Pediatric Sleep: Current Knowledge, Gaps, and Opportunities for the Future

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Abstract

This White Paper addresses the current gaps in knowledge, as well as opportunities for future studies in pediatric sleep. The Sleep Research Society's Pipeline Development Committee assembled a panel of experts tasked to provide information to those interested in learning more about the field of pediatric sleep, including trainees. We cover the scope of pediatric sleep, including epidemiological studies and the development of sleep and circadian rhythms in early childhood and adolescence. Additionally, we discuss current knowledge of insufficient sleep and circadian disruption, addressing the neuropsychological impact (affective functioning) and cardiometabolic consequences. A significant portion of this White Paper explores pediatric sleep disorders (including circadian rhythm disorders, insomnia, restless leg and periodic limb movement disorder, narcolepsy, and sleep apnea), as well as sleep and neurodevelopment disorders (e.g., autism and attention deficit hyperactivity disorder). Finally, we end with a discussion on sleep and public health policy. Although we have made strides in our knowledge of pediatric sleep, it is imperative that we address the gaps in our knowledge and the pitfalls of our methodologies. For example, more work needs to be done to assess pediatric sleep using objective methodologies (i.e., actigraphy and polysomnography), to explore sleep disparities, to improve accessibility to evidence-based treatments, and to identify potential risks and protective markers of disorders in children. Expanding trainee exposure to pediatric sleep and elucidating future directions for study will significantly improve the future of the field.

Keywords: adolescent sleep; attention deficit hyperactivity disorder; autism; cardiometabolic health; circadian rhythm disorders; insomnia; insufficient sleep; narcolepsy; pediatric sleep; sleep apnea

Statement of Significance

This paper's intent is to explore the current knowledge of the field of pediatric sleep. The Sleep Research Society's Pipeline Development Committee assembled a group of experts to provide information across the scope of pediatric sleep, exploring epidemiological studies, development of sleep and circadian rhythms, insufficient sleep, clinical sleep disorders, neurodevelopment disorders and sleep, and public policy. Gaps in knowledge, road maps for trainees, and suggested readings provide more direction for those individuals interested in pursuing pediatric sleep as a field of study. This work is significant to the field of pediatric sleep because it serves as a launching point for those interested in not only learning the scope of the field, but how to improve moving forward.

Executive Summary

This White Paper is a collaborative effort of pediatric sleep experts initiated by the Sleep Research Society's Pipeline Development Committee. The committee identified key areas of pediatric sleep that would serve as a launching point for trainees interested in studying and practicing in the field, including (1) current knowledge, (2) future directions, (3) critical gaps in the knowledge, and (3) a road map for trainees to further their knowledge in each niche subject.

First, we explore the epidemiological studies among pediatric populations. There is discussion on how to improve pediatric sleep health measurement and better understand the social and contextual determinants of pediatric sleep. Next, we cover the development of sleep and circadian rhythms in both early childhood and adolescence, providing thoughtful guidance on the future directions of sleep disparities, sleep as an early predictor of health and development, digital medias, methodologies, brain maturation and development, school involvement, and access to evidence-based treatments. The consequences of insufficient sleep and impact on mood, emotion, and cardiometabolic health are discussed, including a spotlight specifically on delayed sleep phase and puberty's impact on affective functioning. There is considerable dialogue regarding clinical sleep disorders (circadian rhythm disorders, insomnia, restless leg syndrome and periodic limb movement disorder, narcolepsy, and sleep apnea), as well as neurodevelopmental disorders (autism spectrum disorder and attention deficit hyperactivity disorder). Finally, we end with public health policy and the importance of sleep.

We begin the White Paper with a Foreword by Mary A. Carskadon, who provides a brief introduction to the broad field of pediatric sleep, as well as encouraging words for new trainees exploring this area.

Foreword

Section author: Mary A. Carskadon

In my career, I have engaged in sleep research and later in circadian rhythms research in many ways and not just with children/adolescents, though not babies. [I was terrified when asked by Christian Guilleminault, MD, to watch over preemies in the NICU making sure they kept breathing…and one stopped. I learned quickly that infants were not for me, but the research need remains, as you'll see in this document below.]

With encouragement from my primary mentor, William C Dement, MD, PhD, I got involved in developing methods for studying sleep that resulted most notably in the Multiple Sleep Latency Test (MSLT). This measure arose from a clinical need, yet it played an important role in my research to explore daytime sleepiness in the elderly, adults, emerging adults (college students), adolescents, and children under conditions of extended and restricted sleep and sleep loss, and of course narcolepsy. So, I wasn't always a just child person, and you, too, may be moving into pediatrics from another area…don't be shy.

Measurement tools are critical to our research and need to be evaluated for reliability and validity, so beware of shiny new tools that may not be suitable to your needs. Thus, as you spread your wings into sleep/circadian research, you also need to identify the best measures and variables for your work…with luck, you may be the person to fill measurement gaps useful to the field. You may also find yourself, as have I, needing to stick to your guns to perform the study or studies you feel are needed. When I wanted to run forced desynchrony studies in kids, for example, I was told it couldn't be done...I did it. Don't give up.

Because of sleep's central role in emotional, cognitive, behavioral, and physical health, you'll be advised to keep your training focused, but I urge you to keep your interests

broad. For me, working across many ages provided a deeper perspective for adolescent research. Don't ignore basic science literature or findings from allied fields either.

Remember, too that among the most important components of successful science are curiosity, creativity, and good writing! I give my graduate students, postdoctoral fellows, and junior faculty mentees my favorite book on writing well—the same book Dr. Dement gifted me a half century ago and that I refer to even today—Strunk and White, *The Elements of Style*.

My hope for the future of sleep and circadian science in children and adolescents is that coming generations of scientists will expand our knowledge in unpredicted and unanticipated ways. Yet I urge trainees to ground yourselves in the current knowledge and then start your exploration in the gap areas identified by these authors or other gaps as you see them.

Epidemiological studies

Pediatric Sleep – Health Epidemiology

Section Lauren Hale and Ariel A. Williamson.

The multidimensional concept of sleep health often includes measures such as sleep duration, regularity, satisfaction, quality, and timing [1]. Among pediatric populations, most epidemiologic studies rely on caregiver- or self-reported data primarily limited to sleep duration [2], with occasional measures of snoring, sleep quality, and napping. Population-based research shows several broad trends, including a shift from biphasic sleep to monophasic sleep around ages 3-5, decreasing sleep duration across development, and later timing starting in puberty through adolescence. Two consensus panels provide recommended sleep duration starting at 14-17 hours per 24 hours (including naps) for infants moving to 8-10 hours per night for adolescents [3, 4] for optimal health and well-being. Across epidemiologic studies, there are notable sleep disparities, with children of racial/ethnic

minority backgrounds or those of lower socioeconomic status (SES) more likely to evidence poor sleep health [5, 6].

Epidemiologic studies of sleep health in early childhood (0-5 years) suggest considerable variability in total (24-hour) sleep duration and timing, particularly between birth and 36 month [7-9]. In a large, cross-cultural sample of families from 17 countries/regions, infants and toddlers from predominantly Asian (e.g., China, Korea, Vietnam) contexts had significantly later caregiver-reported bedtimes and shorter total sleep duration than those from predominantly Caucasian (e.g., Australia, Canada, US) contexts [9]. Bedtimes ranged from 19:27 (New Zealand) to 22:17 (Hong Kong), while total sleep duration ranged from 11.6 hours (Japan) to 13.3 hours (New Zealand) [9]. In a US study of primarily lower-SES and racial/ethnic minority preschoolers, over 20% of caregivers reported insufficient child sleep duration (<10 hours) [10]. Another US study of caregiver-rated child sleep duration from birth to age 7 found that children of Black, Hispanic/Latinx, and Asian backgrounds were more likely than non-Latinx White children to exhibit chronic sleep curtailment (below recommended sleep duration thresholds) although adjustment for SES attenuated some of these racial differences [11].

Cross-sectional, population-based research on school-aged children (6-11 years) in the US indicates a high prevalence of insufficient sleep [12]. On school nights, an estimated 55% of children get less than the recommended 9 hours of sleep [13]. In the one of the few studies to longitudinally assess actigraphy-derived sleep in school-aged children, Black children exhibited shorter actigraphic sleep duration and endorse more sleep problems compared to White youth [14, 15]. Children of lower-SES backgrounds also showed shorter sleep duration compared to those of higher-SES [14, 15].

National and community-based studies show that more than half of US teens obtain less than the recommended 8 hours of sleep per night [16, 17]. However, overall absolute

estimates for insufficient sleep vary according to measurement strategy (self-report and actigraphy) and sample characteristics [16-19]. Actigraphic studies of teens have identified differential sleep duration by race/ethnicity and sex [17-19]. In particular, compared to White teens, Black teens sleep approximately 20-30 minutes less per night, and male teens sleep about 20 minutes less than female teens [17-19]. Further, there has been a slight increase in inadequate sleep among adolescents during the past decade, which has been attributed to an increase in smartphone use in the bedroom environment [20].

Future directions: Critical gaps in knowledge

Improve pediatric sleep health measurement

Pediatric sleep health research is often limited to survey questions on a small number of sleep variables. Future epidemiologic research should incorporate measures of sleep regularity and timing, with information about both inter- and intra-individual variation in sleep [21]. The use of videosomnography, actigraphy, and other wearables should also be incorporated into data collection efforts to reduce measurement error from self-reported or caregiver-reported data, particularly in early childhood and school-aged samples.

Estimate the continuity of childhood sleep health to short-term and longer-term outcomes, including adulthood

Most research examining sleep and child outcomes has focused on sleep duration in short-term or cross-sectional studies [2]. Evidence of continuity in a broad range of sleep health parameters from early childhood on short and longer-term outcomes is critical for justifying and supporting future population-based sleep health promotion efforts.

Identify the role of social and contextual determinants of pediatric sleep

Elucidating the role of social and contextual factors, including neighborhood and household environments, is necessary for developing effective and culturally tailored sleep health promotion interventions. Examples of modifiable sleep health factors include bedtime routines, light, noise, physical activity, and screen time.

Road map for trainees

Trainees interested in pediatric sleep epidemiology should seek multidisciplinary training in areas such as sleep, psychology, public health, and the social sciences. Mentorship with hands-on data collection and analytic experience in pediatric sleep epidemiology is also necessary. Trainees will benefit from attending pediatric and general sleep meetings and acquiring skills in translating research findings to actionable sleep health promotion strategies.

Development of sleep and circadian rhythms

Early Development of Sleep and Circadian Rhythms

Section Monique K. LeBourgeois, Sachi D. Wong, and Lauren E. Hartstein.

Brief Summary of the Field

Developmental changes in sleep behavior during the first decade of life are remarkable [22]. On average, newborns sleep for 15-17 h, displaying a polyphasic sleep-wakefulness pattern across the 24-h day. Around 5 months of age, sleep becomes more consolidated, with the longest nighttime sleep episode of ~6 h. By 12 months, infants sleep ~14 h, where ~11 h of these occur at night. By 22 months, most infants have dropped their morning nap [23]. Afternoon naps gradually decline in number and duration across the preschool years, and as a result, sleep becomes consolidated into one nighttime period of 11-13 h. By 8 years of age, sleep duration declines to ~10 h, which on average remains consistent through the end of the first decade of life.

Newborns do not produce overt rhythms as evidenced by the absence of significant circadian rhythmicity in their sleep/wake cycle, body temperature, melatonin, and cortisol [24]. Infants receive time of day cues from their environment through light, as well as maternal signals via diurnal variation in breast milk hormones [25, 26]. Measurable outputs appear throughout the first 2-6 months of life, including the sleep and wakefulness, as well as rhythms in body temperature, melatonin, and cortisol [24]. The timing of the circadian clock delays throughout childhood: melatonin onset occurs at ~19:30 in toddlers and at ~20:40 in 9-to10-year-olds [27, 28]. There is wide individual variability in the timing of circadian development, and factors that influence the emergence of a stable circadian clock remain understudied.

Across infancy and childhood, behavioral changes in sleep are due to increased maturation of the sleep homeostatic and circadian systems in their interaction with individual difference factors (e.g., sex, chronotype, temperament) within the context of social and familial environments (i.e., opportunities, demands, stressors) [29].

Future Directions and Road Map

The following represent current gaps in the literature with regard to sleep, circadian rhythms, and infant and child development. These areas offer rich opportunities for trainees to create their own road map toward a rich independent research career.

- Brain maturation: Further research is needed to determine the association between changes in sleep throughout development and brain maturation and whether it is bi-directional [30, 31].
- Digital media: The increase in digital media use, even in young children, is associated with later bedtimes and shorter sleep durations [32]. Additional experimental studies are critical to understanding the underlying mechanisms and

whether interventions to limit children's screen time lead to improvements in sleep health.

- Sleep disparities: White, non-Hispanic children are more likely to have earlier and more regular bedtimes, longer nighttime sleep durations, and take fewer naps than children of racial/ethnic minorities [6]. More research is crucial to understanding predictors and consequences of sleep disparities and resulting disparities in health outcomes.
- Sleep as early predictor of health and development: Data from longitudinal studies suggest insufficient sleep in early childhood can have lasting impacts on physical health, emotion regulation, and academic performance [33, 34]. The underlying mechanisms and effectiveness of early sleep interventions remain largely unknown.
- Premature birth: Current understanding of whether premature birth has long-term implications for children's sleep and the development of circadian rhythms is limited [35].
- Pre- and peri-natal melatonin: Little is known about whether a pregnant woman's melatonin levels influence rest/activity patterns in the fetus [36]. Additionally, future work should examine how a mother's light exposure and sleep cycles influence the melatonin received by a breast-feeding baby, and whether that in turn impacts the child's sleep and circadian rhythms [26].
- Methodology: Estimating circadian phase and period currently involves challenging procedures that are difficult to perform with young children. Future research should explore whether circadian timing can be estimated through simpler procedures (e.g., a single blood draw) [37], or mathematical modeling from non-invasive measures (e.g., actigraphy, light history) [38].

- Impact of light: Evening bright light suppresses children's melatonin production [39, 40]. How light-induced melatonin suppression affects children's sleep, however, is currently unknown. Additionally, the impact of light timing, spectrum, and duration on children's sleep and circadian rhythms remain unexplored areas of research.
- Stability of chronotype: Chronotype shifts throughout the lifespan and can differ between individuals [41]. However, research on the variability of chronotype throughout childhood and how well individual chronotypes are reflected in parent-selected bedtimes is sparse.

Adolescent sleep

Section author: Jessica C. Levenson.

Many adolescents experience short, poorly timed, and inadequate sleep [42, 43], with only 25% obtaining the recommended duration of 8 hours or greater [44]. Insufficient sleep has serious consequences for adolescents across various domains, such as emotion dysregulation, increased likelihood of depression, suicidality and risky behavior, poorer physical health, and poor school performance [45, 46]. Insufficient adolescent sleep results from a "perfect storm" of biological and psychosocial factors that characterize this developmental period, including delayed circadian phase and slowed accumulation of sleep pressure, increased bedtime autonomy, and social networking, among others [42, 47]. Yet, the biological processes underlying the circadian phase delay and slower accumulation of sleep pressure that characterize adolescence are not fully understood, despite recent advances [48]. Early school start times are a modifiable contributor to insufficient and poorly timed sleep; when start times are delayed, teens demonstrate improvements in weekday sleep duration, sleepiness, weekend oversleep, and school attendance [49-51]. Yet, logistical and financial challenges, among other factors, have contributed to the maintenance of early start times in many districts [52]. Several universal sleep education programs addressing other

modifiable contributors to poor sleep among adolescents have been developed and tested, primarily in schools [53]. While these programs have good accessibility and reach, and are successful in improving sleep knowledge, they have limited impact on improving sleep behavior [54-56].

Sleep disorders frequently emerge during adolescence. Insomnia is the most common at ~11% lifetime prevalence [57, 58]. Though cognitive behavioral interventions for insomnia are efficacious among youth in general, relatively few studies have been conducted among adolescents, with even fewer focused on adolescents with medical or psychiatric comorbidities [59-61]. Recently, an intervention to address adolescent sleep and circadian rhythms transdiagnostically has been developed and tested (TranS-C), and growing evidence supports its efficacy [62-65]. Adolescent sleep concerns are frequently reported in primary care visits [66-68], where youth are likely to first discuss sleep issues [69]. Yet, behavioral treatment for sleep rarely occurs in primary care [67, 70, 71], likely due to lack of clinician training and comfort in addressing sleep, and limited time during adolescent visits [67, 70, 72]. Further, given the shortage of trained pediatric sleep providers in our country [73, 74], there is an urgent need to increase access to evidence-based behavioral treatment for adolescents.

Critical Gaps and Future Directions

1. **Sleep regulation:** Build on recent research to further elucidate the biological processes underlying changes to the homeostatic sleep and circadian systems that characterize adolescence.
2. **School start times:** Partner with school districts and community stakeholders to address barriers to delaying school start times and advocate for policy change.
3. **School-based sleep programs:** Increase the impact of school-based sleep programs on sleep behavior by targeting mechanisms that translate sleep knowledge into

behavior change (e.g., family involvement, tailoring of strategies, creating a culture change). Applying frameworks such as Knowledge to Action (KTA) can support this work [53].

4. **Access to evidence-based treatments:** Increase screening for and treatment of sleep disturbances, especially insomnia, in primary care and among youth with comorbid conditions. Increase access to evidence-based treatments for sleep disorders by enhancing sleep education at various stages of provider training, across clinicians (e.g., school and outpatient nurses, physicians, behavioral health clinicians) and settings (e.g., schools, primary care, adolescent medicine, specialty behavioral health).

Road Map for Trainees

Those interested in adolescent sleep should seek general training in sleep and behavioral sleep medicine, public health, adolescent development, and particularly the role of sleep changes during this period. Specific to the future directions identified here, trainees should seek training and mentorship in: community-based participatory research, especially with stakeholders in schools and primary care; intervention development and adaptation; relevant theories of adolescent behavior change; and dissemination and implementation science.

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Consequences of insufficient sleep and circadian disruption

Neuropsychological (Affective Functioning)

Section author: Misol Kwon.

Brief Summary of What is Known

During pubertal onset (between ages 9 to 14), rapid physical growth occurs, with significant changes in neuropsychological functioning and brain maturation [75]. The adolescent brain goes through a period of heightened affective reactivity characterized by greater sensitivity to

rewards and negative stimuli [76, 77]. These include greater sensitivity to social evaluation and emotional reactions, such as sensation-seeking, risk taking behaviors, intensified focus on social relationships, and desire for independence [75, 78-80]. Simultaneously, dramatic changes in sleep timing, architecture, and homeostasis occur during adolescence [81]. Across puberty, the sleep slow-wave activity sharply declines [82, 83] alongside significant maturation of sleep spindles, which facilitate synaptic elimination and brain reorganization [84]. Few brain regions susceptible to sleep loss include prefrontal cortex and amygdala, which are also areas critical for advancements in emotional reactivity, evaluation, and expression [85, 86]. Insufficient sleep and circadian disruption may pose greater susceptibility and heightened risk in children and adolescents for affective dysfunction and onset of related psychological disorders and affect their life trajectory.

Sleep and its Association with Affective Functioning

Burgeoning evidence indicates that sleep influences affective functioning such as mood, emotion, and emotion regulation among adolescents. Under sleep deprivation (characterized by ≤6.5 h the first night, ≤2 h the second night), adolescents reported less positive affect and more anxiety as a result of catastrophizing compared to rested, than adults [87]. Another experimentally induced sleep deprivation (characterized as ≤6.5 h for 5 nights) found that both parents and adolescents under the sleep restricted condition experienced significantly more negative emotion and poorer emotional regulation than those rested [88]. A similar finding was found where positive moods (i.e., happy, energetic) significantly decreased among adolescents sleep restricted to ≤5 h for 5 nights than those with more sleep opportunity [89]. Bidirectional and temporal associations between sleep and affective functions have also been reported [90]. For instance, in a naturalistic environment, longer self-reported sleep duration was associated with lower negative affect among adolescents, though this association differed on sleep measurement and affect dimensions [91].

Delayed sleep phase and sleep loss experienced during adolescence may further enhance developmental tendencies towards increased sensitivity, impulsivity, and lack of control [92-94]. Significant bidirectional associations between sleep problems and increased difficulties with impulse control were found among adolescents [95], and reciprocal associations between sleep problems and self-control during childhood [96]. In a similar context, adolescents are at an increased likelihood of engaging in risk-taking behaviors, including consuming highly caffeinated drinks and/ use of substance use to perceive positive effects on their mood, performance, and alertness or energy level [97] thereby, perpetuating and worsening existing sleep deprivation problems [93].

Critical Gaps and Future Directions

Future studies are recommended to integrate multimodal sleep assessment methods measured both objectively and subjectively. For instance, incorporating chronotype and sleep health assessments [98], especially sleep timing and regularity, including frequencies of unintentional and intentional naps, intra-individual variability of sleep health using ecological momentary measures will allow researchers to better understand and refine temporality as well as interrelationships between sleep and affect.

The aggregated research suggests a complex, bidirectional interplay between sleep and affective functioning, however, focus often lies on sleep and single dimensions of affective function such as mood, and is limited in the areas of emotion and emotion regulation [99]. Firstly, future studies can benefit and build upon existing research by utilizing standardized measures of affect such as the Positive and Negative Affect Schedule (PANAS) [100], and using consistent terminology when describing different affective functioning constructs (i.e., mood, positive and negative emotions, emotional regulation) [99]. Additional work could also address the bidirectionality between sleep and affective

function among clinical and non-clinical samples of adolescents, particularly those with history/ diagnosis of neurological, developmental, mood, and substance use disorders.

Identifying potential risks and protective markers, the distal and proximal social determinant factors that takes the family context into consideration related to sleep and affective functioning may represent an important future direction for research and translational benefits.

Sleep, Circadian Disruption, and Cardiometabolic Health

Section Chantelle N. Hart and Ashley Greer.

Brief Summary of What is Known

There is increasing recognition of the importance of sleep duration, and more recently the potential role of sleep timing, in the promotion of cardiometabolic health. Meta-analyses of observational studies demonstrate prospective associations between shorter sleep duration and increased risk of obesity in children and adults [101, 102]. Short sleep in adults (e.g., 6 hours or less) has also been associated with increased risk of type 2 diabetes mellitus (T2DM), hypertension, and cardiovascular and coronary heart diseases [103] while shorter sleep duration in children has been associated with disturbances in insulin sensitivity and elevations in blood [104]. Experimental studies with adults lend further support to disturbances in glucose regulation and insulin sensitivity that result from short sleep [105, 106], and also demonstrate that sleep restriction leads to increased caloric intake that predisposes to weight gain [107] - a finding also observed in pediatric samples [108, 109]. Taken together, extant findings provide compelling evidence for the important role of achieving sufficient sleep for cardiometabolic risk reduction.

Beyond sleep duration, emerging work is demonstrating the potentially important role of the circadian timing system for cardiometabolic health as well. Ample evidence has demonstrated the negative impact of night shift work on obesity, diabetes, and cardiovascular

disease [106]. Experimental studies in rodents and adults underscore the negative impact of misaligned sleep on weight regulation and impaired glucose metabolism [106, 110]. Although less work has been conducted with children, observational studies have shown that both the timing of sleep, particularly bedtimes, as well as greater variability in sleep-wake times are associated with less healthy eating and activity behaviors and increased risk for obesity [111]. It is also of note that both of the above-noted pediatric experimental studies that observed changes in eating behaviors when sleep was restricted, restricted sleep by delaying bedtimes [108, 109], thus calling into question the relative impact of the circadian timing system versus sleep duration on study outcomes. In sum, although less attention has been paid to the role of the circadian timing system in cardiometabolic risk, emerging work is underscoring the importance of future work in this area.

Critical Gaps and Future Directions

There are a number of important future directions for this work, some of which are highlighted below.

- Most evidence to date that has supported the importance of optimal sleep duration for cardiometabolic health has relied on cross-sectional and prospective observational studies or experimental studies that have assessed how large changes in sleep duration acutely effect cardiometabolic outcomes within tightly controlled laboratory settings. As such, an important next step is determining the clinical utility of enhancing sleep within real world contexts for reducing cardiometabolic risk.
- It will also be important to determine the importance of enhancing sleep duration and timing for disease risk reduction relative to other health behaviors. For example, how interventions to enhance sleep can independently contribute to disease risk reduction relative to those focused on eating and activity behaviors - or together with such approaches - could inform extant treatment approaches.

- Overall, fewer studies have focused on the importance of circadian rhythms on cardiometabolic outcomes, yet a number of lines of research point to the potentially important role of sleep timing and consistency for optimizing cardiometabolic health. It will therefore be important to further explore the role of the circadian timing system (both within well-controlled laboratory settings as well as in real-world settings, and that focus on work across the lifespan) for cardiometabolic risk reduction.
- Given observed sleep-related health disparities, it will also be important to understand the potential role of enhancing sleep for decreasing observed disparities in obesity, type 2 diabetes, and cardiovascular disease.

Roadmap for Trainees

Trainees interested in the role of sleep and circadian influences on cardiometabolic health should consider not only seeking foundational training in sleep and circadian science, but also additional training in cardiometabolic health, including risk and protective factors for development of obesity, T2DM, and cardiovascular disease, as well as effective approaches for prevention and treatment. Hands on training with an experienced mentor in the field can provide a well-rounded skillset grounded in scientific rigor and that offers the opportunity for exposure to the day-to-day management of research in this area. Gaining hands-on experience not only in the conduct of research, but also in presentation of findings will provide a strong foundation for continued work in this area.

Pediatric clinical sleep disorders

Circadian Rhythm Disorders

Section Cele E. Richardson and Michael Gradisar.

Brief Summary of What We Know

The ability of our endogenous circadian rhythm to adjust to a new timezone is a wonderful example of our body's ability to adapt. Unfortunately, one's circadian rhythm can travel to a

different timezone, even though the physical body remains steadfast. This decoupling mainly strikes those living in their second decade – adolescents. The adolescent phenotype is one of falling asleep late, an inability to obtain sufficient sleep on school nights, and difficulty waking for morning commitments [47].

Whilst delayed sleep timing is common amongst adolescents, the prevalence of Delayed Sleep-Wake Phase Disorder (DSWPD) likely ranges between 1.1-4.0% [33, 112, 113]. Compared to their "better"-sleeping peers, teenagers with DSWPD are at greater risk of substance use (alcohol, caffeine), being more sedentary, school non-attendance, and higher anxiety levels [33, 112, 113]. Fortunately, these ill effects can be reversed using interventions such as bright light therapy, exogenous melatonin and chronotherapy [114, 115].

Gaps and Future Directions

Here, we posit the 3 Ms (*see also Figure 1*):

(1) *Motivation*. Anyone who has worked with a sleepy teenager knows how much harder it is for them to muster motivation. Yet motivation is essential to behaviour change, particularly in the morning (e.g., getting up earlier, exposure to bright light). Whilst there have been a burst of new studies investigating teens' motivation in the context of treatment [64, 116-119], it is not yet clear whether Motivational Interviewing enhances treatment outcomes.

(2) *Melatonin*. An expert panel review concluded that the recommended treatment for DSWPD in children and adolescents is "strategically-timed melatonin" [120]. However, the state of the evidence was considered weak. Whilst many studies demonstrate the efficacy of immediate-release melatonin for children with delayed sleep [121], more well-designed clinical trials are needed to understand the efficacy of various formulations of melatonin for DSWPD in adolescents. For instance, more evidence is needed to address concerns about the efficacy and

safety of over-the-counter versions of melatonin. Finally, whilst some pharmacologic formulations are not to be prescribed for those under 18 years (e.g., Ramelteon), this may change if suitable evidence from clinical trials demonstrates their efficacy in adolescents of all ages with DSWPD.

(3) *Mental Health*. There is a close association between circadian rhythm disorders and mental health issues in young people, especially depression [122]. Science investigating the etiology and natural course of delayed circadian rhythms in youth, the mechanisms linking circadian mistiming/poor sleep with emotional symptoms, and the effects of chronobiological treatments on sleep, circadian and mental health is needed. Such research could inform of whether chronobiological treatments (e.g., bright light therapy, melatonin) should be considered before psychological treatments (e.g., cognitive-behavior therapy) for mental health disorders.

A Road Map for Trainees

A trainee may become aware and interested in adolescent circadian rhythm disorders at the undergraduate, graduate, or postgraduate level. Undertaking one's PhD in this area will certainly lay an excellent foundation. Seeking supervision from an experienced and knowledgeable mentor in this area is essential. We also encourage mentees to publish their work throughout their studies. Optimally, combining research with clinical training to diagnose and treat circadian rhythm disorders in teenagers will accelerate one's knowledge, skills, and career satisfaction.

Pediatric Insomnia

Section Michelle A. Clementi and Stacey L. Simon.

Pediatric insomnia, characterized by difficulty initiating and/or maintaining sleep despite age-appropriate time and opportunity, is common and associated with numerous

consequences for children and their families, including poor physical health and psychological dysfunction [57, 70, 123, 124]. Etiology is varied and pediatric insomnia often co-occurs with neurodevelopmental disorders, chronic medical conditions, and psychiatric disorders [125-127]. In young children, insomnia may present as dependency on specific sleep conditions (e.g., stimulation, objects, settings) and/or bedtime resistance resulting in prolonged sleep onset. Substantial caregiver intervention is often necessary for initiating or returning to sleep. In adolescents, insomnia is often characterized by heightened physiological and/or cognitive arousal interfering with sleep onset.

Strong empirical evidence exists for the efficacy of cognitive and behavioral interventions for treating pediatric insomnia [59, 128, 129]. These interventions typically focus on training and modifying parental behaviors (e.g., withdrawing reinforcement/excessive parental involvement) to promote the child's ability to self-soothe for sleep onset and reduce unwanted behaviors such as bedtime resistance [129, 130]. In adolescents, cognitive-behavioral therapy for insomnia (CBT-I) has demonstrated initial efficacy for improving a range of sleep indices and daytime consequences [128]. CBT-I techniques include sleep restriction, stimulus control, relaxation, and cognitive interventions to reduce sleep-interfering cognitions (bedtime worry, rumination) [131].

Currently, no medications are approved by the US Food and Drug Administration for the treatment of pediatric insomnia, though medications are frequently prescribed off-label or available over-the-counter [132]. Insufficient data and lack of controlled studies are available to demonstrate efficacy and safety of many of these substances [133, 134]. However, recent evidence does support the efficacy and safety of melatonin for sleep-onset insomnia in youth [135].

Future Directions

Future research on treatment for pediatric insomnia should focus on understanding mechanisms of change, dose-response, and evaluation of individual treatment components through dismantling studies. Exploration of clinically-meaningful biomarkers may help inform treatment outcomes and evaluation. Our understanding of treatment for adolescent insomnia is less robust than that of behavioral interventions for younger children. Examination of appropriate adaptations of CBT-I and considerations of motivation and treatment adherence for adolescents is necessary in the context of significant developmental changes during this period. Adaptation and study of insomnia interventions in youth with neurodevelopmental, medical, and psychiatric comorbidities is also imperative, as controlled studies in these populations are generally lacking [129] despite exceedingly high rates of comorbidity [127]. Moreover, addressing health disparities in treatment development and implementation is important to address recent findings implicating socioeconomic status, race, ethnicity, and sex in persistence of insomnia symptoms across childhood [136]. Consideration of alternative forms of behavioral intervention delivery (e.g., internet-delivered CBT-I) is important to study from a dissemination, implementation, and cost-effectiveness perspective. Finally, more rigorous study of the safety and efficacy of pharmacologic intervention for pediatric insomnia (including in combination with behavioral intervention) is important for standardizing practice parameters and ensuring long-term safety.

Road Map for Trainees

Trainees interested in pediatric insomnia are encouraged to gain clinical experience in behavioral sleep interventions across the developmental spectrum. Providers that possess this skillset may include psychologists working in pediatric specialty clinics such as sleep centers and primary care settings. Interested trainees may also consider pursuing the Diplomate in Behavioral Sleep Medicine (DBSM) credential granted by the Board of Behavioral Sleep

Medicine. Eligibility for the DSBM credential requires a graduate degree in a health-related field and documentation of specialized training experiences. Additional information may be found at www.bsmcredential.org/.

Pediatric Restless Legs Syndrome (RLS) and Periodic Limb Movement Disorder (PLMD): Common Disorders, Commonly Misunderstood

Section Lilith M. Reuter-Yuill and Daniel L. Picchietti.

Pediatric restless legs syndrome (RLS) and periodic limb movement disorder (PLMD) are common, complex, neurologic disorders that negatively impact sleep and daytime function [137, 138]. RLS is characterized by an uncontrollable urge to move the legs, usually accompanied by uncomfortable and unpleasant sensations, which are worse at night and alleviated by movement [137, 138]. Although new research suggests that the underlying pathophysiological mechanisms may be similar, PLMD is diagnosed by polysomnographic findings associated with adverse clinical consequences, while RLS is a clinical diagnosis elicited by careful history [137, 138]. It is estimated that ~85% of children with RLS experience sleep disturbance.[139] RLS and PLMD are treatable [138]. However, it is common for RLS to be disregarded as “growing pains” by pediatricians, and PLMD may not be considered, even if polysomnographic findings are present. In addition, many aspects of these disorders are yet to be discerned. Consequently, greater attention to RLS and PLMD from the medical and research communities is needed to better understand these disorders.

Epidemiology

Population-based studies estimate a high prevalence of 2-4% for pediatric RLS, which exceeds other common childhood disorders such as pediatric diabetes (<1%) and seizure disorders (~0.5%) [138, 139]. Approximately one-third of children are affected by moderate-to-severe RLS symptoms, impacting sleep and daytime function. However, very little is known about the incidence or natural course over time, including ameliorating or

exacerbating factors [140]. Further work assessing quality of life and comorbidities with standardized instruments, and the inclusion in prospective cohort studies would be worthwhile. Although very little is known about the epidemiology of PLMD, periodic limb movements and PLMD are commonly reported at pediatric sleep centers [141, 142].

Diagnosis

Expert consensus on the pediatric diagnostic criteria for RLS was formalized in the medical literature in 2002 and updated in 2013 [137]. The 2013 update integrated unique inductive and qualitative research methods to access useful diagnostic information directly from pediatric RLS patients [143]. In addition, pediatric and adult diagnostic criteria were harmonized, and subsequently accepted by the International Classification of Sleep Disorders (ICSD-3) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Recommendations for diagnostic interviews with pediatric patients include semistructured approaches with straightforward diagnostic prompts that allow the child to describe the symptoms in their own words or through drawings (see Figure 2) [137, 138]. Furthermore, diagnostic criteria for PLMD were updated [137].

Based on these diagnostic criteria, development of validated diagnostic and severity tools are needed for pediatric RLS [144] Such instruments will help substantially to standardize clinical care and research. The Clinical Global Impression Scales are not specific to RLS but have been used in some pediatric RLS studies, lacking other measures. In addition, new tools for the diagnosis and longitudinal assessment of PLMD are needed, such as portable accelerometers, video devices, or innovative wearable technology for limb movements, to compliment polysomnography. Children who are less than 6 years of age or developmentally delayed are particularly challenging to diagnose, although further work on PLMD evolving to RLS [145] and the new defined restless sleep disorder [146], will likely be productive.

Pathophysiology

Genetics, brain iron deficiency, and neurotransmitter dysfunction are all probably involved in the pathophysiology of RLS and PLMD based on work in adults [147]. The highly familial nature of RLS [141] provides a unique opportunity to explore these aspects in pediatric populations, particularly genetic and epigenetic factors.

Clinical treatment

Oral iron therapy and alpha-2-delta ligands have shown promising results in the treatment of pediatric RLS and PLMD [138, 148, 149]. However, these data are predominated by limited retrospective case reports and series rather than prospective controlled trials, and no therapies have been approved by US or European regulatory agencies for children. Additional case series are needed for these and other potential treatments, including behavioral interventions, intravenous iron [150], and vitamin D, which could then provide a sound basis for large randomized clinical trials. Also, therapeutic approaches need to be investigated for pediatric RLS that is comorbid commonly with Attention Deficit Hyperactivity Disorder (ADHD), anxiety, or depression [145, 151]. The clinical response to iron therapy of the sleep movement disorders RLS, PLMD, and restless sleep disorder merits further investigation, as well [152, 153].

Future directions and roadmap for trainees

In addition to the topics mentioned above, comorbidity of RLS and PLMD with other conditions, such as autism spectrum disorders [154], parasomnias [155], chronic kidney disease [156], nocturnal enuresis, and migraine headaches, merits further research. Basic science aspects of RLS and PLMD could be unlocked using recently developed animal models [157]. New imaging techniques for brain iron deficiency, like transcranial ultrasound, could provide valuable information in both adults and children.

Trainees should seek intra- and interprofessional collaboration to address complex clinical problems (e.g., cross-discipline practitioner-practitioner, practitioner-basic researcher, and patient-practitioner collaborations). Expand what you know and who you know! Seeking mentorship is crucial to developing skills and perspective in a new area. In addition, affiliation with groups dedicated to research in RLS and PLMD, may prove invaluable as a way to network with like-minded individuals and find career support. The International RLS Study Group (young investigator awards), the Restless Legs Syndrome Foundation (seed grants), the Sleep Research Society, and the American Academy of Sleep Medicine (mentorship grants) are all dedicated to advancing sleep science.

Pediatric Narcolepsy

Section Salome Wild and Leila Tarokh.

Narcolepsy is a rare neurological disorder characterized by disruption to the sleep-wake cycle and excessive daytime sleepiness. Narcolepsy is often overlooked and underdiagnosed in youth given its rarity, developmentally changing manifestation, and symptoms resembling psychiatric conditions [158, 159]. A first peak in emergence is seen during puberty with more than half of patients reporting symptoms before the age of 18 [160, 161]. However, often the interval between first onset of symptoms and correct diagnosis is a decade or more later [162, 163]. Although the precise etiology is unknown, narcolepsy is currently conceptualized as an autoimmune condition marked by a dysfunction or loss of orexin neurons in the hypothalamus, leading to a disrupted sleep-wake cycle [160]. Both genetic and environmental influences are involved in its initial manifestation; a genetic predisposition coupled with environmental factors, such as psychological stressors, head injury, or infection with a seasonal influenza virus, may cause the disease to unfold [164, 165].

Typical symptoms of narcolepsy include excessive daytime sleepiness, fragmented sleep, hallucinations, sleep paralysis, as well as cataplexy [163, 166]. More specifically, in children and adolescents, narcolepsy might manifest in an increased duration of nighttime sleep, a need for daytime naps, sleep attacks during the day, as well as hyperactivity and irritability [167]. Correct diagnosis in children and adolescents is challenging because symptoms might be misattributed to mental health problems, parasomnias (e.g., nightmare disorder), or even considered normal in the course of development [167, 168]. Moreover, cataplexy, the most specific symptom of narcolepsy, presents differently in pediatric as compared to adult patients, further complicating the correct detection of the disease in adolescence.

Being a chronic, non-progressive disorder, narcolepsy most often necessitates continuous treatment [169]. Symptoms of narcolepsy impact the daily lives of children and teens by negatively affecting cognitive performance and mood regulation as well as peer and family relationships [163]. Therefore, treatment options generally aim at improving quality of life and include behavioral interventions, education, and medication. However, evidence on safety and efficacy of different treatment approaches in children is limited. For instance, the beneficial effects of behavioral interventions such as scheduled naps or exercise have not sufficiently been subject to scientific study. Furthermore, medications are frequently used "off-label" due to a lack of randomized controlled trials in child and adolescent samples [169, 170]. Preliminary evidence on hypocretin receptor antagonists as well as treatments considering the immune-mediated nature of the disease are encouraging [171]. Yet, future research is required to determine the appropriateness, efficacy, and risk-to-benefit ratio of both pharmacological and behavioral treatments in youth [169] at different developmental stages (e.g., pre- versus post-pubertal). Moreover, accurate diagnosis and treatment of comorbid physical (e.g., metabolic upset) and mental conditions (e.g., mood disorders) is

paramount to lessen the burden of disease and to enable optimal development for affected youth [172, 173].

Sleep Disordered Breathing in Children

Section author: Kathy Sexton-Radek.

The International Classification of Diseases (ICD) manual recognizes Pediatric Sleep disordered breathing as an array of ventilator disorders from multi-organ involvement [174, 175]. Sleep apnea in a pediatric population is included in this diagnostic grouping. Specifically, obstructive sleep apnea (OSA) within this category is associated with neurocognitive disorders, medical conditions of obesity, elevated blood pressure, diabetes, cardiovascular disorders, and increased mortality [176-178]. Sleep apnea is experienced qualitatively distinctly in children as compared to adults. The daytime sleepiness and fatigue are absent in children with OSA [175]. Children with OSA display behavioral issues of hyperactivity and poor concentration due to the compromise in sleep quality. OSA is a disorder of breathing where tissue in the upper larynx/pharynx areas has become flaccid and stents the airway. A disruption in ventilation and oxygen/hemoglobin becomes substantially disturbed [175].

OSA in a pediatric population is common [179]. The prevalence of OS is increased in populations of children diagnosed with medical conditions that compromise breathing such as intellectual disability, cerebral palsy, prematurity, craniofacial abnormalities, and obesity. The scope of OSA diagnoses in a pediatric population is further intensified by empirically measured clinical findings in both short and long-term medical complications. Thus, diagnosis and preventative treatment are essential for a child with OSA health [180]. Specifically, Duman et al. [181] identified short-term medical complications of OSA in the pediatric population as the following: perioperative edema and need for mechanical ventilation and/or intubation [182]. Medical long-term complications of OSA further

intensify for the child with OSA; they are cognitive deficits of attention, concentration, excessive daytime sleepiness, hyperactivity, cardiovascular complications (i.e., cor pulmonade, elevated blood pressure, autonomic instability), and metabolic syndromes (i.e., serum insulin-like growth factor (IGF) decreases [183, 184]. Some genetic evidence of pediatric OSA suggests a familial tendency [183, 184]. Additional studies have examined the probability of inflammation factors such as CRP, dL-6, IFN-γ, and TNF- and anti-inflammatory cytokine dL-10 decreases [185]. In some genetic conditions, OSA is at higher risk. The Pierre Robin syndrome 22q11 deletion (DeGeorge syndrome) both have been studied with increased risk for OSA due to craniofacial changes that result from these conditions (e.g., micrognathia) [186].

Second-hand smoke was identified by studies as the highest in China, Bangladesh, Indonesia, India, and the Philippines. Children's respiratory conditions of asthma, allergies, and respiratory infections are at substantial risk from secondhand smoke as well as OSA [177, 187, 188].

A nocturnal polysomnograph (PSG) is used to study and diagnose obstructive sleep apnea (OSA). Per Association for Sleep Medicine guidelines, a positive airway pressure therapy titration may be conducted during the all-night PSG [179]. Also, the assessment may continue with a daytime nap study/multiple sleep latency test (MSLT) to further assess sleep and daytime sleepiness level. Kothare et al. [189] suggest using electronic medical records to ensure quality treatment with a thorough review of medical examination data. A snoring assessment is to be conducted for all screenings as a screening measure as well as physical exam measures of obesity and adenotonsillar hypertrophy [174].

Gozal et al. [190] presented treatment approaches for the removal of enlarged upper airway lymphadenitis tissues, use of anti-inflammatory therapy, orthodontic intervention, rapid maxillary expansion, myofunctional therapy, and continuous positive airway pressure

[174, 185, 191]. The treatment approaches are decided on a case-by-case basis depending on the symptom severity [176, 179, 191]. Some children with OSA may receive continued positive airway treatment (CPAP) as part of their assessment and as a treatment. In other cases, surgical consultation and treatments such as tonsillectomy/adenoidectomy maybe considered [174, 189, 190].

For the neonate, sleep has been measured to be 55% to 65% active sleep that transforms into rapid eye movement (REM) by 2-3 months of age [192]. Apnea of prematurity occurs whenever the birth weight is below 1500g or less than 28 weeks old and breathing is expressed with prolonged apnea of 20 or more seconds or brief response accompanied by reduction in oxyhemoglobin saturation or bradycardia [192]. In children under 18 years, Upper Airway Resistance Syndrome presents as an arousal preceded by an episode lasting two breaths of one of the following factors: increased respiratory effort, flattening of the inspiratory pressure signal, snoring, or elevated tidal $PaCO_2$ [193]. An analysis of all night polysomnogram findings particular to respiratory events and nasal pressure transducers is sometimes considered an additional factor. In Obesity Hypoventilation Syndrome, morbidly obese patient present with hypercapnia during wakefulness due to excess carbon dioxide produced from inefficient ventilation.

Central, obstructive, and mixed apnea is considered to possibly be present in cases of apnea in prematurity [192]. In situations where the infant is under one year, Sudden Infant Death syndrome is diagnosed. An attenuation of central arousal mechanism leading to overheating, prime position, and environmental maternal and prenatal factors are considered for etiology components of the diagnosis. Research has been focused on the serotonergic network in the control of breathing [192]. Some cases of central apnea in childhood are caused by Congenital Central Hypoventilation Syndrome, a rare genetic condition determined by the homeobox gene PHOX2b mutation on chromosome 4p12. A secondary form may

occur from developmental malformations such as in Arnold-Chiari type II, Zellweger syndrome, and Leigh Syndrome [192].

The diagnosis and treatment of Childhood Obstructive Sleep Apnea and Sleep Related Breathing Disorders in Childhood are to be evaluated by the Physician using a history, examination, and PSG sleep study if needed. Additional testing of laboratory tests, nap study, and repeat night of a PSG sleep study can be determined from preliminary findings. The examination is to include oropharyngeal exam findings. The following are to be considered in the evaluation: nocturnal or day symptoms, oropharyngeal exam findings, body mass index, growth level, medication usage, sleep environment, and association to other disorders (e.g., Craniofacial disorders, Down Syndrome, Cerebral palsy, Neuromuscular disorders, Chronic Lung Disease, Sickle Cell disease, Central Hypoventriculation Syndrome, Genetic Diseases, Cardiorespiratory Failure).

The Physician/Sleep Fellow in the conduction of the history, exam, and oropharyngeal examination may want to consider a referral for an all-night PSG. Several studies and clinical recommendations suggest in the case of moderate/severe OSA in children suggest management with an adenotonsillectomy surgery. In mild cases of OSA, position therapy and weight reduction with sleep log follow up are to be conducted. With persistent sleep-related breathing disorders, a positive airway pressure device is recommended. In some cases, pharmacological intervention with nasal steroid and leukotrienes antagonists may be medically successful. Currently, the small amount of literature that focuses on dental appliances and procedures for children with OSA suggest deferment to a more empirically validated procedure.

Partial Arousal Disorders of Sleep in a Pediatric Population

Section author: Kathy Sexton-Radek.

Partial arousals disorders of sleep are a group of behaviors that occur alongside sleep. There is an abrupt departure from slow wave sleep or REM sleep that results in transitional states of sleep and wake, which the sleeper is usually amnestic to [194]. Further, the partial arousals are positioned at the beginning of the night in terms of slow wave sleep incomplete arousals and, during the last or second to last cycle of REM, during the second half of the sleep interval. In general, the factors influencing partial arousals are thought to be both internal physiological factors of immature sleep homeostat, dysregulation of circadian rhythm from sleep disorder/disorder, and behavioral factors that reduce overall inhibition such as high stress, anxiety conditions, some medications, substance use, and, commonly, sleep deprivation [195]. Sleep deprivation from sleep loss and fragmentation of sleep schedules pressures the sleep homeostat. Additionally, the pediatric population has higher prevalence due to the maturity of their sleep cycle; also, Obstructive Sleep Apnea in children increases their risk for partial arousal from sleep [196, 197].

The following partial arousals of sleep in the non-rapid eye movement (nREM) sleep cycle occur in slow wave stages 3 and 4 sleep: Sleep Terrors, Somnambulism, Confusional Arousals, and Sleep-Related Eating. *Sleep Terrors* are characterized by a shrill, loud cry and a behavior of marked upset. There is no responsiveness from the sleeper and they are amnestic for the episode(s). Mason and Pack [195] described PSG results of a Sleep Terror episode as high-amplitude slow waves of stage 4 nREM sleep, then a sudden arousal with an admixture of electroencephalographic frequencies and muscle movement. Treatments include safety of the environment and the provision of gentle guidance back to bed without waking the sleeper. The prevalence drops to less than 1% of the adult population for Sleep Terrors; a maturity of the sleep cycle is presumed to facilitate this recovery [195, 198].

With *Confusional Arousals*, the pediatric sleeper may experience nighttime and or daytime napping bouts of confusion characterized by vocalizations, sitting up in bed, decreased responsiveness on awakening, amnestic for the episode, and normal autonomic activity [196]. Mason and Pack [195] reported a 4.2% prevalence for Confusional Arousals, which are more common in childhood than adolescence (1-17% prevalence), Somnambulism with a peak between 8-12 years, and 2.2% Sleep Terrors in childhood. Sleep disorders such as restless legs/periodic limb disorder or obstructive sleep apnea can precipitate confusional partial arousals and other parasomnias [196, 199].

In *Somnambulism*, the sleeper is partially awakened in usually the first third of the night, they have vocalizations, move in familiar motor movements with decreased responsive, and amnesia for the event(s). The parasomnias typically have a positive family history of parasomnia [195]. *Rhythmic Movement Disorder* is expressed as a burst from slow wave sleep with repetitive large muscle movements. Jactatio capitis nocturna (head banging), head rolling, and body rocking represent some of the rhythmic movements [197, 200, 201]. The treatment is a thorough clinical study of medical history and clinical study of PSG findings. Pharmacological agents that lower arousal threshold, such as selective serotonin reuptake inhibitors (SSRI), must be considered [194].

In *Sleep-Related Eating partial arousal*, the sleeper consumes peculiar food(s) and is amnestic for the event. Fleetham and Flemming [196] report all parts of the sleep cycle and stages 2-3-4 departures with vocalizations. Treatments are behavioral to establish a safety plan to reduce self-injury. Sleep Eating Disorder co-occurs with Somnambulism, Restless legs/Periodic Limb disorder, and Sleep-Related Breathing Disorder. Prevalence is higher in females than males and eating disorders versus no eating disorder population [195, 200].

The *REM Behavior Disorder (RBD*) emerges from REM sleep, mainly the last third of the night interval. There is no autonomic activity, and the person is responsive on awakening.

The prevalence of RBD is estimated at 0.38% of general population. Fleetham and Fleming [196] reported RBD as more common in men. Treatment for RBD is thorough assessment and clinical study, treatment of coexisting condition of Parkinson disease if evident, and palliative care to reduce factors that may be contributing to the loss of inhibition. Behavioral sleep medicine interventions are effective in treating sleep hygiene, sleep deprivation, and inadequate sleep schedules of RBD patients.

In *Nightmare disorder*, the pediatric patient's partial arousal is from REM sleep of the last third of the night, sometimes occurs with vocalizing. Psychiatric issues must be discerned; Watson et al. [202] identified the use of the Anomalous Sleep Experiences scale to distinguish Nightmare Disorder experiences with and from psychopathology. Treatment considerations included thorough medical history, clinical study of PSG, and medication evaluation to consider threshold elevating medications (e.g., Lithium, SSRIs, Antihistamines) that alter REM. Behavioral treatment using Imagery Rehearsal has been successful, as well as CBT [175, 194, 202].

In the disorder of *Sleep Paralysis*, the partial arousal from REM sleep occurs from any of the REM episodes. A slight groaning vocalization may occur, and there is no autonomic activity or post event confusion. There is no movement or injury risk concerns [196]. Prevalence figures of 15%-40% among students have been reported [196].

In summary, REM partial arousals most often occur in the last third of the night. As in nREM partial arousals, REM partial arousals are to be distinguished from other sleep and medical disorders such as seizures with a thorough history, examination, and PSG. Parasomnias are not stereotyped, do not have an automatic component, and have distinguished times of the burst from slow wave or REM sleep by comparison to seizures. General treatment guidelines for the Practitioner with Partial Arousals from sleep (Parasomnias) in a pediatric population is thorough evaluation with history, clinical study of

PSG findings, evaluation of current medications and medical conditions of patient, reassurance, and in some cases such as severe nightmare disorder or REM behavior disorder, prescribed medications (e.g., Prazosin, Clonidine). Medical treatment and diagnostic issues are comprehensively addressed in Fleetham and Fleming [196], Ferber and Kryger [203], and Mason and Pack [195]. Reviews of Behavioral treatments for pediatric parasomnias can be found in Mindell et al. [198], Sexton-Radek and Graci [175], and Galbiati et al. [199].

Pediatric sleep and neurodevelopmental Disorders

Autism Spectrum Disorder and Sleep

Section author: Kristina P. Lenker.

Autism Spectrum Disorder and Sleep

Current estimates are that 1 in 68 children has an autism spectrum disorder (ASD) with prevalence rates continuing to rise yearly. In children with ASD, 50-80% have sleep problems, which, when treated, often have a profoundly positive impact on daytime behaviors in the child and parent functioning. Those with ASD and other neurodevelopmental conditions have been identified as a high priority group for sleep research. Others have identified sleep disturbance as a valuable phenotype for defining those with ASD. Therefore, the study of sleep in ASD provides an unprecedented opportunity to work in a rapidly developing field while contributing to the health and well-being of affected individuals and their families.

Mechanisms are multifactorial; see Figure 3 for a representation of the biological, medical, and behavioral factors involved with ASD and sleep. Basic mechanisms that tie autism and brain chemistry together include differences in circadian regulation patterns, genetic contributors, or arousal patterns. For example, mutations in circadian-relevant genes (such as TIMELESS and CLOCK) affecting gene function are more frequent in patients with

ASD than in controls [204]. Individuals with ASD have also been shown to have higher heart rates, including during sleep, than typically developing controls [205].

- **Areas for future research** into these mechanisms may include work in genetics (identification of polymorphisms predictive of sleep disturbance in individuals with ASD), imaging of brain circuits common to sleep and ASD, comparison of indicators of arousal (such as heart rate variability, cortisol, and catecholamine levels), or measurement of biomarkers implicated in sleep and ASD (evening or overnight levels of blood, saliva, or urine melatonin or melatonin metabolites). Behavioral or medication trials [206] focused on improving sleep may include these measurements as biomarkers of treatment success.

Family systems are also strongly impacted by the birth of a child with significant developmental delays. The dynamics between parents and siblings can be significantly burdened and contribute to sleep disturbance [207]. Emergence of anxiety at bedtime, and the process of implementing rituals and routines all require study to guide intervention and to identify the pathophysiology of sleep disturbance in ASD. See Figure 4 for a sample visual schedule that may be used during an intervention to implement healthy routines.

- **Areas for future research** into these mechanisms may include cross-sectional, longitudinal, or interventional studies focused on the relationship between parenting stress and sleep in children with ASD, including behavioral approaches to improve sleep [208].

Road Map for Training

If an MD...

- As part of your sleep fellowship, seek out rotations where you can get exposure to children, teens and/or adults with Autism Spectrum Disorder (ASD). For children and teens, seek out a developmental medicine clinic in pediatrics, or clinics in child

neurology or child psychiatry. For adults, neurology or psychiatry clinics may have subspecialty clinics for autism spectrum disorder, or for individuals with intellectual and developmental disabilities.

- Work with a psychologist or another faculty member with expertise in behavioral therapies - including applied behavioral analysis, developing visual schedules or other routines. This will be helpful in working with individuals with ASD and their family members.
- Some institutions have LEND (Leadership Education in Neurodevelopmental and Related Disabilities) or UCEDD (University Centers of Excellence in Developmental Disabilities) programs that you can participate in as a postdoctoral fellow (2nd year after sleep fellowship). You can look up participating institutions at these websites.

  LEND website: https://www.aucd.org/template/page.cfm?id=473

  UCEDD website: https://www.aucd.org/directory/directory.cfm?program

If planning a PhD or in a postdoctoral program...

- Seek out institutions for graduate or postdoctoral training with IDDRCs - (Intellectual and Developmental Disabilities Research Centers) or neuroscience departments or institutes.
- Talk with your sleep mentor about getting exposure to training within the IDDRC on neuroscience department/institute.
- Getting clinical exposure to patients with ASD (see resources above under MD) will also benefit you in a similar way to getting exposure to sleep patients.

Attention Deficit Hyperactivity Disorder and Sleep

Section Kristina P. Lenker and Susan Calhoun.

The prevalence of sleep disturbances and disorders in youth with Attention Deficit Hyperactivity Disorder (ADHD) is high, ranging from 25-70% [209]. Insomnia symptoms

are the most frequently parent/self-reported sleep problems, while sleep disordered breathing, restless legs syndrome, periodic limb movement disorder (PLMD) or circadian rhythm sleep disorders are the most common sleep disorders. Both ADHD and sleep problems negatively impact many aspects of youths' lives including risk for psychiatric morbidities [210].

Emerging evidence suggests that there is symptom overlap (e.g., inattention, hypoarousal) of sleep problems and ADHD, which may indicate shared underlying neurobiological mechanisms. Indeed, the cortical and brainstem regions most involved in the regulation of sleep/arousal are also the major sites implicated in the pathophysiology of ADHD, given their role in the regulation of attentional processes [211]. There is an overlap in the neurotransmitter systems involved in the regulation of sleep, arousal and attention; both dopamine and norepinephrine are involved in maintaining activation of the prefrontal cortex during wakefulness as well as the impact of deficient sleep associated with specific sleep disorders on the prefrontal cortex. The identification of physiological and behavioral sleep disorders, regulation, and differences early in life may help in the development of phenotyping of children with ADHD based on the presence of specific sleep disorders [212] that may lead to identification of predictors of ADHD, description of developmental trajectories of ADHD or prediction of the prognosis of ADHD. The development of phenotype-based treatments will also improve the care of youth with ADHD through the application of specific sleep interventions such as cognitive-behavioral therapy (CBT-I), chronotherapy, and/or pharmacotherapy. Recent cutting-edge research has proposed that a disruption in normal circadian regulation may be a core mechanism in some youth with ADHD [213] and that the presence of PLMD may be associated with specific behavioral/neurocognitive phenotypic presentations [214]. Other research is underway to confirm these physiological-behavioral relationships by identifying biomarkers such as heart rate variability or cortisol levels in ADHD [215]. Recent evidence also suggests that sleep

disorders may be related to genetic differences linked to ADHD. Common genetic substrates leading to widespread dopaminergic dysfunction is a possible shared etiopathogenic mechanism for both ADHD and sleep disorders [216]. Moreover, an innate catecholaminergic dysregulation or specific alterations in "clock" genes may be common in both ADHD and sleep disorders [217]. Epigenetic studies will be critical in answering whether sleep disturbances and disorders play a role in the etiology of ADHD in children.

The bidirectional relationship between ADHD and sleep disturbances poses challenges for clinicians and researchers in the evaluation and development of treatment strategies [218]. From an etiological perspective, the distinction between sleep disorders and disturbances in ADHD is blurred given the ongoing debate of whether sleep problems are intrinsic to ADHD, a result due to a co-morbid sleep disorder, or cause ADHD-like symptoms that may result in a misdiagnosis. Advances in sleep and ADHD pathophysiology and assessment measures in both fields may impact clinical practice if early identification and treatment of sleep disorders proves to decrease symptom severity and/or need for stimulant medication in children with ADHD. Longitudinal studies are needed to establish whether sleep disturbances in early childhood are a pre-morbid neurophysiological or behavioral sign of ADHD [219] while randomized clinical trials addressing ADHD and behavioral sleep disorder overlap should compare the effectiveness of behavioral therapies, use of off-label medications (e.g., sedating antidepressant) and supplements (e.g., melatonin), and examine the PLMD and ADHD overlap and treatment options (iron supplements, gabapentin).

Future studies including youth with and without ADHD, as well as subclinical ADHD symptoms, are necessary to examine the psychosocial, biologic, epigenetic, contextual factors, and biomarkers that intersect with sleep functioning. It is unclear how sleep problems contribute to clinical, neurocognitive, and psychosocial presentations in ADHD, and impacts the persistence of ADHD symptoms over the lifespan. An enhanced understanding of the

proposed underlying neurophysiologic systems and relationships between the regulation of sleep, attention, arousal, genetic vulnerabilities, and environmental influences on both areas may shed light on shared mechanistic pathways and in turn influence the development of patient-centered, novel therapeutic approaches that are translatable to daily clinical practice.

Special Consideration for Trainees

- Gain clinical exposure through working in various specialty clinics (e.g., behavioral health, sleep, developmental pediatrics, psychiatry) and with psychologists/other faculty members whose expertise is in behavioral therapies for sleep problems and ADHD such as behavioral parent training or CBT.
- Seek out working with faculty members in training programs including clinical, school, health, and pediatric psychology.
- Participate in conferences special interest groups within research institutions.
- Seek funding from NIMH, NICHD, NINR, NINDS, PCORI.

Sleep and public health policy

Pediatric Public Sleep Health Research and Priorities

Section Dayna A. Johnson and Daniel Lewin.

Overview

Public health research may be considered the final step of translational research. There have been many adult and a few pediatric sleep and circadian health initiatives that have advanced into national and public policy. In pediatric research there have been some notable advances based on established and emerging science over the past decade, but as with all research in pediatrics there tends to be a time-lag behind adult research. This brief article provides definitions, summarizes some recent pediatric sleep public health research initiatives, poses questions about translation of basic and clinical science to the public health sector, and poses some key priority or gap areas that exist in pediatric sleep and circadian public health.

Public health research

Public health research (PHR) encompasses several methodologies that aim to improve efficacy, effectiveness, and efficiency of public health interventions to improve population health. Another important aspect of PHR is to identify the multi-level determinants of health (i.e., social, environmental, genetic) which shape population health. PHR can estimate the impact of interventions or guidelines on the health of large communities and populations and guide implementation and tracking of public health initiatives. There are models, frameworks and theories that can aid in the understanding of sociological, diversity, and economic risks and benefits of health indicators and initiatives. Surveillance and epidemiologic data collection and economic models are some of the key methods to conducting PHR, always an interdisciplinary effort that may include epidemiology, health behavior/education, environmental health, sociology, psychology, implementation specialists, as well as other domain specific specialists who understand measurement of key underlying variables and methodology. Examples of public health initiatives related to sleep and circadian health include: Healthy People, 2020 and 2030, the Back-to-Sleep campaign for healthy infant sleep [220]; guidelines for sleep duration [221] and healthy school start times [222]. These initiatives are often developed based on epidemiologic surveillance datasets that include pediatric sleep and circadian health data.

Public health importance of sleep

Healthy sleep is a public health priority. Pediatric sleep health was first included in Healthy People 2020 and was expanded in Healthy People 2030 with objectives to (1) increase the proportion of children and high school students who get sufficient sleep, (2) reduce drowsy driving, (3) increase the proportion of infants who are put to sleep on their backs and in a safe sleep environment, and (4) increase the proportion of secondary schools with a start time of 8:30 AM or later. Inclusion of sleep was a major advancement for the field of sleep and

circadian medicine made possible by large surveillance data sets that facilitate longitudinal tracking and demonstrated a high prevalence of short sleep duration (<9 hours for children aged 6–12 years and <8 hours for teens aged 13–18 years) [16]. The preponderance of evidence identified dire consequences of deficient sleep including unhealthy diet and metabolic dysregulation, poorer academic performance, mood disturbance, sleepiness, injury, risky behavioral, and other health consequences [111, 223, 224], aided in the immediate need to make sleep a public health priority.

Healthy sleep initiatives

Championing a public health initiative requires understanding of when a body of scientific evidence is sufficient for large scale implementation (e.g., safe infant sleep practices). In some cases, public health initiatives may be based on a weaker evidence base and common-sense recommendations intended to educate and change behavior (e.g., the food pyramid), which then has the benefit of spawning decades of PHR. There is undoubtedly strong evidence from clinical and epidemiologic studies that greater screen time, inconsistent bedtimes, physical inactivity, secondhand smoke exposure, minority race, early school start times, lower socioeconomic status, and adverse neighborhood environments are associated with increased risk and disparities in sleep duration, circadian misalignment, and sleep disorders such as obstructive sleep apnea [225-231].

Cultivating public health initiatives and messages require collaborations by sleep and circadian scientists who can define essential biomarkers and relevant outcome variables, epidemiologists, public health implementation expertise in lobbying, marketing to the public, associations, and policy makers to name a few. A recent example is healthy school start times initiatives that draw on indirect science (i.e., impact of deficient sleep), direct science (i.e., outcomes in specific school districts), national advocacy from providers (AAP statement) and activists (e.g., StartSchoolLater.org) and legislative effort championed by politicians (e.g.,

California, Bill 328). These initiatives have resulted in increases in weeknight sleep duration, optimized sleep period timing, as well as improved school performance and fewer motor vehicle crashes [228].

Future directions

Advancing public sleep and circadian health requires developing interdisciplinary collaborative teams including sleep and circadian scientists and public health scientists. There are national data available from many sources developed by the Center for Disease Control (CDC; Youth Risk Behavior Survey), National Institutes of Health (NIH; NEXT Generation Study, ECHO, Children's Health Study), State Departments of Education (youth health and risk surveillance studies), The Census Bureau (American Time Use Survey) that require effort, but minimal funding to analyze and contribute to sleep and circadian science. Support for larger scale studies may come from special interest groups (e.g., automobile insurance companies interested in drowsy driving laws); federal agencies (NIH), and funding components such as Patient-Centered Outcomes Research Institute (PCORI) and the US Department of Education.

To continue to advance of the field of sleep and circadian science with a public health lens, we recommend the following areas for PHR policy:

- Translate sleep/circadian health to valued public health outcomes
- Study social determinants including structural barriers such as access to care
- Drowsy driving laws and guidelines
- Lighting in schools
- Safe places to sleep
- Supplement regulation
- Pediatric sleep health education in schools
- Community sleep awareness campaigns

- Equating public health recommendations of sleep/circadian with exercise and nutrition
- Understand the mechanisms linking sleep/circadian health to disease
- Partner with policy makers to inform public policy

It is imperative to intervene during these formative years. Improving sleep health and creating safe sleep environments should be a top public health priority. Pursuing the recommendations of this article could potentially inform new research and intervention efforts.

Conclusion

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The value of this document lies primarily in identifying research gaps for studying the roles of sleep and circadian timing for pediatric wellness. No single section provides a deep literature review; however, each includes a rich overview of current knowledge, and the cited papers provide an excellent launch point for the interested trainees. That said, trainees need to dig deeper and not take for granted what may be presented as ground truth; the low numbers of scientists and clinicians engaged in pediatric sleep and circadian rhythms work increases the propensity to accept conclusions at face value. The field of psychology science has gone far to recognize the need for replication, and we cannot deny the need in our own science as well.

In the context of pediatrics, the nature of the core behavioral patterns of sleeping and waking are influenced by poverty, climate change, war, trauma, and so forth; as small and large shifts in cultural values and opportunities arise, they likely to play major roles in the kinds of sleep and circadian outcomes we are examining. For example, child sleep before television, Internet, smart phones, YouTube, and so on occurred on a different playing field from today. I also note that the overwhelming amount of information on pediatric sleep and

circadian rhythms comes from mostly industrialized, wealthy, and largely white countries, notwithstanding emerging information from other regions of the world, as noted in the opening section of this document highlighting epidemiological findings from many regions.

As you have read this brief overview of the field, its lists of gaps and opportunities, and roadmaps for trainees to use in pursuing research in each area, do not forget that virtually every specialty has roles to play. Whether you intend to train in a medical specialty, you crave fundamental neuroscience research, your interest lies in model organisms, your field is more oriented to omics research, you are drawn to clinical psychology and mental health, you want to focus on sleep disorders, your desire is to use experimental manipulations, or many hundreds of other approaches, pediatric sleep and circadian rhythms research needs you and your skills and creativity.

One final note is to recommend that all pediatric sleep and circadian scientists/clinicians read a paper written by one of my dissertation advisors. This article has influenced me and my thinking about how cross-sectional studies—which are necessary and form the bulk of our pediatric sleep knowledge—may constrain or skew our conclusions about developmental processes: "How Can We Learn About Developmental Processes from Cross-Sectional Studies, or Can We," (HC Kraemer, JA Yesavage, JL Taylor, and D Kupfer. Am J Psychiatry, 157:163-171, 2000).

I wish you all the rich rewards of scientific exploration!

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Figure 1. The 3 Ms for Circadian Rhythm Sleep Disorders Future Directions

The 3 Ms for future research directions: motivating teens to change sleep behaviors; evaluating the efficacy of strategically-timed melatonin for delayed circadian rhythms; mechanisms linking delayed circadian rhythm disorders and mental health.

Figure 2. Drawing and Description from a Pediatric Sleep Patient

A 15-year-old female: ‘‘My bed, and my pillow, and (inaudible). My head is usually somewhere around here. Sometimes at night, I just have to flip my whole body around or else it just bugs me. So then, I just sleep at the bottom of the bed for like a week, and then I can go back to sleeping like I’m supposed to. Feeling tired; (inaudible) blue eyes, and they’re bloodshot because I didn’t get any sleep; (inaudible) all over them. And my legs, they’re like tingly, (inaudible) wavy. And my arms kind of do the same thing. So I just have to keep moving them, or else it just bugs me all night long, and then I definitely don’t get any sleep.’’

From J Child Neurol. 2011;26:1365-76. Reproduced with permission from SAGE Publications.

Figure 3. Biological, Medical, and Behavioral Overlap in Autism Spectrum Disorder and Sleep

Visual representation of the biological, medical, and behavioral overlap and the multifactorial nature of autism spectrum disorder and impact on sleep.

Figure 4. Visual Schedule for Healthy Routines

Sample visual schedule that could be used in an intervention setting to promote healthy implementation of rituals and routines for children.

Figure 1

Figure 2

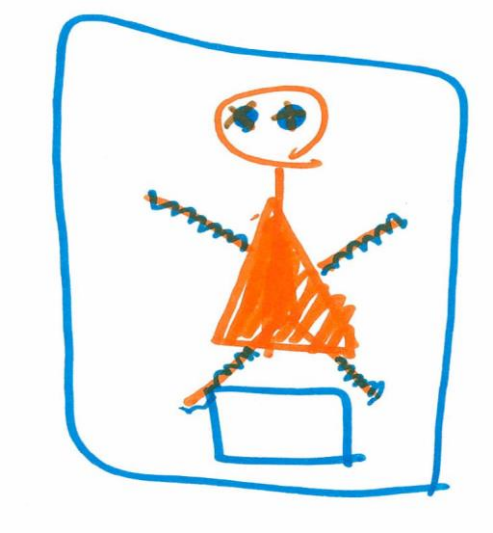

Figure 3

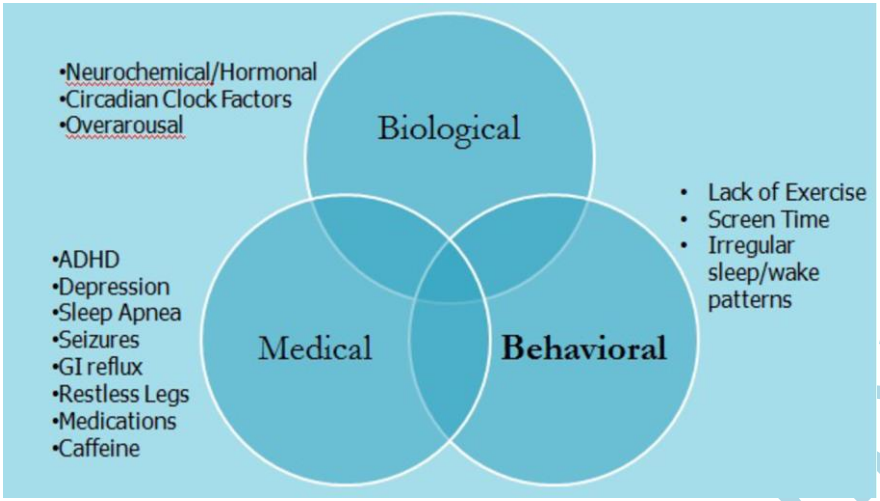

Figure 4