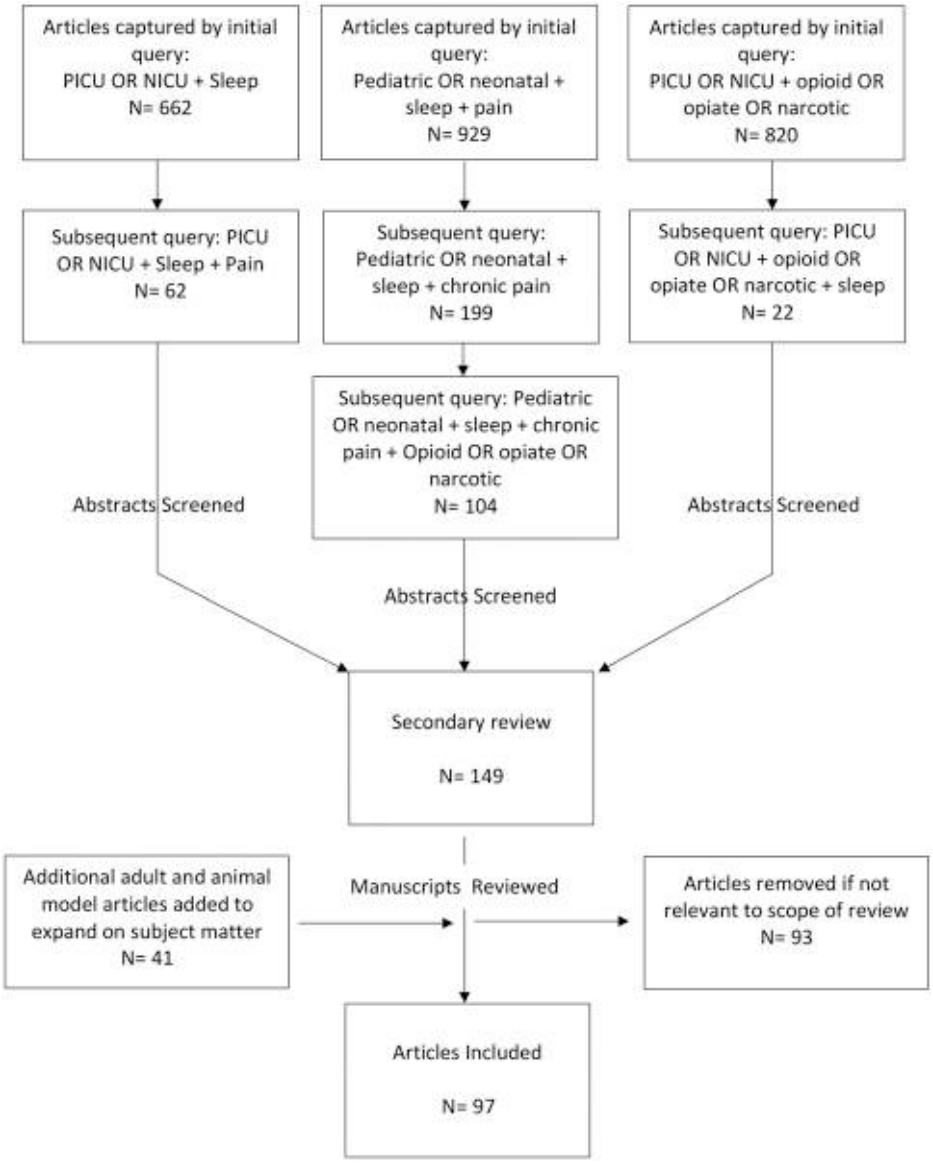
In all, 188 abstracts were screened, and of those, 149 were further reviewed. Articles were excluded if not relevant to the scope of the review. Ninety-eight articles were cited in this review and prospective clinical trials were emphasized. Additional articles were addended in areas not captured by the search. Highlighted articles are summarized in **Table 1**.

RESULTS

Scrutinizing the bidirectional relationship between sleep and pain in pediatrics

The adult literature has explored the sleep and pain relationship with several randomized studies, to understand if sleep and pain have an equally bidirectional or predominantly unidirectional relationship. In an adult review article from 2013,[13] analysis of adult literature indicated that, while sleep and pain do have a reciprocal relationship, there is a stronger influence of sleep on pain than pain on sleep. The conclusion is supported by recent basic scientific studies indicating the role in which poor sleep promotes chronic pain across the neuraxis. Investigations have demonstrated that sleep restriction and sleep disorders exacerbate pain through the activation of inflammatory mediators

Figure 1—Flow diagram of studies reviewed for inclusion.



NICU = neonatal intensive care unit, PICU = pediatric intensive care unit.

Table 1—Highlighted pediatric articles in support of the sleep and pain relationship.

Study	Pain Condition	Study Assessment	n	Highlighted Findings
Chronic pain leads to poor sleep				
Vendrame et al,[18] July 2008	Headaches	Polysomnography	90	Sleep-disordered breathing is more frequent among children with migraine and nonspecific headache.
Lopes et al,[19] October 2008	JIA	Polysomnography	24	Patients with JIA had increased short awakenings and an increase in overall cyclic alternating pattern rate compared with healthy controls.
Lewandowski et al,[38] August 2010	Adolescents with chronic pain	Prospective study—sleep actigraphy + pain diary	97	Longer sleep duration and more sleep awakenings predicted next day pain. Neither nighttime sleep quality nor sleep efficiency predicted pain the following day.
Poor sleep exacerbates pain				
Palermo and Kiska,[5] March 2005	Chronic headaches, JIA, sickle cell disease	Questionnaire	86	Low correlation between pain dimensions (frequency, intensity) and subsequent sleep patterns and behaviors. High correlation between sleep disturbances and depressive symptoms, functional limitations, and health-related quality of life.
Butbul et al,[24] August 2011	JIA and juvenile dermatomyositis	Questionnaire	125	Sleep disturbance and fatigue are strongly associated with increased pain and decreased quality of life.
Pavlova et al,[31] July 2017	Youth with chronic pain	Questionnaire	147	Poor sleep quality was associated with increased pain intensity and pain interference. Anxiety and depressive symptoms are mediators.
Bromberg et al,[2] March 2012	JIA	Prospective longitudinal study, sleep diary	51	Poorer sleep quality associated with higher next day pain. Daily pain did not predict nighttime sleep quality. Improvements in mood weakened sleep's effect on pain.
Lewandowski Holley et al,[37] August 2017	Youth with acute musculoskeletal pain	Sleep actigraphy + pain diary	67	Shorter sleep duration and poorer sleep quality predicted higher morning pain intensity. Evening pain did not predict nighttime sleep.
Harrison et al,[3] September/October 2014	Healthy adolescents	Prospective population-based study + questionnaires	2,493	Association between sleep problems in adolescence and musculoskeletal pain at a later stage in adolescence.
Logan et al,[45] July 2014	Pediatric pain rehabilitation patients	Prospective cohort study—questionnaire	274	Greater sleep duration, less sleep-onset delay, and fewer night awakenings correlated with lower pain intensity ratings at discharge.
Bidirectional/neutral association				
Fisher et al,[20] March 2018	Sickle cell disease	Questionnaire and actigraphy	30	Greater pain severity associated with worse sleep efficiency and night awakenings that night. Worse sleep efficiency was associated with the occurrence of more severe pain the next day.
Van Dyk et al,[86] July 2021	Adolescents with insomnia	Questionnaire	375	Parent-reported somatic/pain complaints are prevalent in > 50% of adolescents seeking behavioral insomnia treatment.

JIA = juvenile idiopathic arthritis.

(primary prostaglandin and interleukin 6),[14,15] lower levels of endogenous opioids and the downregulation of opioid receptors,[16,17] limbic changes resulting in cingulate cortical changes that correlate with adverse emotional responses to pain, and by promoting a chronic wind-up of the pain system at the level of the thalamus, lowering the threshold for pain signals to be transmitted (**Figure 2**). Indeed, several large prospective adult studies suggest that sleep problems can precede the development of chronic pain disorders and improved sleep can increase the chance that chronic pain will decrease over time.[13] In children, it is known that poor nighttime sleep leads to worse next-day pain, and daytime pain is associated with disrupted sleep; however, a detailed look into the nature of this bidirectional relationship in pediatrics has not been completely explored.

Most studies on sleep and pain in pediatrics have been done in patients with diseases causing chronic pain or sleep disruption such as sickle cell disease, juvenile idiopathic arthritis (JIA), migraine, intellectual and developmental disabilities, and cancer. Few studies investigating chronic pain use electroencephalography or polysomnography for sleep measurement due

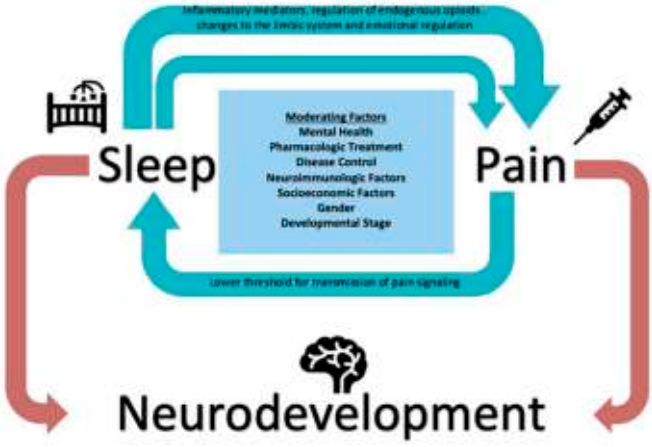
to cost and invasiveness. One investigation found that children with migraines had shorter sleep time, longer sleep latency, and shorter rapid eye movement (REM) sleep on polysomnography.[18] A second polysomnography study found that patients with JIA and chronic pain experience frequent sleep disruptions and more frequent cyclic alternating patterns during sleep.[19] Actigraphy is more frequently used as an objective sleep measurement because of its relatively lower cost and decreased invasiveness and provides prolonged sleep-wake monitoring (weeks) in the home environment. Actigraphic findings suggest that children with chronic pain experience lower sleep efficiency than their healthy counterparts.[5,20–22] Patient-reported measures also demonstrate poor sleep among individuals with pain from chronic diseases such as intellectual and developmental disabilities,[23] JIA,[24–26] sickle cell disease,[25] Rett syndrome,[27] and unspecified chronic pain conditions.[1,28–31] Importantly, while these associations between pain and sleep abnormalities were noted, none of these investigations were designed to identify whether pain led to poor sleep or whether poor sleep caused or exacerbated the patient's pain.

Poor sleep exacerbates pain

Poor sleep has been associated with both worse next-day pain and later development or worsening of chronic pain. Sleep deprivation in healthy adults increases nociceptive sensitivity,[32–36] which may contribute to the development of chronic pain. In studies of pediatric patients, shorter sleep duration and poorer sleep quality correlate with worse next-day pain.[2,21,37] In 1 study looking at adolescents, longer nighttime sleep duration and poorer sleep quality was associated with worse next-day pain.[38] This suggests that sleep quality rather than sleep duration alone has a stronger impact on pain; it also may indicate that adolescent populations sleep more as a method of coping with chronic pain. Furthermore, sleep-disordered breathing, such as obstructive sleep apnea—which decreases sleep quality and efficiency, often resulting in longer sleep duration—worsens pain as well.[18,26,39] It is unclear whether this effect is purely due to sleep disruption or if respiratory features such as the intermittent hypoxemia along with the sympathetic activation of obstructive sleep apnea lead to more pain. Clinically, these findings suggest that all pain patients should be screened for sleep-disordered breathing, as these conditions are reversible.

Researchers have studied the effect of poor sleep on subsequent development of pain. One important study demonstrated that poorer sleep quality was associated with higher next-day pain ratings, but importantly, daily pain did not predict nightly sleep quality.[2] Another investigation demonstrated that sleep problems in early adolescence have been found to predict development of chronic pain in later adolescence.[3] Conversely, looking specifically at the development of musculoskeletal pain, a systematic review of 13 prospective studies suggested that sleep problems were not a risk factor for later development of musculoskeletal pain in childhood.[40] This phenomenon is more established in the adult population, where the relationship has been more closely investigated. Studies in adults have shown that poor sleep can predict development of chronic pain conditions up to 5 years later.[4,41–44] There is a need for prospective studies to follow children with sleep disorders along with healthy controls into adulthood to further characterize the relationship between poor sleep and subsequent risk for chronic pain disorders.

Figure 2—Relationship between pediatric sleep, pain, and neurodevelopment.



Demonstrates moderating factors as well as the way in which sleep restriction and sleep disorders exacerbate pain through the activation of inflammatory mediators, decreased lower endogenous opioids and the downregulation of opioid receptors, and limbic changes resulting in cingulate cortical changes that correlate with adverse emotional responses to pain, and by promoting a chronic wind-up of the pain system at the level of the thalamus lowering the threshold for pain signals to be transmitted.

Importantly, optimizing sleep among children with pain syndromes may decrease pain as increased sleep has been associated with a subsequent reduction in pain.[37] In 1 study, longer sleep duration, improved sleep latency, and fewer night awakenings over the course of pediatric pain rehabilitation were correlated with decreased pain intensity at discharge.[45] These findings suggest that sleep improvement should be an important target for pediatric pain management.

Does chronic pain lead to poor sleep?

While acute pain leads to hypervigilance along with shortened and fragmented sleep, most clinicians intuitively assume that chronic pain must also lead to chronically poor sleep. However, close scrutiny of the literature, on balance, does not support this relationship.

Studies of chronic pain on sleep demonstrate conflicting results in both the pediatric[10,12,15,20,28,40] and adult[34,41–45] chronic pain populations. Discrepancies in the literature may relate to distinct mechanisms underlying the etiology of pain (arthritic pain, migraine pain, etc) as well as whether the recruited population was struggling with an acute exacerbation of chronic pain. It is possible that, in the setting of a chronic pain disorder, acute exacerbation of pain may lead to a subsequent effect on sleep, whereas a consistent pain baseline allows for sleep adaptation. It is also plausible that these mechanisms evolve over the course of the lifecycle and manifest differently in adult and pediatric populations.

Animal models have also explored the relationship between sleep and pain, although few studies have focused on neonatal or pediatric models. Sleep deprivation, particularly REM sleep deprivation, in adult animal models increases nociceptive sensitivity.[46–51] This increased sensitivity appears to be regulated by decreased dopaminergic and increased adenosinergic activity in the nucleus accumbens[52,53] and modulation of the descending antinociceptive pathway in the periaqueductal gray.[54] In reverse, acute pain decreases gamma-aminobutyric acid (GABA) and increases glutamate activity in the cingulate cortex, leading to hypervigilance and a subsequent sleep disturbance akin to the insomnia seen in human patients.[55,56]

In conclusion, the pediatric literature appears to support the relationship between poor sleep and subsequent risk for pain. This relationship is most strongly described among children with existing chronic disease and not as well delineated among otherwise healthy children. The reverse effect of pain on sleep is not clear. Studies confirm the general wisdom that acute pain can lead to acutely disrupted sleep,[23,28] while the contention that chronic pain leads to chronic sleep disruption[5,25] is inconsistently supported by the evidence. Complicating factors include uncertainties regarding childhood adaptations to chronic pain. Our group is currently evaluating the relationship between sleep and pain in premature infants using electroencephalography (NCT04286269).

Further studies are clearly needed to better define the relationship between sleep and pain as greater insight to the causal relationship will help identify therapeutic strategies.

Consideration of moderating factors in pediatric sleep and pain

Perhaps some of the inconsistencies in the pediatric sleep and pain literature are due to wide variation in pain etiology as well as multiple physiologic and psychologic factors that influence sleep and pain, making the relationship difficult to study. In particular, mental health, pharmacologic and nonpharmacologic treatments, along with underlying comorbidities are important moderating factors.

Psychologic health

It is well known that underlying depression and anxiety are critical factors to consider in the management of both pain and sleep disorders. Underlying mental health disorders mediate the effect of sleep quality on pain intensity, health-related quality of life, functional disability, and health care utilization.[31] Additionally, depressive symptoms in adolescents with chronic pain are predictive of the severity of sleep disturbances.[5] Further, many of the treatment approaches to pain, sleep, and mental health disorders overlap and all include cognitive behavioral therapy (CBT).[57] These strategies provide clinicians with opportunities to use tools that synergistically address multiple conditions. For example, improvements in depression and anxiety symptoms weaken the relationship between poor sleep quality and worsening pain.[2]

Pharmacologic therapies

The majority of pediatric data on pharmacologic treatment of pain and sleep comes from the inpatient setting and may be biased by more acute conditions. Patients in the pediatric intensive care unit (PICU), particularly those taking opioids and benzodiazepines for pain management and sedation, experience severely reduced REM sleep,[7,58] frequent awakenings,[59,60] sleep-disordered breathing,[61] and obliteration of diurnal, circadian variations in sleep.[7,58,62] Due to these factors, sleep in the PICU is likely not restorative, which may subsequently hinder rehabilitation and recovery.

There are similar findings of sedation-induced alterations and disruptions to sleep in the neonatal population. Oxycodone decreases sleep during the first hour after administration and alters the sleep architecture by decreasing time spent in REM sleep.[6] Studies assessing the impact of pain medications and sedation on neonatal sleep have found alterations in electroencephalography activity[63,64] and most electroencephalography abnormalities resolve after discontinuation of opioid infusion.[64]

Few studies have focused on the effect of chronic opioid use on sleep in pediatric patients. The existing data suggest that opioid use in children may alter and impair sleep. A 2011 study found that children with intellectual and developmental disabilities undergoing pharmacologic management of pain had worse sleep than children with intellectual and developmental disabilities without medication[23]; however, it is unclear whether poor sleep in this sample was simply due to opioid use or whether those children were managed with opioids because they had worse pain, which may have been associated with poor sleep. A 2016 Chinese cross-sectional study found a significant association between nonprescription opioid use and self-reported poor sleep in adolescents[65]; however, mediating and moderating factors such as chronic pain or psychiatric disorders were unclear.

Similarly, a few studies have focused on pediatric animal models of opioid administration and later changes to sleep or pain sensitivity. Existing adult animal model research suggests that opioid use significantly affects sleep, either by suppressing REM sleep,[66–69] shifting the circadian rhythm,[70] or by causing central sleep apnea.[71] Prenatally, exposure to low doses of morphine and methadone decrease quiet sleep and REM sleep and the withdrawal of morphine additionally caused sleep disturbance.[72] In a prospective study, morphine administration in neonatal rodents at baseline resulted in lower basal mechanical and thermal nociception in adolescence,[73] Of note, in the early neonatal period, delta opioid systems seem to predominantly modulate sleep and wake, whereas later mu receptors predominate both circadian rhythms and REM sleep regulation.[16,66,74–77] Finally, neonatal exposure to opioids has long-lasting effects on development and intelligence and ultimately on educational achievement.[78,79] However, there are large gaps in our knowledge of how opioid-related neurobiological changes chronically affect sleep and pain in children.

Nonpharmacologic therapies

The range of nonpharmacologic therapies for pain in pediatrics is broad, ranging from sucking interventions in infants to CBT for older children and adolescents. For acute pain, there is evidence that kangaroo care, swaddling/facilitated tucking, rocking/holding, and sucking interventions are effective for preterm infants and

newborns,[80] although for older infants and young children it has been more difficult to identify evidence-proven nonpharmacologic interventions for acute pain.[80] A systematic review evaluating psychological interventions for needle-related procedural pain in children highlights distraction, distraction + suggestion, and hypnosis as effective in reducing self-reported pain and additionally found CBT, hypnosis, and a nurse coach + distraction as effective in reducing behavioral measures of distress.[77] Simply providing information about a painful procedure did not appear to be helpful.

Many nonpharmacologic interventions for chronic pain include psychotherapy. Pain-reduction psychotherapy combined with treatment of concurrent depression and anxiety have shown promise in pediatric headache disorders, but this combined treatment has been less effective for other mixed pain etiologies.[81] Additionally, clinical anxiety is a risk factor for worse response to pain-focused CBT.[82] A smaller study implementing CBT for patients with JIA has also shown this to be a feasible therapy and to increase quality of life and reduction in pain catastrophizing despite an increase in disease severity.[83]

Considering the compelling evidence that improved sleep attenuates pain, nonpharmacological sleep therapies such as circadian realignment with timed bright light exposure and CBT for insomnia (CBT-I) provide clinicians with evidence-based strategies to relieve pain.[13,84,85] Further, these strategies have been demonstrated to be effective among pediatric patients dealing with chronic pain.[86]

Etiology as a moderating factor

The underlying specific pain disorders and associated mechanisms are key factors mediating the relationship between chronic pain and sleep. For example, a study on sleep disruption in relation to type of pediatric headache found that children with tension headache exhibit a prolonged slow-wave sleep time compared with children with migraine, chronic migraine, and nonspecific headache.[18] Slow-wave activity is an electroencephalographic marker of deep non-REM (N3) sleep and is characterized by synaptic depotentiation, or pruning of synaptic connection.[87] It is uncertain whether increased slow-wave activity of children who experience tension headaches is a biophysiological marker of disease or quite possibly a compensatory mechanism.

Conversely, numerous inflammatory mechanisms, seen in disrupted and poor-quality sleep, are pain promoting and well known to contribute to the development of chronic pain syndromes. Sleep restriction in healthy pain-free individuals is associated with elevated interleukin-6, C-reactive protein, cortisol, and prostaglandin E2, and tumor necrosis factor alpha, which play a role in increasing pain sensitivity, fatigue, and observed decline in self-reported health status.[14,15] Prospective studies of sleep and inflammation in both healthy children and children with underlying chronic pain disorders are needed.

Other moderating factors have been proposed in the pediatric sleep and pain literature, including socioeconomic factors, developmental stage, and sex. For example, socio-contextual factors have been linked with poor sleep patterns in chronically ill children.[8] These factors are currently less represented in pediatric research and warrant further investigation as they may play an important role in treatment.

The impact of childhood sleep and pain disorders on neurodevelopment

Much of the neurodevelopmental literature surrounding sleep and pain is derived from the neonatal intensive care unit (NICU) population. Both painful procedures and sleep disruption are common for infants admitted to the NICU, especially in contrast to the in utero environment. Many NICUs have adopted neurodevelopmental care bundles for preterm infants to decrease the frequency of disruptive procedures and external stimuli such as light and noise. These care bundles are aimed at reducing disruptions in sleep, but despite this, infants in the NICU are awakened frequently and often experience apnea of prematurity and intermittent hypoxemia during REM sleep.[88] Of significance, premature infants with decreased duration of REM sleep have shown lower developmental scores at 6 months corrected age as compared with infants with more time in REM sleep.[89] Prematurity itself may be a risk factor for disrupted sleep architecture, disrupting a critical window of sleep maturation with long-term effects on sleep structure and childhood brain development.[90]

In addition, acute pain early in life likely also impacts neurodevelopment.[91] Premature infants are especially vulnerable, as pain transmission is well developed early but pain modulating and sensitizing mechanisms are immature, altering the infant's ability to cope with pain impulses. Repetitive painful experiences can result in a hyperinnervation of pain synapses that would otherwise be pruned back at this stage of development.[92] This is further complicated by the concern that opioid interventions for pain management disrupt sleep and neurodevelopment,[66] heightening the need for nonpharmacologic means for neonatal pain management.

These findings have been confirmed with animal model research that provides insight into the pathophysiological mechanisms behind observations made through clinical investigations. Poor sleep in the early developmental period appears to have lasting impacts on sensitivity to painful stimuli later in life.[93] Sleep deprivation in neonatal mice has been associated with higher nociceptive sensitivity in adolescence; similar to results found in adult studies, these behavioral changes are associated with reduction in neural activity in the periaqueductal gray, an area implicated in inhibitory pain control.[93] Furthermore, REM sleep deprivation in adult rats reduces neurogenesis in the hippocampal dentate gyrus[94]; sleep deprivation in neonatal or pediatric rats likely contributes to similar neurogenic changes, a potential mechanism by which sleep disorders affect neurodevelopment. In reverse, painful stimuli in early neurodevelopment appear to have lasting impacts on pain and sleep later in life. Nociceptive insult in neonatal rats was associated with higher sleep disruption and altered sleep structure after nociceptive insult in adulthood.[95]

DISCUSSION

Overall, strong evidence supports a relationship between sleep and pain in the adult literature. Chronic poor sleep at baseline exacerbates pain. Acute pain leads to poor sleep. Less certain is the relationship between chronic pain and whether it independently leads to the development of chronic sleep disorders.

Among children, there are some inconsistencies regarding risk of development of future chronic sleep and pain disorders, and these clearly warrant further study.

Most studies have limited the scope of their investigations to symptoms or objective sleep monitoring with polysomnography or wrist actigraphy without appropriately considering mental health impact or functional limitations. A greater understanding of moderating factors including mood, pharmacologic treatment, socio-contextual factors, and underlying disease etiology would drive insight and possible therapeutic interventions. Most importantly, there is a need for comprehensive longitudinal studies of pediatric patients to further understand these relationships.

The need for sleep and pain research is further heightened for the neonatal and later pediatric periods of neurodevelopment when alterations to a normal sleep structure can potentially linger for a lifetime. The impact of sleep on a developing brain has been clearly established[96] and we know that poor sleep is associated with the development of chronic pain conditions later in life.[9,32] Thus, an increased understanding of both the effect of sleep on development as well as interventions to improve pain and sleep are of high importance in the neonatal and pediatric populations. Intriguingly, pediatric patients, with their robust neuroplasticity, may be uniquely resilient to some of the long-term effects of sleep and pain disorders despite occurring at a critical time in neurodevelopment.

Implications for clinical practice

In the neonatal population, the existing research highlights the importance of conscious decision making to limit unnecessary painful interventions and prioritize uninterrupted sleep when clinically appropriate. Circadian health can be augmented in the NICU and PICU by maintaining 24-hour light dark and physical activity cycles. As benzodiazepines, opioids, and related analgesics have been shown to alter sleep architecture, attempts should be made to maximize nonpharmacologic interventions for pain and discomfort.[6,60–63]

For pediatric patients, screening for sleep disturbances should be a routine part of primary care as well as pediatric subspecialty care. Rheumatologists, neurologists, and other specialties caring for children with chronic pain conditions should routinely screen for sleep disorders in high-risk pediatric populations. The BEARS (B = Bedtime issues, E = Excessive Daytime Sleepiness, A = Night Awakenings, R = Regularity and Duration of Sleep, S = Snoring) pediatric sleep screening tool has been proposed as a user-friendly sleep screening tool for use in the primary care setting.[97] Hospital systems and payers should enhance access to sleep clinics and increase availability of treatments, including CBT, which can treat both pain and sleep disorders.[57] Inpatient providers should work toward prioritizing sleep and circadian health in the hospital environment, decreasing nighttime noise and light exposure, enhancing natural sunlight, bundling care when appropriate, and prioritizing sleep when making choices regarding sedation and pain.[54–59]

Directions for future research

To address limitations of the current evidence, future research should include comprehensive longitudinal studies following pediatric patients for both sleep and pain into adulthood assessing neurocognitive development, mental health, and underlying disease factors in addition to propensity for development of future sleep and pain disorders. It is critical that these studies include neonates due to the unique growth and development during infancy. We also encourage basic science animal model research to explore and to identify neurochemical processes altered in the setting of sleep and pain disorders. These findings can then be used in clinical translational studies with the aim to find therapies that prevent and treat sleep and pain disorders in pediatric patients.

ABBREVIATIONS

CBT, cognitive behavioral therapy
JIA, juvenile idiopathic arthritis
NICU, neonatal intensive care unit
PICU, pediatric intensive care unit
REM, rapid eye movement

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