Clinical Child and Family Psychology Review (2018) 21:482–499
https://doi.org/10.1007/s10567-018-0267-4

(Re)Conceptualizing Sleep Among Children with Anxiety Disorders: Where to Next?

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Published online: 22 August 2018

Abstract
Children with anxiety disorders (AD) characteristically complain of sleep problems and the extent to which cognitive behavioral treatments (CBT) for childhood anxiety produce sleep-based improvements is a topic of increasing interest. The current paper reviews available evidence for subjective sleep complaints and objective sleep alterations in children and adolescents with AD, including investigations of potential changes in sleep following anxiety-focused CBT. Despite pervasive complaints of poor sleep, the empirical literature provides minimal evidence for actual sleep–wake alterations in this population of youth and evidence for sleep-based changes following treatment for anxiety is minimal. In line with calls for more comprehensive models of the role of sleep in developmental psychopathology, several fundamental gaps in understanding are described and highlighted as essential avenues for clarifying the nature and consequences of poor quality sleep among youth with clinical levels of anxiety. In a second section of the paper, an emerging body of novel, translational research investigating more intricate sleep–anxiety relationships is introduced with potential implications for both etiological models and treatment design and delivery.

Keywords Anxiety disorders · Sleep · Child · Adolescent · Development · Treatment

Introduction

In a seminal paper published more than two decades ago, Dahl (1996) proposed sleep and vigilance be viewed as opposing processes in a larger system of arousal regulation, owing to the shared neurobiological systems governing both emotional processes and sleep–wake regulation. Since then, an expansive body of research has emerged providing a more intricate view into the complex bidirectionality of these bio-regulatory systems. In otherwise healthy individuals, just one night without sleep has been shown to increase neurobiological activation of the amygdala (a limbic structure central to the development and maintenance of fear; LeDoux 1996) by as much as 60% (Yoo et al. 2007). Limbic activation is in turn compounded by diminished connectivity with the medial prefrontal cortex (mPFC), rendering heightened emotional reactivity more difficult to modulate when sleep is deficit (Yoo et al. 2007). Conversely, when anxious arousal, either cognitive or physiological, is experimentally induced prior to the overnight sleep period, initiation of sleep is prolonged and overall sleep duration is reduced (Tang and Harvey 2004).

Despite consistent and compelling evidence of acute and longitudinal reciprocity between sleep and anxiety across development (reviewed in numerous studies including Brown et al. 2018), the sleep of youth with anxiety disorders (AD) has largely been viewed through only one side of this lens. That is, while the presence of both global and discrete types of sleep complaints has been documented in multiple studies of clinically anxious youth (Alfano et al. 2006, 2007, 2010; Chase and Pincus 2011; Mullin et al. 2017), the ways in which distinct aspects of sleep might impact upon clinical symptoms of anxiety, both acutely and over time have scarcely been explored. This one-sided view of sleep is further exemplified by ubiquitous interest in whether anxiety-based treatments improve sleep. Questions as to whether clinicians need to target sleep directly as part of cognitive behavioral treatments (CBT), which aspects of sleep show the greatest improvements following a course of CBT, and/or whether anxiety-based outcomes are enhanced when sleep

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problems are reduced represent important questions for clinical research, and studies exploring these empirical questions have begun to emerge (Caporino et al. 2017; Clementi et al. 2016; Peterman et al. 2016; Wallace et al. 2017). Nevertheless, in the absence of a broader understanding of the role of sleep–wake processes in the development and maintenance of early-onset AD, the meaning and implications of specific treatment-based findings remain obscure.

The first goal of the current article is to synthesize available research examining the presence of subjective sleep problems and objective sleep–wake patterns among children and adolescents with AD. The growing number of studies investigating the extent to which anxiety-based CBT impacts sleep is also reviewed. Second, building on these findings, several fundamental gaps in knowledge are highlighted as critical directions for future research aimed at elucidating the transactional role of sleep–wake regulation among youth with clinical levels of anxiety. Lastly, an emerging body of translational research investigating sleep–anxiety relationships is introduced with relevance for both developmental models and treatment. In particular, findings from several novel investigations in adults are presented where sleep is leveraged to facilitate fear extinction via enhanced emotional memory. To begin, sleep behavior and physiology is briefly reviewed, including salient changes across childhood and adolescence, and validated methods for measuring sleep.

An Overview of Sleep and Development

Sleep is a highly dynamic activity best understood as a composition of biologically organized states that both influence and are influenced by a wide range of intrinsic and extrinsic factors. At a basic level, sleep consists of different types and stages including rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep stages 1 through 3. NREM stage 1 (N1) occurs during the transition from wakefulness to sleep and occupies only a small portion of the overnight sleep period. NREM stage 2 (N2), the predominate stage of sleep, is associated with the appearance of highly characteristic sleep phenomena known as sleep spindles and K-complex electroencephalograph (EEG) wave forms. NREM stage 3 (N3), also referred to as slow wave sleep (SWS), is the deepest form of sleep and dominates during the first half of the night. Sleep architecture refers to the cyclical pattern in types and stages of sleep that occurs predictably throughout the nighttime period. Both the proportion of specific sleep stages and their timing during the night are critical for healthy sleep.

Two separate but interactive biological processes are involved in the regulation and timing of sleep and wakefulness (Borbély 1982). A circadian process governed by an internal 'biological clock' acts as an alerting signal over a 24-h period and regulates the timing of sleep, particularly REM sleep. This internal clock is coordinated by both endogenous (e.g., melatonin release) and exogenous (e.g., light/dark cycles) factors. A second homeostatic process governed by an internal biochemical system exerts sleep pressure based on prior wakefulness and sleep. Homeostatic sleep drive is 'gated' by the circadian drive for arousal. Thus, alignment of these two processes is necessary for sleep to occur at optimal times. A third, shorter ultradian process occurs within the sleep episode and is represented by the repeated alternation of sleep types and stages across the night.

Sleep need, architecture, and timing change dramatically across early development. For example, homeostatic sleep pressure builds rapidly in infants (creating need for diurnal sleep periods) but gradually slows throughout childhood and into adolescence. By the school-aged years (e.g., around age 5 or 6), daytime naps are no longer needed and sleep is consolidated into one overnight sleep period, ideally 9–10 h in duration (Paruthi et al. 2016). Recommended sleep duration remains relatively stable through the school-age years including adolescence. Most teenagers do not receive an adequate amount of sleep, however (Owens 2015; Twenge et al. 2017) in part due to biological sleep changes following puberty that include a delay in circadian timing and slowing of homeostatic sleep pressure (Darchia and Cervena 2014; Wolfson and Carskadon 1998). Alterations in underlying sleep architecture are also observed. For example, whereas REM sleep comprises about 50% of total sleep time in newborns, it gradually decreases over the first 2 years of life until it reaches about 25% of sleep; a proportion that is generally maintained through adolescence. A dramatic decrease in the percentage of N3 or SWS is also observed, including a decline by about 40% from childhood to adolescence (Campbell and Feinberg 2009; Colrain and Baker 2011). More intricate characteristics of SWS, including slow wave activity (SWA; an indicator of slow wave intensity) also decrease markedly during adolescence (Jenni et al. 2005).

Measurement of Sleep in Children

Generally, evaluation of sleep in children is more complex than in adults due to constant changes in sleep duration and timing, the influence of caregivers and environmental factors on sleep–wake schedules, and the possibility of discrepancy between parent and child perceptions of what constitutes a 'sleep problem.' Multi-method approaches to assessment are therefore considered optimal. A range of methods for assessing sleep are available, each of which offers both strengths and limitations.

Child/Parent Sleep Questionnaires

Questionnaires are perhaps the most commonly used method for assessing child sleep patterns and problems. Major advantages of questionnaires include their low cost, ability to attain information about sleep-related behaviors unlikely to be captured by objective sleep measures (e.g., bedtime resistance, sleepwalking), and time frames that span extended periods. A number of validated questionnaires developed for children and adolescents are available, though they differ in terms of informant (e.g., child/adolescent or caregiver-report), specific sleep variables/behaviors assessed, and time frames used. However, measurement invariance, or the degree to which items on a scale are interpreted in a conceptually similar manner across respondents from different cultural backgrounds, has not been established for most questionnaires.

Sleep Diaries

A sleep diary or log is a prospective record of an individual's sleep–wake patterns and related information across at least 1 week, thereby capturing night-to-night variability in sleep. Typical information collected includes specific bed and wake times, sleep onset latency, number and duration of nighttime awakenings, and perception of quality of sleep. Although several forms of sleep diaries have been used and no standardized format exists, this method is often regarded as the gold standard of subjective sleep assessment (Buysse et al. 2006). However, recency effects and recall biases can occur when diaries are completed retrospectively rather than prospectively. Sleep diaries are often completed in conjunction with actigraphy.

Actigraphy

Actigraphy provides objective estimates of sleep and wake periods. An actigraph is an accelerometer-based monitor resembling a wrist watch that collects data continuously for up to several weeks. Data are downloaded and scored using reliable algorithms for distinguishing sleep from wake. Some actigraphs feature an event button that allows for more precise assessment of total time in bed and sleep onset latency. Common variables derived from actigraphy include total sleep time, sleep onset latency, sleep efficiency (total time in bed divided by time spent sleeping), and total wake minutes after sleep onset. Actigraphy is well-validated in youth and offers the advantage of assessing typical sleep patterns in the home environment. It does not, however, provide information about sleep stages and physiology, and multiple nights of recording are needed to provide valid sleep estimates (Acebo et al. 1999).

Polysomnography

Polysomnography (PSG) measures the biological and physiological changes that occur during sleep, enabling the scoring of specific sleep stages. Basic PSG assessment uses electrodes for the measurement of electroencephalography (EEG) to record brain activity, electrooculography (EOG) to assess eye movements, and electromyography (EMG) to assess muscle tone. Additional measures provide information on respiration and cardiovascular functioning (e.g., chest/abdominal respiration belts, pulse oximetry, electrocardiogram) necessary to diagnose certain medically based sleep disorders such as obstructive sleep apnea. Although considered the gold standard of sleep measurement, the cost of PSG limits its utility for research purposes. In addition, a single night of PSG monitoring may not provide reliable estimates of sleep variables.

Sleep Problems and Patterns in Youth with AD

Subjective Sleep Reports

Sleep problems are included as a diagnostic criterion for several AD common in children including generalized anxiety disorder (GAD) and separation anxiety disorder (SAD), but affect youth with all forms of anxiety. In fact, even when other psychiatric disorders are primary, the presence of comorbid anxiety uniquely predicts the presence of sleep problems (Hansen et al. 2011). The vast majority (up to 85%) of parents of youth with AD report problems related to sleep (Alfano et al. 2006, 2007, 2010; Chase and Pincus 2011; Mullin et al. 2017). Specific types of problems vary but most commonly surface at or around bedtime, including resistance/avoidance of getting into bed, nighttime fears, problems initiating sleep, and refusal to sleep independently. Problems that manifest during the actual sleep period, such as parasomnias (e.g., night terrors, enuresis), nightmares, and prolonged awakenings are somewhat less common but still occur at higher rates than the general population (Alfano et al. 2006, 2007, 2010; Chase and Pincus 2011; Reynolds and Alfano 2016).

Youth with GAD evidence the highest incidence of sleep problems, with significantly higher rates of parent-reported insomnia, bedtime resistance/fears, nightmares, parasomnias, and difficulty waking in the morning than found for other childhood AD and among healthy controls (Alfano et al. 2006, 2007, 2010; Chase and Pincus 2011; Hudson et al. 2009; Mullin et al. 2017). Findings based on

child reports are similar, with one study showing nearly 90% of children with GAD endorse trouble sleeping; a significantly higher rate than found among children with SAD, obsessive–compulsive disorder (OCD), or social anxiety disorder (SOC; Alfano et al. 2010). However, rates of subjective sleep complaints in youth with SAD and OCD are still higher than rates found in the general population of youth (Alfano et al. 2010; Johnson et al. 2006; Storch et al. 2008). Findings for sleep problems in youth with SOC are more mixed. There is some evidence to suggest that youth with SOC experience sleep problems at a rate similar to healthy children (Alfano et al. 2010). However, other researches have reported rates of insomnia among adolescents (13–16 years) with SOC (32%) to be similar to rates among youth with GAD (30%), panic disorder (36%), and agoraphobia (30%) (Johnson et al. 2006).

Notably, agreement between child and parent sleep reports is often poor. Chase and Pincus (2011) found a small but statistically significant correlation between parent and child reports of overall sleep problems in youth with GAD, SOC, SAD, and OCD, but overlap between specific types of problems endorsed was minimal. In a study of children with these same AD, 85% of parents endorsed the presence of a sleep problem in their anxious child, whereas only 53% of children reported problems sleeping (Alfano et al. 2010). Overall, parents tend to endorse higher rates of child sleep problems relative to their anxious children, though the use of different measurement instruments may to some extent influence discrepancies. However, the types of problems endorsed by parents tend occur during the pre-sleep and early sleep period (e.g., bedtime resistance, requests to co-sleep) and may not be considered problematic from the viewpoint of children (Alfano et al. 2015, 2010).

Fewer data are available examining subjective sleep–wake patterns among children with AD. One study using 1-week sleep diaries found children with various AD went to bed significantly later and got less sleep (about 30 min on average) on school nights as compared to a non-anxious control group (Hudson et al. 2009). In addition, only anxious youth reported shorter sleep onset latency (SOL) and less time spent awake during the night on weekends compared to weekdays, suggesting greater recovery of lost sleep on weekends. Conversely, another study using sleep diaries did not find any differences in sleep variables between youth with GAD and controls (Mullin et al. 2017). Findings based on parent-reported sleep patterns similarly indicate bedtime, total sleep duration, and morning wake times that are equivalent among children with GAD and controls (Alfano et al. 2015).

Objective Sleep Measurement

Very few studies overall have utilized polysomnography (PSG) to investigate sleep–wake patterns and architecture among youth with AD, but those conducting PSG in the sleep laboratory setting have found evidence of sleep abnormalities. In a sample of children and adolescents with various AD (primarily GAD), anxious youth exhibited decreased N3 sleep compared to both depressed and healthy control groups (Forbes et al. 2008). The anxious group also experienced more awakenings during the night than the depressed group. In a study of pre-pubescent children with GAD, results showed reduced latency to the first episode of REM sleep in comparison to age-matched healthy controls (Alfano et al. 2013a). Marginally increased total REM sleep was also found among the GAD group; however, because sleep onset occurred almost 30 min later on average among anxious children, differences in REM sleep may have been underpinned by circadian timing. In the only published study to utilize ambulatory PSG in the home environment, pre-pubescent children with GAD exhibited significantly fewer REM sleep periods and better sleep efficiency compared to controls (Patriquin et al. 2014), but no other sleep-based differences were found.

A greater number of studies have used actigraphy over 1 week to evaluate more typical sleep–wake patterns in youth with AD. Alfano et al. (2015) examined potential differences between children with GAD and controls across several sleep variables including bedtime, total time in bed, total sleep duration, and wake-up time on both weekday and weekend nights. Non-significant differences were detected for all parameters. Mullin et al. (2017) similarly reported non-significant differences in bed and wake times across 1 week between children and adolescents with GAD compared to healthy controls. Unexpectedly, longer average sleep duration (by approximately 30 min) was detected in the GAD group. Another study found no differences in actigraphy-based sleep–wake patterns between adolescents with and without SOC (Mesa et al. 2014).

Although studies utilizing actigraphy have largely failed to detect significant sleep differences between children with AD and typically developing youth, SOL, or the amount of time required to initiate sleep after getting into bed, is one exception. Objective estimates of SOL corroborate subjective reports of difficulty with the wake-to-sleep transition. Across studies, youth with various types of AD, GAD most commonly, require 5 to 15 min longer on average to initiate sleep than healthy controls (Alfano et al. 2015; Cousins et al. 2011; Mullin et al. 2017). Differences in SOL are even more apparent in the sleep lab setting. Both Forbes et al. (2008) and Alfano et al. (2013a) showed youth with various AD and GAD, respectively, required approximately twice as long as healthy controls to initiate sleep, with differences ranging

from 10 to 25 min. Parent- and child-rated anxiety symptoms have also been shown to correlate postively with objective SOL (Forbes et al. 2008; Mullin et al. 2017).

Does Sleep Improve with Treatment for Childhood Anxiety?

Cognitive Behavioral Treatment for Anxiety

Because CBT for anxiety shares several overlapping principles and features with behavioral interventions for insomnia (e.g., strategies for reducing problematic avoidance behaviors, negative ways of thinking, and levels of arousal), purely anxiety-focused interventions might improve sleep. A meta-analysis of anxiety-focused CBT studies among anxious adults found an overall moderate effect on co-existing sleep problems (Belleville et al. 2010), though research in this area is relatively limited overall (i.e., only 2% of more than 1200 potential studies reported a sleep-related outcome).

A handful of child studies published in the last few years have investigated potential changes in sleep in relation to CBT (Caporino et al. 2017; Clementi et al. 2016; Donovan et al. 2017; Peterman et al. 2016; Wallace et al. 2017). Using the same validated parent- and child-report sleep scales, two separate studies including children and adolescents with various AD identified significant improvements in parent-reported bedtime resistance and sleep anxiety as well as child-reported pre-sleep arousal following CBT (Clementi et al. 2016; Peterman et al. 2016). Still, a majority of youth in both studies continued to report clinically significant sleep problems at post-treatment. One study found parent-reported daytime sleepiness to be most resistant to change during treatment (Clementi et al. 2016) while the other reported improvements in parent- but not child-reported sleep problems (Peterman et al. 2016).

Peterman et al. (2016) also examined changes in sleep–wake patterns using 1-week sleep diaries. Average total sleep duration, SOL, sleep efficiency, nighttime awakenings, and daytime sleepiness were not significantly impacted by treatment, and changes in sleep hygiene behaviors were not observed. Consistent with other studies, these authors concluded that behavioral problems manifesting at bedtime, rather than quantitative aspects of sleep, may be most amenable to anxiety-focused CBT.

Caporino and team (2017) examined sleep-related outcomes using data from the Child/Adolescent Anxiety Multimodal Study (CAMS; Walkup et al. 2008) including youth with GAD, SOC, and SAD. Composite sleep scales from other validated parent- and child-report measures were constructed to assess two dimensions of sleep problems; dysregulated sleep (e.g., trouble sleeping) and separation-based sleep problems (e.g., sleeps next to someone in the family). Treatments that included CBT (alone or in combination) significantly reduced dysregulated sleep according to children but not parents (contrasting findings reported by Peterman et al. 2016). Conversely, compared to pill placebo, all active treatments (CBT, sertraline, CBT + sertraline) produced significant reductions in separation-related sleep problems as reported by parents, but not children.

In a recent study utilizing questionnaires, sleep diaries, and actigraphy, McMakin et al. (2018) examined the impact of anxiety-focused CBT or child-focused therapy (CCT) on the sleep of youth (ages 9–14 years) with GAD, SOC, or SAD. There were no effects of anxiety treatment condition (CBT, CCT) on sleep outcomes and significant reductions in parent- and child-reported sleep-related problems were apparent at post-treatment. However, the proportion of youth with scores greater than or equal to the clinical cutoff on a validated sleep problems measure did not decrease significantly; 75% of youth remained above the clinical cutoff. Based on sleep diaries, total sleep time increased, wake minutes after sleep onset was reduced, and sleep quality improved at post-treatment relative to baseline. No changes in actigraphy sleep variables were observed over the course of anxiety treatment.

Surprisingly, few child anxiety treatment studies have explicitly investigated sleep-related outcomes based on development. Following completion of an online CBT program, one study found children but not adolescents with AD (GAD, SOC, SAD, or specific phobias) demonstrated a significant decrease in sleep-related problems (Donovan et al. 2017). Such findings are consistent with results from multiple sleep intervention trials showing sleep–wake patterns to be particularly resistant to change during the teenage years (Bei et al. 2013; Schlarb et al. 2011). Specifically, although adolescents often report improved sleep-related knowledge following treatment, modifications in sleep-interfering behaviors and actual sleep–wake patterns are more modest (Cain et al. 2011; Moseley and Gradisar 2009; Tan et al. 2012).

Wallace et al. (2017) explored whether sleep–wake patterns prior to anxiety-focused treatment serve as predictors and/or moderators of treatment outcomes among youth ages 9–14 years with GAD, SOC, or SAD. Longer sleep duration, based on both parent reports and actigraphy predicted greater anxiety reduction following treatment. Additionally, the authors used a novel statistical approach to explore specific moderators that might identify youth for whom CBT (compared to child-centered therapy) is a preferable intervention approach. Youth reporting worse sleep at baseline (e.g., sleep quality, ease of waking, and sleep efficiency) fared better in the CBT group. Although replication studies are needed, these results dovetail with studies showing more sleep problems to correspond with more severe anxiety (Alfano et al. 2007; Chase and Pincus 2011) and more

severe anxiety at baseline to predict better CBT response (Compton et al. 2014).

Integrated and Sequential Treatments of Anxiety and Sleep

Available studies investigating the efficacy of integrated treatments for anxiety and sleep problems in youth are even more scant. In one pilot study, the initial efficacy of an integrated behavioral intervention for anxiety and sleep problems was examined among four children with primary GAD, ages 7–11 years (Clementi and Alfano 2014). Targeted Behavioral Therapy (TBT), a 14-week exposure-based treatment, included two sessions focused on sleep prior to initiating exposures. Sleep sessions focused on adequacy and regularity of sleep, sleep hygiene practices, and other idiographic strategies for reducing child sleep problems (e.g., limit setting). Using a reliable change index (i.e., change relative to measurement error), three of four children (75%) at post-treatment and two of three children (67%) assessed 3 months later reported improvements on a validated parent-reported sleep measure. The number of children falling above the clinical cutoff for sleep problems decreased from 75% children at baseline to 25% at post-treatment, and 33% at follow-up. The small sample size and lack of a comparison control group preclude firm conclusions, but the authors observed that inclusion of only two sessions explicitly focused on sleep was likely inadequate for producing sustainable changes in sleep–wake patterns and behaviors.

A small, follow-up randomized, controlled treatment trial comparing TBT to a well-established treatment for childhood AD (Coping Cat; Kendall et al. 1997) was recently completed (Clementi and Alfano 2018). Twenty children (ages 6–12) with primary GAD were randomly allocated to 16 weeks of treatment with either TBT or Coping Cat. Two additional sessions focused on sleep were added to the original TBT protocol (Clementi and Alfano 2014) allowing for more intensive and prescriptive sleep intervention. Assessments completed at pre-treatment, post-treatment, and 6 months later included structured diagnostic interviews, parents and child reports, and 1 week of sleep monitoring at home using actigraphy. At pre-treatment the groups showed equivalent levels of anxiety, sleep problems, and rates of co-sleeping, and at post-treatment and 6 months later, comparable significant improvements in anxiety and functioning were observed in both groups. In terms of sleep reports, equivalent improvements in child- and parent-reported sleep problems were observed in both groups at post and follow-up. Based on actigraphy, SOL was the only objective sleep parameter to show improvement after treatment, decreasing in both groups by approximately 6 min on average compared to pre-treatment. The latter finding notably aligns with other findings revealing similar differences in SOL between untreated anxious children and healthy controls (Alfano et al. 2015; Cousins et al. 2011).

In the treatment study by McMakin et al. (2018), youth completing anxiety-focused treatment who continued to evidence clinically significant sleep complaints at post-treatment were offered a sleep enhancement intervention called Sleeping TIGERS, including 6–8 sessions focused on duration and regularity of sleep, good sleep hygiene, and motivation for improving sleep. Of the 47 youth completing at least 6 sessions, significant reductions in parent, child and clinician-rated sleep-related problems were observed following treatment, and the proportion of youth with scores greater than or equal to the clinical cutoff on a parent-report measure of sleep problems fell significantly from 90% (at baseline) to 67.5%. Sleep diary data revealed significant reductions in sleep quality ratings across treatment but no significant changes in actigraphy sleep variables were found.

Summary of Sleep-Based Treatment Outcomes

Emerging research suggests that purely anxiety-focused CBT reduces some of the most common sleep complaints found among anxious youth; specifically, those that occur at or around bedtime. Parental perceptions of improvement are not always shared by children however (Caporino et al. 2017; Peterman et al. 2016) and there is minimal evidence overall that reported changes in sleep correspond with actual sleep–wake alterations. Such findings are unsurprising in light of the broader literature finding common discrepancies between parent and child perceptions of sleep and objective sleep patterns mirroring those of healthy control youth. It is important to point out nonetheless that, with only one exception (McMakin et al. 2018), the anxiety-based treatment studies reviewed here have not included sleep as part of a priori study designs and hypotheses. Methodological limitations also abound, including narrow assessments of sleep-related behaviors and patterns, and lacking attention to developmental changes in sleep.

A few recent studies have examined integrated and sequential treatments for sleep among youth with AD. In a small study comparing an integrated behavioral treatment for anxiety and sleep to 'gold-standard' CBT, similar reductions in subjective sleep problems and objective SOL were found across the groups (Clementi and Alfano 2018). In a larger, open trial of a sleep enhancement intervention administered following anxiety-based CBT, large within-subject effects were found for multiple subjective sleep measures based on parent, child, and clinician reports. Although actigraphy-based sleep changes were not observed, sleep diaries revealed significant improvement in two variables; average sleep quality and variability of morning waking difficulty. Collectively, these data signal the possibility that sequentially ordering anxiety and sleep-focused treatments may be

more beneficial than integrated treatments that split their focus across these targets.

Broadening Conceptualizations of Sleep Among Anxious Youth

One primary question to arise from review of this literature is why youth with AD persistently complain of sleep problems in the general absence of altered/abnormal sleep patterns. Several important points regarding sleep measurement first warrant comment. First, actigraphy is not a direct measure of sleep since it relies on accelerometer-measured movement to determine sleep–wake periods. It cannot therefore easily distinguish lack of movement from actual sleep states. For populations prone to worry and rumination at night, this may be particularly problematic in that estimates of SOL and total sleep time might underestimate degree of sleep difficulty (Tang and Harvey 2004). Home-based PSG, which has rarely been utilized among clinically anxious youth, has limitations as well. Despite measuring sleep in a more naturalistic environment than a sleep laboratory, the amount of equipment that children must wear during this procedure can result in a non-typical night of sleep, both in terms of overall sleep time and underlying sleep architecture, obscuring potential abnormalities and differences between different populations.

Further, objective sleep measures do not provide information about the sleep environment; meaning that the role of numerous contextual factors known to impact sleep quality, such as noise, sleeping surface, room temperature, and parent–child interactions surrounding sleep cannot be appreciated. Where children sleep, with whom they sleep, and the interactions that occur in the sleep setting set the tone for sleep. Parent–child conflict and certain sleep practices including co-sleeping are routinely linked with subjective sleep problems in children (e.g., Alfano et al. 2013b; Stein et al. 2001) and may compromise overall sleep quality. In a recent study of children with GAD and age-matched healthy controls, one-third of the anxious group reported co-sleeping with parents at least twice a week compared to only 5% of controls (Palmer et al. 2018). Unfortunately, most investigations of sleep among youth with AD have failed to either examine or consider the potential influence of co-sleeping behavior on subjective sleep reports and objective sleep parameters.

Sleep is a multi-dimensional behavior encompassing physiological, cognitive, and psychosocial facets. Thus, while certainly a worthy starting point, total sleep problem scores derived from a single questionnaire or sleep parameters averaged across several nights provide only a snapshot of overall sleep health. The boundaries of optimal sleep, particularly in children for whom changes in sleep–wake regulation are ongoing, are remarkably elusive and debate regarding the role of sleep quantity versus quality ensues (see Blunden and Galland 2014 for a review). Attempts to define optimal sleep in children fall outside the scope of the current paper, but most sleep researchers underscore a fundamental need to consider a range of sleep-based indices for conceptualizing individual sleep health (Buysse 2014; Blunden and Galland 2014). Unfortunately, many of these indices have scarcely been examined in the context of childhood AD. Below, several specific dimensions and aspects of sleep are considered in relation to childhood anxiety.

Subjective Sleep Quality

The term ‘sleep quality’ is ubiquitous in both the popular and research literatures despite the fact that consensus for a definition does not exist (Krystal and Edinger 2008). Sleep quality has sometimes been inferred from a collection of quantitative sleep measures including total sleep time, SOL, sleep efficiency, and wake time during the night. Other studies have sought to identify PSG-based correlates of sleep quality (Buysse et al. 2008; Keklund and Akerstedt 1997; Westerlund et al. 2016). The limited utility of purely objective approaches is nonetheless exemplified by the fact that many individuals complain of unsatisfying sleep in the presence of sleep patterns similar to good sleepers—prime example including the roughly one-half of adult insomniacs who evidence normal objective sleep patterns despite chronic complaint of non-restorative sleep (Edinger and Fins 1995). In reality, individuals rely upon different aspects of sleep and daytime experiences in providing estimates of overall sleep quality, including latency to sleep onset, ease of waking in the morning, degree of daytime sleepiness, and performance ability (Argyropoulos et al. 2003; Åkerstedt et al. 1994; Harvey et al. 2008). The perceived quality of one’s sleep is also routinely shown to correlate with emotional states including anxiety and mood (Krystal and Edinger 2008).

Factors and experiences that shape perceptions of overall sleep quality among youth with AD have not been explored empirically. Limited research among adults with AD has found the daytime consequences of poor sleep to be among the most robust influences of sleep quality ratings (Ramsawh et al. 2009), but generalizations to younger patients may be invalid. Further, measurement timing needs to be closely considered. Individual accounts of sleep quality are inherently retrospective and longer assessment periods introduce greater possibility of bias, which may be highly problematic among youth with AD. Apt example comes from a study comparing retrospective versus prospective reports of nightmares in children with GAD and controls (Reynolds and Alfano 2016). Children with GAD retrospectively endorsed more frequent

nightmares than control children, whereas prospective tracking of nightmares across a 1-week period revealed no difference and few nightmares overall.

Harvey (2008) has underscored the potential for cognitive processes to distort sleep quality ratings in adults, particularly among those with psychiatric disorders. Cognitive biases and faulty ways of thinking are endemic to childhood AD (Alfano et al. 2002; Barrett et al. 1996) and might directly influence perceived sleep quality. In fact, cognitive errors characterized by catastrophizing (i.e., expecting the worst possible outcome of an event or situation) and over-generalizing (i.e., believing that a single negative outcome is representative of or will occur in all similar future events) are uniquely found among anxious youth (Bögels et al. 2003; Weems et al. 2001). Catastrophizing has been shown to predict sleep disturbance in children; a relationship that is mediated by symptoms of anxiety (Gregory et al. 2010).

Autonomic features of AD may also influence ratings of overall sleep quality. Heart rate variability (HRV), which results from the dynamic interaction of parasympathetic and sympathetic (vagal) inputs to the sinoatrial node, is commonly used as an index of autonomic activity during both wake and sleep periods. Reduced HRV (i.e., a sympathovagal imbalance), both during rest and in response to a stressor, is a hallmark feature of most AD (Chalmers et al. 2014), reflecting a physiological state of hypervigilance or chronic 'preparedness' for threat (Porges 2007). Initiation of sleep, conversely, is preceded by a reduction in heart rate and an increase in HRV (Van de Borne et al. 1994); autonomic changes shown to contribute to subjective experience of sleep as refreshing (e.g., Irwin et al. 2006). Accordingly, lower resting high-frequency HRV (HF-HRV), an index of cardiac autonomic modulation similar to respiratory sinus arrhythmia, has been linked with greater subjective sleep problems in adults with AD (Hovland et al. 2013). In children, reduced HF-HRV corresponds with lower ratings of sleep quality and reduced sleep efficiency based on actigraphy (Elmore-Staton et al. 2012; Michels et al. 2013).

In an exploratory study including children with GAD and matched controls, Palmer and Alfano (2015) examined heart rate and HRV during the 5 min prior to sleep onset during home-based PSG. Higher heart rate and reduced HRV were found in the GAD group although the small sample size did not yield a statistically significance difference. However, increased pre-sleep HR was associated with significant increases in self-reported arousal during the pre-sleep period in the GAD group. In concert with findings among adults with the disorder (e.g., Andor et al. 2008), children with GAD may be more sensitive to physiological arousal during the wake-to-sleep transition and use this information as an index of overall sleep quality.

Sleep Loss Vulnerability

As is commonly the case in sleep-related research, studies among youth have chiefly relied on group-averaged estimates of sleep—a practice that essentially ignores differences at the individual level. However, the extent to which anxiety might pose heightened vulnerability to even mild levels of sleep disruption warrants attention. Indeed, even when average sleep duration is comparable to that of healthy youth, children with AD endorse significantly greater levels of daytime sleepiness, perceptions of too little sleep, and lower sleep satisfaction (Alfano et al. 2015; Mullin et al. 2017). Just as sleep need differs across individuals, robust inter-individual differences exist with regard to the effects of sleep loss on daytime tiredness and performance (Van Dongen and Belenky 2009; Van Dongen et al. 2004). One study utilizing fMRI in adults provides evidence of heightened sleep loss vulnerability among anxious individuals at the neurobiological level. Following a night of sleep deprivation or normal sleep, anticipatory responses to negative and neutral stimuli (under conditions of certainty or uncertainty) were examined in relation to trait anxiety (Goldstein et al. 2013). Following results from other studies (e.g., Yoo et al. 2007), sleep deprivation increased emotional reactivity in limbic structures for all individuals, but the greatest increases were observed among individuals high in trait anxiety in response to uncertainty or ambiguous cues; a pattern of neural activity characteristic of AD (Etkin and Wager 2007).

A study recently conducted in adolescents with AD examined similar relationships, albeit with somewhat divergent findings. The authors collected self-reported total sleep time among clinically anxious adolescents and healthy controls for three consecutive nights preceding an fMRI scan with negative emotional images in order to examine the interactive effects of clinical levels of anxiety and sleep duration on neurobiological responses (Carlisi et al. 2017). Two brain regions involved in emotion processing, the dorsal anterior cingulate cortex (dACC) and hippocampus were differentially affected by sleep duration across the two groups in response to emotional images. Positive associations were found in the anxious group (i.e., less sleep, less activation), whereas negative associations were observed among controls (i.e., less sleep, more activation). However, less sleep was associated with weakened connectivity between the dACC and dorsal medial PFC among controls but corresponded with strengthened connectivity among adolescents with AD. These same relationships were found for hippocampus—insula connectivity within the groups (i.e., enhanced connectivity in the anxious group with less sleep). Although the direction of findings diverges from those reported by Goldstein et al. (2013), the use of retrospective sleep reports, developmental differences in brain maturation, and greater

variability in sleep estimates among the anxious group may have impacted specific results. Responses to mild, persistent sleep loss may also differ from those following acute periods of sleep deprivation (Rupp et al. 2012). Among teens, short sleep duration every night for 1 week has been shown to double risk for the development of an AD one year later (Roberts and Duong 2017). Overall, evidence of unique relationships between sleep duration and emotional circuitry in youth warrants further investigation.

Heightened vulnerability to sleep loss may emanate from more proximal levels of emotional processing as well. Anxiety sensitivity (i.e., the perception of physiological sensations of anxiety as threatening), a feature of most AD has been shown to predict the presence of subjective sleep complaints in clinically anxious samples of children (Weiner et al. 2015). Similar findings have been reported in anxious adults (Baker et al. 2017) where anxiety sensitivity was shown to moderate the relationship between sleep anticipatory anxiety and SOL (Babson et al. 2008). Thus, when bodily sensations related to anxiety are perceived as a threatening or harmful, quiescence required for sleep initiation (and perhaps maintenance) is likely to be compromised. Similarly, perceived control over anxiety correlates with higher levels of pre-sleep arousal in youth with AD (Parker et al. 2017).

Intra-individual Sleep–Wake Variability

Since some degree of nightly variation in sleep occurs normally in all individuals, aggregated sleep values inevitably provide limited understanding of intra-individual sleep variation. Evidence of linkages between sleep–wake variability and anxiety is available in both child and adult samples (Becker et al. 2017; Robillard et al. 2015). In young children, the absence of a set bedtime at 2 years of age predicts the presence of anxiety 1 year later (Jansen et al. 2011). During the early school-age years, low sleep rhythmicity (i.e., consistency of sleep habits and schedules) predicts the development of anxiety and mood disorders up to 20 years later (Ong et al. 2006). Such relationships are observed bi-directionally. For example, in school-age children, pre-sleep worries related to school, which often afflict anxious youth, are associated with greater sleep schedule variability (Bagley et al. 2016). Other findings insinuate anxiety may be more closely associated with variability of sleep than average total sleep duration (Fletcher et al. 2018).

As the greatest levels of intra-individual sleep variability are often found among anxious individuals (Doane et al. 2015; Mezick et al. 2009), regularity of sleep represents a relatively neglected but critical dimension of sleep for youth with AD as well as youth at high levels of risk. Palmer et al. (2018) examined variability of sleep–wake patterns across 1 week (using actigraphy) in relation to co-sleeping behavior and anxiety among children with GAD and healthy controls. Variability of total sleep time was positively associated with anxiety severity based on both parent and child report. Moreover, frequent co-sleeping with a parent (which was significantly more common in the anxious group) predicted greater intra-individual variability in sleep duration and timing. Together with longitudinal research showing difficulty sleeping alone during the preschool years to be among the most crucial sleep-based predictors of later anxiety (Whalen et al. 2017), findings underscore the role of sleep–wake instability as a putative mechanism of interest in the development of AD.

Consistency of sleep–wake patterns may hold heightened significance for adolescents with anxiety since more variable sleep–wake patterns can give rise to or worsen shifts in circadian timing and impact mood (Acebo and Carskadon 2002; Lewy 2009; Short et al. 2013). Research routinely documents differences in average sleep duration on weekdays versus weekends among adolescents (Carskadon et al. 1998; Crowley et al. 2007), a phenomenon commonly referred to as ‘social jet lag’ (Wittmann et al. 2006). However, variability in night-to-night sleep is also considerable during this developmental period and shown in at least one study to be a more salient predictor of psychological health (including symptoms of anxiety) than sleep discrepancy on school versus non-school nights (Fuligni and Hardway 2006). School start times indisputably exert direct pressure on teens’ sleep schedules, but even during periods when sleep opportunity is unconstrained, more variable sleep patterns predict greater negative mood (Bei et al. 2017).

Sleep and the Transition to Adolescence

Rates of AD reliably increase during the transitional period into adolescence (Costello et al. 2011) and epidemiological data show age 11 to be the median age of onset (Kessler et al. 2005). Nevertheless, the precise impacts of different risk factors vary across specific developmental periods (Bosquet and Egeland 2006) and there is strong indication that this is the case for sleep–wake regulation. Difficulty sleeping alone and prolonged SOL during early childhood presage the development of anxiety between the ages of 9 and 13 years (Whalen et al. 2017). Further, results of a multi-wave longitudinal study showed reduced sleep duration and quality at age 10 to forecast anxiety at age 13 whereas sleep duration at age 8 did not predict anxiety at age 10 (Kelly and El-Sheikh 2014). Likewise, analysis of data from the Great Smoky Mountains Study showed difficulty falling asleep and early morning awakenings during the pre-adolescent years to forecast the development of GAD in adolescence (Shanahan et al. 2014). Unanimously, these data reveal the transitional period from childhood to adolescence as a sensitive

developmental window during which acute or accumulated sleep loss increases the probability of clinical levels of anxiety (see McMakin and Alfano 2015).

Adolescence is a highly precarious time for sleep as well. From the onset of puberty (around 11–12 years) through the late teenage years (17–18 years old), nightly sleep time decreases by about 90 min (Tarokh et al. 2016) notably in the absence of a decreased need for sleep. Several intersecting factors shape an epidemic of insufficient sleep during the teenage years. From a biological standpoint, a reliable delay in circadian timing and slowing of homeostatic sleep pressure that emerge during the pubertal transition produce a shift in sleep timing preferences (i.e., an eveningness chronotype) (Darchia and Cervena 2014; Wolfson and Carskadon 1998) that is at odds with school schedules requiring early wake times. A normative, progressive decline of SWS beginning around the age of 11 also results in sleep that is lighter and more prone to disruption (Campbell and Feinberg 2009; Jenni et al. 2005). Socio-emotional influences, including prioritization of peer and romantic relationships, greater use of electronics/social media, and a drive for greater autonomy compromise sleep time further (Carskadon et al. 1998). Ongoing structural and functional changes of various brain regions provide a dangerous neurobiological backdrop for these developments, rendering young adolescents the most vulnerable to sleep-based cognitive and emotional impairments (Giedd et al. 1999; Powers and Casey 2015). In one experimental study, transitioning adolescents (ages 10–13) but not older adolescents appraised their worries as significantly more threatening after two nights of restricted sleep compared to when rested (Talbot et al. 2010).

The role of development has received superficial attention overall with regard to sleep in childhood AD. When development is considered, arbitrary dichotomizations based on age are used (e.g., 7–11 years, 12–17 years) despite consistent findings from developmental neuroscience revealing sleep-related changes to better align with pubertal than chronological development (Darchia and Cervena 2014; Wolfson and Carskadon 1998). Biologically mediated alterations in sleep are in turn associated with significant elevations in psychological risk. In particular, circadian misalignment (i.e., a mismatch between internal circadian timing and external schedules) is robustly linked with affective disturbances during adolescence (Frank et al. 2013). Relationships with anxiety specifically have received less attention, though cross-sectional and epidemiologic studies provide evidence of a clear link between an evening chronotype and elevated rates of anxiety (Sivertsen et al. 2015; Taillard et al. 2001; Vardar et al. 2008; Willis et al. 2005). In theory, anxiety may be a natural consequence of endogenous sleep–wake patterns that are misaligned with external school/work schedules and demands. For youth who enter adolescence with pre-existing elevations in trait anxiety, social, emotional, and academic stressors may be amplified by alterations in sleep timing and duration, compounding risk for the development of an AD.

Where to Next? Novel Directions in Sleep Research Among Children with AD

In recent years, an increasing number of investigations have shifted their focus toward understanding more acute sleep–anxiety relationships in clinical populations of youth. A few studies have examined interactional effects between sleep and affective symptoms across brief periods. Using 1 week of actigraphy data and daily reports of emotion, Cousins et al. (2011) found that increases in daytime negative affect predicted more time spent awake at night among youth with AD. Further, as positive affect increased during the day, total time in bed at night decreased. Potentially, the presence of better daytime emotional experiences may allow anxious youth to spend less time in bed worrying and ruminating at the end of the day. In the opposite direction, more time spent awake at night predicted greater negative affect the following day, suggesting sleep to play a vital role in emotional recovery from the previous day's emotional events. Mullin et al. (2017) similarly found evidence for a dose–response relationship whereby greater sleep duration was associated with decreases in anxiety the next morning among youth with GAD but not controls. These data reveal unique relationships between broad dimensions of sleep and daytime symptomatology among youth with clinical levels of anxiety that may hold relevance for treatment design and delivery.

In concert, other studies have explored potential sleep-based mechanisms underlying these relationships, focusing on both macro and micro aspects of sleep architecture. Palmer and Alfano (2017) examined daytime affective and somatic symptoms in pre-pubertal youth with GAD (without comorbid depression) and non-anxious controls across 1 week in relation to sleep architecture. Although the groups showed similar proportions of SWS across a night of PSG, duration of SWS was inversely related to negative affective symptoms in the GAD group but not controls. Forbes et al. (2008) also found a negative correlation between SWS and depressive and anxiety symptoms in a mixed sample of children and adolescents with AD. These cross-sectional findings are bolstered by longitudinal data showing a greater amount of SWS in pre-pubertal children at high risk for depression to buffer against the development of mood disorders in early adulthood (Silk et al. 2007).

Whereas REM sleep preferentially supports the formation of emotional memories, SWS plays a fundamental role in the consolidation of hippocampal-dependent, 'emotion-free' declarative memories (Walker and van der Helm 2009). Amount of SWS has also been shown to predict dissipation of emotional distress the next day (Talamini et al. 2013).

Importantly however, slow waves, the major electrophysiological features of NREM sleep, undergo considerable alteration across development in direct parallel with cortical maturation. Specifically, slow wave amplitude increases across the childhood years, peaks right before puberty, and then declines progressively across adolescence, corresponding with changes in the synchronization of cortical neurons (i.e., stronger and denser synapses give rise to faster, more synchronized slow waves; Esser et al. 2007). The long-term protective functions of SWS for affective disorders may therefore exist within a relatively brief, developmental window (i.e., prior to pubertal onset) corresponding with the greatest levels of brain plasticity. In addition to the role of development, the ways in which pre-existing psychiatric symptoms/risk might modulate the interplay between sleep and declarative memory in childhood awaits investigation.

With regard to more micro aspects of sleep physiology, sleep spindles, defined as bursts of oscillatory brain activity that primarily characterize NREM stage 2 sleep, are of increasing interest to child psychopathology researchers. Sleep spindles are believed to synchronize the flow of information from limbic structures to the cortex (Clemens et al. 2007; Siapas and Wilson 1998) fostering consolidation of newly acquired traces into durable memories (Schabus et al. 2004, 2006). Wilhelm et al. (2017) recently examined the presence of slow (9–12 Hz) and fast (13–16 Hz) sleep spindles among youth with SOC and healthy controls. A marked reduction in fast spindles was detected in the SOC group as well as a negative correlation between fast spindle activity and social anxiety severity. Other child-based findings similarly link sleep spindles to child emotional health. Both at-risk and depressed youth show less spindle activity than matched healthy controls (Lopez et al. 2010; Sesso et al. 2017) and greater sleep spindles among preschool-aged children are associated with better emotional health both concurrently and longitudinally (Mikoteit et al. 2013). Sleep spindles might therefore mark a child's ability to adequately process emotionally challenging information/events, in turn minimizing or increasing psychiatric risk.

Because an additional function of sleep spindles is to aid in sleep maintenance, research in this area might also provide insights into perceptions of sleep quality among clinically anxious children. EEG and functional neuroimaging studies demonstrate cortical transmission of external (e.g., acoustic) stimuli is drastically diminished during sleep spindles (Dang-Vu et al. 2011), contributing to the preservation of sleep. Individuals with lower spindle density show greater vulnerability to sleep disruption due to noise in the sleeping environment (Dang-Vu et al. 2010) and are more susceptible to insomnia symptoms during periods of high stress (Dang-Vu et al. 2015). Whether the sleep oscillation characteristics of youth with AD might contribute to perceptions of poor sleep quality therefore represents a worthy question for future study.

Another novel study utilizing the same socially anxious sample as Wilhelm et al. (2017) investigated the role of memory reactivation during sleep. Participants were taught associations between pictures of ambiguous social situations and positive or negative words (Groch et al. 2017). Half of the words were then re-presented auditorily during SWS in the sleep lab that night. Despite no group differences in ratings the next morning, when re-assessed 1 week later, SOC youth provided less positive ratings for negative words presented during sleep compared to controls. The authors conceptualize these findings as reflective of the previous (negative) social learning experiences of youth with SOC such that preferential abstraction of negative emotional information during sleep might account for memory biases characteristic of the disorder (Morgan 2010). Thus, although sleep is known to facilitate emotional memory consolidation generally (Walker and van der Helm 2009), the prior emotional experiences of those with AD may impair memory reconsolidation, or the process by which memories are updated over time.

Re-Conceptualizing the Role of Sleep in Treatment

Treatment research among anxious youth has for the most part considered sleep in terms of problem reduction. Although certainly pragmatic, such an approach overlooks the fact that aspects of sleep might be harnessed to enhance overall treatment response. Since exposure has been shown as the 'essential ingredient' of CBT for childhood AD (e.g., Walkup et al. 2008; Kendall et al. 1997) and sleep occupies an essential role in emotional learning and memory, research in anxious adults has begun to explore sleep's potential for enhancing extinction learning. Fear extinction—the goal of exposure—refers to the loss of a conditioned fear response following repeated, controlled presentation of a feared stimulus. Guided by results from numerous experimental studies showing extinction trials flanked by sleep to result in greater fear reduction (e.g., Graves et al. 2003; Hagewoud et al. 2010; Vecsey et al. 2009), two published studies have investigated sleep-enhanced extinction in clinically anxious adults. Kleim et al. (2014) found spider phobics who napped after a single virtual-reality exposure session evidenced enhanced extinction compared to non-nappers during a behavioral assessment 1 week later. In another study where spider phobics completed an exposure session either in the morning or in the evening (in close proximity to the overnight sleep period), greater extinction based on both subjective and physiological (e.g., skin conductance) decreases in

fear/arousal was apparent the next morning among subjects who completed evening exposures (Pace-Schott et al. 2012).

Other research suggests cumulative wake time prior to exposure to impact fear extinction. In a sample of healthy adults, Pace-Schott et al. (2013) found that exposure sessions conducted in the morning (when homeostatic sleep pressure is lowest) as compared to later in the day resulted in significantly greater fear reduction. Similar findings were recently reported in a sample of adults with post-traumatic stress disorder (PTSD) where hours-since-waking moderated the relationship between fear extinction and PTSD symptoms such that participants with greater symptoms showed significantly poorer extinction the longer they had been awake prior to exposure (Zuj et al. 2016). Since homeostatic sleep pressure increases across the day and reduces efficiency of various regulatory functions, extinction potential may be heightened when sleep pressure is low (Hobson and Pace-Schott 2002). Replication in clinically anxious child samples awaits but strategically timing exposure sessions in relation to sleep could optimize extinction learning and maximize treatment benefit.

Finally, fear extinction in the clinic must also generalize to situations/stimuli in the real world in order for meaningful treatment improvements to occur. Most childhood AD are characterized by a broad range of fears, many of which cannot be directly targeted during clinic-based exposures (e.g., tests, school performances). A vital question then is whether sleep-enhanced extinction learning generalizes to feared situations/stimuli encountered outside of the clinic setting. Available findings in animals and healthy adults provide evidence that post-learning sleep promotes generalization of extinction from targeted fears to non-targeted fears (Kuriyama et al. 2010; Pace-Schott et al. 2009). In their study of spider phobics, Pace-Schott et al. (2012) provide preliminary evidence of extinction generalization in a clinically anxious sample. Specifically, those who completed evening rather than morning exposures showed no evidence of subjective or physiologic arousal when later presented with a novel spider. These sleep-based effects may in part reflect consolidation of between-session learning.

Summary and Future Research Directions

Pediatric sleep researchers have called for more integrative models incorporating knowledge from developmental psychopathology, affective neuroscience, and sleep science to fully explicate the functions of sleep in the context of both healthy and maladaptive child trajectories (El-Sheikh and Buckhalt 2015; Meltzer 2017). Disturbances of sleep are linked diagnostically with anxious psychopathology and youth with AD pervasively complain about their sleep, primarily difficulty with the wake-to-sleep transition and non-restful sleep. A majority of this research has relied on subjective reports however and sleep abnormalities have proven more challenging to capture with standard PSG and actigraphy. These discrepancies notwithstanding, fact remains that detection of simple cause and effect relationships between sleep and anxiety is unlikely given the complexities of these intersecting bio-regulatory systems. Indeed, decades of investigation among various adult psychiatric populations reveal distinct sleep alterations rarely align with specific disorders (Baglioni et al. 2016; Benca et al. 1992). Taken as a whole, there are numerous potential, mutually inclusive reasons for discrepancies between subjective and objective sleep findings but none that should be viewed to diminish the significance of reports of poor sleep and its potential detrimental effects on children with AD. It is more accurate to state that anxious children's experience and perceptions of sleep are shaped by factors that remain largely unknown at this time.

In light of the opposing nature of sleep and arousal states, it is unsurprising that certain types of parent-reported sleep complaints tend to show improvement with anxiety-focused CBT, including reports of bedtime resistance and sleep anxiety. Still, symptom agreement between children and parents both before and after treatment is poor and no substantive evidence exists to suggest that sleep patterns are meaningfully altered following a course of CBT. A pilot study examining the efficacy of an integrated behavioral treatment targeting both anxiety and sleep problems produced similar findings. More compelling evidence comes from a study that sequenced anxiety and sleep interventions where improvements in several sleep variables were found including subjective ratings of sleep quality. Nevertheless, the fact that these reports did not correspond with objective sleep changes bolsters many of the conceptual and methodological points raised in the current paper. A pressing question for clinician and researchers therefore is which aspects of sleep to prioritize during treatment. The current paper highlights several specific avenues for future investigation aimed at filling these gaps in knowledge, collectively rooted in a broader, multi-dimensional view of sleep.

First, precise factors that shape perceptions and reports of sleep quality among youth with AD remain to be distinguished. The contribution of broad objective sleep parameters, such as sleep duration and efficiency is a valuable starting point, but adult-based studies reveal unidimensional (i.e., objective) approaches to be of limited usefulness in this regard. In the context of clinical levels of anxiety, cognitive and physiologic influences must concurrently be considered. Youth with AD possess cognitive biases and distortions characterized by over-generalizing and catastrophizing, and the latter has been shown to predict reports of sleep problems in children. Cognitive biases also necessitate greater attention to measurement timing and the possibility

that extended assessment periods may obfuscate more proximate relationships. The presence of heightened autonomic arousal, a core feature of AD, may additionally render the wake-to-sleep transition highly precarious for youth with AD and contribute to reports of poor sleep quality. Finally, micro-architectural aspects of sleep, such as sleep spindles, known to preserve depth of sleep await exploration in relation to subjective sleep quality.

Second, a nascent body of research suggests the presence of elevated levels of anxiety to pose heightened vulnerability to the effects of sleep loss. Studies in children are limited but youth with AD endorse significantly greater levels of daytime sleepiness, too little sleep, and poorer sleep quality even when sleep parameters are equivocal to healthy youth. Since sleep directly impacts brain structures and circuits underlying emotional arousal and regulation, even subtle amounts of sleep loss or alterations in sleep timing might exacerbate pre-existing neurobiological vulnerabilities in this population. In support of this thesis, emerging studies using fMRI have demonstrated the presence of anxiety to moderate degree of neurobiological vulnerability related to sleep. A heightened sensitivity to sleep loss may further emanate from more down-stream cognitive processes including anxiety sensitivity, perceived control over anxiety, or catastrophizing struggles with sleep.

Third, examination of mean sleep variables and one-time sleep reports provides little insight into the regularity of children's sleep. The greatest levels of intra-individual sleep variability have been found in anxious populations making this a critical dimension of overall sleep health for youth with AD. Across developmental stages, greater night-to-night variability in sleep predicts anxiety both concurrently and prospectively and variability of total sleep time is positively associated with anxiety severity among youth with AD. These relationships are likely reciprocal as anxiety and worries prior to sleep have also been associated with greater sleep schedule variability in non-clinical populations of youth. The sleep context may exert direct influence on sleep regularity (as well as sleep quality) since bedtime resistance, co-sleeping, and contentious family interactions set a negative 'emotional tone' for sleep generally. Periodic co-sleeping is remarkably frequent in pre-pubescent children with AD and has been shown to predict greater intra-individual variability in both sleep duration and timing. Unfortunately, most published studies have failed to either examine or consider the influence of co-sleeping on sleep–wake regularity. Variability in night-to-night sleep is also considerable during the adolescent years and linked with intensified psychological risk.

With regard to development, vast changes in the biology and behavior of sleep that emerge with the transition to adolescence command greater attention in the context of clinical levels of anxiety. The neurobiological, hormonal, social, and environmental alterations that underlie peri-pubertal changes in sleep intersect with emotional systems to produce heightened levels of affective risk in all youth. For youth with AD, a delay in circadian timing, slowing of homeostatic sleep pressure, and declines in SWS may act synergistically with pre-existing levels of anxiety to produce negative cascading effects on emotion across adolescence. Importantly, since pubertal timing, as compared to chronological age, provides a more reliable marker of these sleep-based changes, there is general need for a shift in assessment practices and conceptual approaches for studying sleep among youth with AD. The role of circadian misalignment (i.e., social jetlag), a frequent result of competing endogenous and exogenous influences on sleep during the teenage years, has received remarkably little attention among clinically anxious youth despite the possibility of greater sensitivity to sleep-based disruptions in daily routines and activities (i.e., low rhythmicity). Low sleep rhythmicity in childhood has nevertheless been shown to predict the onset of AD during adolescence.

Other emerging, novel studies reviewed herein represent promising areas of inquiry as well. Several studies have explored reciprocal relationships between macro and micro aspects of sleep and daytime symptomatology among youth with AD, revealing unique sleep–emotion relationships. Accumulating evidence also suggests that duration and/or depth of SWS may shield youth with (and without) AD from subsequent depression. Accordingly, the degree to which normative developmental decline in SWA that begins with the pubertal transition intersects with elevations in anxious and affective symptomatology is an important question for future research. In addition, sleep spindle activity during NREM sleep might provide a neurobiological index of anxiety risk and/or severity. Based on the thesis that sleep spindles provide evidence of encoding emotional information/events, examination of spindles in relation to CBT-based outcomes for anxiety could provide mechanistic insight into successful/unsuccessful treatment. More sophisticated analysis of PSG parameters among children with AD therefore represents an exciting avenue for future research.

Finally, rather than merely representing a direct target of treatment, various dimensions of sleep might be leveraged to enhance anxiety-based treatment outcomes. Sleep is essential for emotional learning and memory including extinction learning, a core mechanism of exposure-based treatments. A wealth of research in animals and adults provides evidence of enhanced fear reduction when extinction training (i.e., exposure) is conducted in close proximity to a sleep period. These learning effects are independent of circadian influences and appear to generalize to non-targeted fears. Although developmental variation in extinction learning (Kim et al. 2009; Kim and Richardson 2010) necessitates replication of these findings in child samples, the fact that CBT, the 'gold standard' treatment for childhood AD

is effective for less than 2/3 of youth (James et al. 2013) underscores a need for novel, practical strategies to enhance its effects.

Conclusions

Cross-sectional, longitudinal, epidemiological, and experimental work emphasizes the presence of complex bidirectional relationships between sleep and anxiety across the life-span. Sleep disruption is a manifest feature of clinical levels of anxiety but also independently forecasts the development of an AD. These reciprocal impacts make clear the need to better understand the nature and consequences of sleep–wake patterns associated with early-onset AD to inform developmental models as well as comprehensive assessment and treatment approaches. The current paper highlights several fundamental questions for future research including the possibility of sensitive developmental periods wherein dimensions of sleep might intersect most intensely with anxiety symptomatology. The questions raised here are by no means exhaustive however, as other noteworthy gaps in understanding persist. For example, significant cross-cultural differences exist with regard to children's sleep (Jenni and O'Connor 2005) but the ways in which these differences might interact with anxiety is largely unknown, even in the face of evidence for such relationships (e.g., Alfano et al. 2010). As such, findings included in the current review are mainly based on Caucasian youth from western cultures. Other valuable questions relate to whether and to what extent specific forms of anxiety might be more susceptible to circadian rhythm disturbances across development. Overall, probing of these and other questions ultimately rests upon an understanding of sleep that surpasses mere symptoms and problems to include appreciation of more intimate relationships with emotional health.

Compliance with Ethical Standards

Conflict of interest The author declares that she has no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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