SLEEP Advances, 2025, 6, zpaf072
doi:10.1093/sleepadvances/zpaf072
Advance Access publication 12 November 2025
Protocol Papers

Protocol Papers

Exploring the association between sleep and fear extinction learning in adolescents with anxiety and/or OCD: a study protocol

Kathrin Renschler[1], Giulia R. Righi[1,2,3,*], Kristen G. Benito[1,3], David H. Barker[2,3], Mary A. Carskadon[2,3] and Jared M. Saletin[2,3]

[1]Pediatric Anxiety Research Center, E.P. Bradley Hospital, Providence, RI, USA, [2]Sleep Research Laboratory, E.P. Bradley Hospital, Providence, RI, USA and [3]Department of Psychiatry and Human Behavior, Warren Alpert Medical School of Brown University

*Corresponding author: Giulia R. Righi, 1011 Veterans Memorial Parkway, East Providence, RI, 02915, USA. Email: giulia.righi@brownhealth.org.

Abstract

Pediatric anxiety disorders (including Obsessive Compulsive Disorder) are prevalent and impairing. Youth with anxiety disorders frequently experience sleep disturbances. Exposure, the primary component of gold-standard Cognitive Behavioral Therapy (CBT) for treating anxiety disorders, works by harnessing fear extinction learning. Given that sleep plays a critical role in the consolidation and retrieval of emotional memories, we hypothesize that shorter sleep quantity and greater sleep disruption are associated with psychophysiological responses indicating reduced fear extinction learning and reduced fear extinction recall in adolescents with anxiety and OCD. In this protocol paper, we describe a pilot study testing this hypothesis in a clinical sample of adolescents participating in a CBT-based partial hospital program (PHP) dedicated to the treatment of anxiety disorders. Participants complete a multi-method sleep assessment over 10 days during the first portion of their admission in the program (within the first 4 weeks) and at the end of their stay (at least over 5-7 days before discharge). Standardized clinical interviews and sleep questionnaires are coupled with multi-modal at-home sleep monitoring using sleep diaries, patch-based actigraphy, and wearable sleep electroencephalography (EEG). Participants also complete a computerized task assessing initial fear learning (day 1), fear extinction learning (day 2), and extinction recall (day 3) as measured by skin conductance responses (SCR). This use of multi-method sleep assessments in a clinical sample of youths with more clinically severe anxiety disorders is innovative and, to our knowledge, has not yet been done.

Key words: anxiety; sleep; fear conditioning; adolescents

Statement of Significance

Results of this study will provide data for understanding sleep problems in relation to one of the underlying mechanisms of exposure therapy among adolescents with anxiety disorders, and evidence for feasibility of multi-method sleep assessments in a relatively acute mental health setting. If this line of research is successful, it will allow for the development and evaluation of augmentation strategies that target specific aspects of sleep that contribute to suboptimal fear extinction learning. Results from this work may serve as proof-of-concept for identifying sleep targets to guide the augmentation of behavioral treatments.

Introduction and Rationale

Pediatric anxieties disorders (including obsessive compulsive disorder) are some of the most prevalent of childhood onset psychiatric disorders, with anxiety affecting up to 30% [1] and OCD affecting up to 4% of adolescents [2, 3]. Symptoms are unremitting into adulthood and associated with later emergence of mood and substance problems as well as disproportionately high disability [4, 5].

Problems with sleep are common in anxiety disorders [6–8] and sleep problem severity has been associated with greater degree of clinical symptoms and poorer clinical outcomes [9–12]. The majority of youth with anxiety report at least one sleep-related problem (e.g. insomnia, reluctance to sleep alone, reluctance to sleep away from home, nightmares, being-overtired, etc.) and more than half report three or more [7, 13].

Subjective sleep complaints have shown poor agreement with objective sleep patterns to date, and traditional actigraphy and polysomnography in youth with anxiety disorders show few consistent differences from healthy controls [14]. For example, whereas some actigraphic investigations have observed differences in total sleep duration, sleep fragmentation and night-to-night variability [15–18], others have reported no group

Submitted: 14 August, 2025; **Revised:** 26 September, 2025; **Accepted:** 4 October, 2025

differences between anxious youth and controls [19, 20]. Findings are also inconsistent with polysomnography [21, 22]. Of note, these studies have been primarily conducted with youth with mild-to-moderate levels of symptoms, and very limited research is available in youth with more severe challenges.

While sleep complaints are commonplace in pediatric anxiety clinical settings, understanding the nature of sleep disruption and its potential role in the maintenance of clinical symptoms has yet to be established. In this study, we hypothesize that the nature of sleep disruptions present in anxiety disorders impairs the mechanism underlying by gold standard behavioral treatment for these disorders, which relies heavily on generating new learning. Exposure-based CBT is the first-line treatment for anxiety disorders [23, 24], but more than 40% of youth do now show adequate improvements and only about half experience remission [25-27]. Even intensive daily CBT (e.g., provided by partial hospital programs or intensive outpatient treatment) produces low remissions rates [28]. Exposure involves approaching a feared stimulus in a gradual and controlled manner, followed by the prevention of ritualistic or avoidant strategies utilized by an individual to reduce their distress. Exposure is functionally related to fear extinction learning, which allows for a fear response to be diminished by associating the triggering stimulus with a new outcome [29]. This process most likely does not involve a reversal of a fear association, but new learning [30]. Initial fear extinction learning takes place during an exposure situation, where youth learn that feared situations are not as dangerous or distressing as they had predicted. Consolidation of this learning occurs after the exposure, likely over the next several hours and during subsequent sleep [31]. Recall of new fear extinction memories then occurs when individuals encounter similar contexts going forward, which no longer elicit strong distress. In order for exposure therapy to succeed, consolidation and recall of extinction learning acquired during therapy are essential [32]. Fear extinction learning is often measured with a combination of involuntary psychophysiological responses and subjective ratings. In youth, skin conductance responses (SCR) have been shown as the most reliable index of initial learning, consolidation and recall [33].

Ample evidence from work with adults and animal models links sleep with emotional memory consolidation [34]. In experimental paradigms, sleep loss compromises the ability to commit new experiences to memory [35], and sleep deprivation can impede forming memories of emotional content [36]. Sleep after learning promotes key neural processes required for memory consolidation [37–39]. Thus, sleep problems may exacerbate and/or maintain anxiety symptoms by interfering with the consolidation and generalization of fear extinction memories. Longer sleep duration the night before exposure predicts lower symptoms at the next session, after controlling for symptoms at the previous session [40]. Furthermore, greater self-reported "restedness" after exposure-based therapy sessions uniquely predicted subsequent symptom reduction in adults [41].

A number of studies have experimentally manipulated sleep duration to determine its effects on phases of fear extinction learning (initial learning, recall, generalization) during lab-based exposure paradigms or computerized tasks, quantifying fear extinction using psychophysiological variables such as SCR and/or startle responses. Longer sleep prior to the task can facilitate initial learning (i.e., encoding information) [42, 43] . Sleep deprivation can impair initial extinction learning and recall and also reduces ability to generalize extinction learning [44-48]. Sleep following lab-based exposure can promote retention and generalization of extinction learning [49].

Sleep stage distribution may also influence fear extinction learning. Neural circuitry associated with the processing of emotional stimuli and emotional memories is activated during REM sleep, which has led to the hypothesis that REM sleep may influence the consolidation of emotional memories [42]. In healthy adults, REM sleep deprivation was associated with reduced recall of fear extinction, [39] and REM sleep percentage during the intervening night between initial learning and subsequent recall has been positively associated with retention of extinction learning [42]. A relationship between REM sleep parameters and altered fear extinction learning has also been observed in adults with insomnia [50] and adults with PTSD [51, 52]. Higher slow wave sleep (SWS) percentage in healthy adults was also associated with lower reactivity to the safety stimulus, indicating better initial learning [43]. Altogether, these studies suggest that both REM and SWS may influence learning during exposure. It is important to note that these studies involved adults, and none has examined these associations in a clinical sample of youths.

The available literature supports a causal role for biobehavioral sleep indices across multiple phases of fear extinction learning. Even with the theorized importance of sleep for therapeutic learning during exposure, this relationship is not directly addressed during treatment, especially in those with more impairing clinical symptoms. Sleep may be an important pathway through which exposure outcomes could be improved; however, the promise of this approach is limited by the sleep methods traditionally available in clinical settings (e.g., reliance on self-report of sleep quality). Our multi-method approach to sleep assessment has the potential to yield specific information about the most promising sleep targets that could then be used to guide the development of matching augmentation strategies.

Actigraphy, an objective measure, is capable of capturing broad indices of sleep-wake rhythms (i.e., diminished sleep duration [53] or alterations to circadian timing [54]). The strength of such methods lies in their ease-of-use, validation (e.g [55–59].), and ability to capture sleep across multiple nights. Even with the advent of more advanced analytics capable of detecting subtle shifts in sleep regularity across days [60–63], all actigraphic sleep estimates eschew both sleep macrostructure (e.g., sleep stages) and microstructure (e.g., the electroencephalographic (EEG) power spectrum). For advancing insight into potential differences, EEG is a requisite although often burdensome (in the context of polysomnography) addition. The current study attempts to bridge this methodological gap by introducing multiple sleep measurements across multiple nights in the home environment.

Current Study

Building on this literature we present the methods and protocols of an ongoing study to determine whether multi-method sleep indices relate to fear extinction learning in youth with moderate to severe anxiety disorders. The central hypothesis is that shorter sleep quantity and greater sleep disruption are associated with reduced fear extinction learning and reduced fear extinction recall in these youth as indexed with psychophysiological responses. Our first aim (aim 1) is to characterize sleep problems with a multi-methods examination of sleep, as there is very limited data available on youth with more prominent clinical symptoms of anxiety and related disorders. We hypothesize that participants will present with a variety of sleep problems, including reduced overall sleep duration and increased sleep disruptions, when compared to similarly aged healthy peers.

Aims 2 and 3 examine the association between these adolescents' sleep and fear extinction learning (aim 2) and recall (aim 3) respectively. We hypothesize that lower sleep duration and greater sleep disruption during the night preceding fear extinction learning predict reduced learning indexed with skin conductance responses (SCR), and lower sleep duration and greater sleep disruption during the night before the recall phase predict impaired fear extinction recall as indexed with SCR. Exploratory hypotheses include an examination of the quality and quantity of REM and Slow Wave Sleep (SWS) sleep during the night preceding each experimental phase and their relationship to SCR during the respective phase of the task. Finally, we examine the association between sleep problems and treatment outcomes (aim 4) and expect that treatment responders and non-responders show significant differences in reported sleep problems at the beginning of treatment.

Methods and Analysis

Participants

We plan to enroll a total of 84 treatment-seeking adolescents between the ages of 11 and 18 years. The age range is intentionally broad, as this study is also intended to evaluate the feasibility of our protocol to support the utilization of similar methods in future projects with more targeted aims. Participants are recruited from the Pediatric Anxiety Research Center (PARC) Intensive Program for OCD and Related Disorders located within Bradley Hospital in East Providence, Rhode Island. PARC Intensive Program treats youth with moderate to extreme anxiety and/or OCD for 4-6 hours/day Monday through Friday. During the active phase of treatment generally starting during the second week of admission, participants complete 1-2 hours of exposure therapy per day along with other adjunctive therapies (e.g., motivational interventions, peer-support group, family therapy). Youth return home each day after the program and medications (most frequently SSRI, antipsychotics, benzodiazepine, stimulants [28]) are taken at home. The program is considered a partial hospitalization level of care, which is intended for children with severe or refractory symptoms. Median length of stay is 6-8 weeks. To be eligible for the study participants must be between the ages of 11 and 18 and have primary diagnoses of anxiety disorders (Social Anxiety Disorder, Generalized Anxiety Disorder, Separation Anxiety Disorder, Phobia, Panic Disorder, Illness Anxiety Disorder) and/or OCD. Youth and one parent must be able to speak English. Exclusion criteria include a diagnosis of autism spectrum disorder, and/or cognitive or developmental delay.

Procedures

Participants are recruited in person after they are admitted to PARC's partial hospital program (PHP) for anxiety and related disorders. Prior to approaching potential participants, the study team applies a three-step process of determining eligibility.

Determination of eligibility. First, the study staff screen newly admitted patients' intake information for age and diagnoses. If a patient is younger than 11 years, was previously diagnosed with autism spectrum disorder (ASD), or does not have a legal guardian who speaks English, they are considered ineligible. Second, the study team confirms that the patient has not previously participated in the study, as this is another exclusion criterion for participation. Third, if admission criteria are met, the study team contacts the patient's treating clinicians to assess any concerns about the patient being offered enrollment in the study. Our standard operating procedure is to wait at least three program days before reaching out to the clinical team to allow for sufficient familiarization with the patient's clinical presentation. Reasons for exclusion at this stage can include: 1) participation being clinically contraindicated (e.g., patients for whom study participation would interfere with treatment); or 2) the patient might discharge too quickly to complete the different parts of the study (e.g., it is unclear at admission if the Intensive Program is the best fit for the patient's symptom presentation).

Study Enrollment. If a participant is determined eligible following the above-described procedure, the study team, which does not overlap with their clinical team, approaches them in person during their daily stay in the intensive program. The study team provides a brief overview of the study and allows time for questions. If the patient expresses interest in participation, the study team schedules a meeting to do the informed consent process with the patient and at least one legal guardian, if the patient is under the age of 18. In line with IRB and HIPAA guidelines, trained study staff obtain informed consent from legal guardians or adult participants (i.e., those 18 years old) and assent from minors after initial contact and prior to data collection. If a participant turns 18 years old while participating in the study, they are re-consented as an adult. As part of the consent process, legal guardians (or participants, if 18 years old) provide their email address and, if relevant, the patient's email address which is used to send study measures at the beginning, during, and at the end of study participation. The first participant was enrolled on 9/15/2022, and we anticipate data collection to be completed by February of 2026. No substantial changes have been made to the protocol since data collection started.

Study participation. Once the consent process is completed, participants and their caregivers take part in clinical interviews and complete self-reports to assess clinical symptoms and sleep characteristics. All measures and devices used are described in detail in the following section. Clinical interviews are administered by research assistants who are trained to criterion on study measures and participate in weekly supervision for criterion maintenance. Self-report measures are completed in electronic form.

Youths participate in a 10-day sleep assessment in their homes that includes daily sleep diaries and actigraphy monitoring. On day 8, youths begin a computer-based fear learning and extinction paradigm, which will take place in three distinct phases. On the first day, youths participate in the fear acquisition phase; the following day, they participate in the fear extinction phase, and on the final day, they participate in a fear extinction recall phase. For the last 4 days of the study, youths also undergo at-home electroencephalogram (EEG) recording during sleep. Within the last week of participation in the intensive program, we collect self-report and parent-report sleep characteristics, clinical symptom severity measures, and 3-5 days of actigraphy data and sleep diaries. See figure 1 for the complete study flow.

Measures

Clinical and self-report measures. Study assessment measures are listed in Table 1.

Demographics: Standard demographic information is collected at the beginning of the study. This information includes age, gender, puberty status, education, race, ethnicity, and family composition.

Clinical Measures: The following is a description of clinical measures that are administered prior to collecting sleep and task

Figure 1. Study flow.

data (see Table 1). All clinical assessments occur either in person at PARC, by teleconference, or by phone to minimize barriers for patients/families.

Diagnosis and Symptom Severity. Mini-Kid [64] is a brief, structured
interview measuring psychiatric diagnoses in children according to DSM-V and ICD-10 criteria. Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) [65] is a clinician-administered, "gold standard" assessment of OCD symptom severity with excellent psychometric properties. Total scores for obsession and compulsion subscales range from 0 (no symptoms) to 40 (severe). Pediatric Anxiety Rating Scale (PARS) [66] is a clinician-rated measure of anxiety symptom severity for use with multiple anxiety disorders that have good psychometric properties including sensitivity to change in treatment. Clinical Global Impression Scales (CGI) [67] are brief, clinician-rated measures of global severity and improvement in treatment for children and adults and have good psychometric properties.

Sleep Functioning. PROMIS Sleep Disturbance and Sleep-Related Functioning [68] are two short-form 8-item measures of sleep problems that are completed by caregivers and adolescents. Munich Chronotype Questionnaire (MCTQ) is a self-report measure filled out by participants to collect information on sleep-/wake patterns and to assess chronotype. Modified Children's Chronotype Questionnaire (CCTQ) [69] is administered to caregivers to get information about their child's sleep/wake patterns and chronotype. Pediatric Sleep Questionnaire [70] is a 22-item measure administered to the caregiver that asks about snoring frequency, loud snoring, observed apneas, difficulty breathing during sleep, daytime sleepiness, inattentive or hyperactive behavior, and other pediatric obstructive sleep apnea features.

Measure of broad emotional, cognitive and behavioral functioning. PROMIS Anxiety, Depressive Symptoms, Anger, Cognitive Function, Positive Affect, Family Relations, Peer Relationships, Life Satisfaction and Psychological Stress [71] are completed by caregivers and adolescents. These measures are designed to assess psychiatric symptoms, emotional distress, and social role participation within family and community. Difficulties Emotion Regulation Scale (DERS) [72] is an 18-item measure used to identify emotion regulation issues.

Table 1. Complete list of clinical and sleep functioning measures including times of administration

Measures	Construct	Acquisition Time
CLINICAL ASSESSMENTS		
Mini-Kid (Clinician Administered)	Psychiatric Diagnoses	Baseline
CYBOCS and/or PARS (Clinician Administered)	Symptom Severity	Baseline & End of Treatment
CGI Severity (Clinician Rating)	Symptom Severity	Baseline
CGI Improvement (Clinician Rating)	Symptom Improvement	End of Treatment
PROMIS full youth battery (Self-report)	Broad Psychological Functioning	Baseline & End of Treatment
DERS (Self-report)	Emotion Regulation	Baseline & End of Treatment
SLEEP FUNCTIONING		
PROMIS Sleep Short-Forms (Youth/Parent)	Sleep-related problems and impairment severity	Baseline & End of Treatment
Munich Chronotype Questionnaire (Self-report)	Sleep-Wake Patterns	Baseline & End of Treatment
Modified Children's Chronotype Questionnaire (Caregiver)	Sleep-Wake Patterns	Baseline & End of Treatment
Pediatric Sleep Questionnaire (Caregiver)	Contextual Sleep Factors	Baseline & End of Treatment

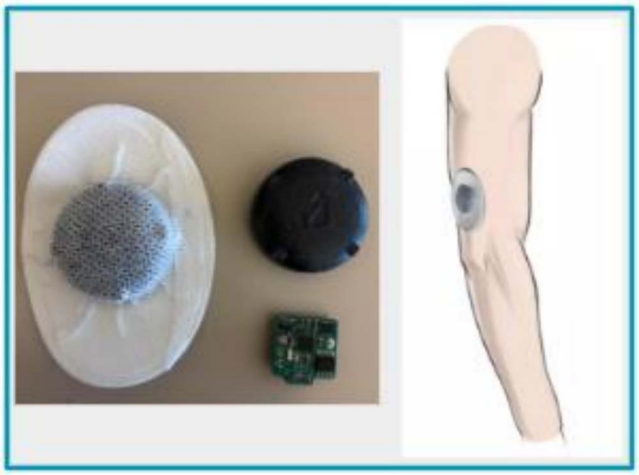

Figure 2. Actigpatch device (left) and location on participant's body (right).

Figure 3. ZMax wearable EEG device (top) and electrodes (bottom).

Measures of treatment course. We collect the length of stay in the intensive program. Any prescribed psychotropic medications and relevant dosage is recorded at the beginning of treatment, during the 10-day study window, and at discharge. A significant portion of youth with high-impairment ARD are treated with medication [28] supported by the American Academy of Child and Adolescent Psychiatry. Given these treatment requirements and ethical concerns about restricting access to medications, as well as feasibility of recruiting youth who are willing to forgo medication trials. As such we allow participants to have changes to or initiation of psychiatric medications while participating.

Sleep and laboratory-based assessments

Actigraphy & Sleep Diaries. To assess daily sleep-wake patterns we employ a novel triceps-worn compact activity monitor (Actigpatch, Circadian Positioning Systems, Inc., Newport, RI; see figure 2) adhered to the skin with an adhesive patch. This device has been validated against traditional wrist-worn actigraphy and polysomnography [73]. Participants wear the Actigpatch for 10 days at the beginning of study participation and for three to five days at the end of study participation, prior to their discharge from the intensive program. An advantage of this patch-based monitor is continuous wear for the course of the study, facilitating data retention in a clinical sample.

While wearing the Actigpatch, adolescents complete online sleep diaries. Logs contain daily information about bedtime, attempted sleep time, nighttime wakings, wake up time, out of bedtime, naps, caffeine, life events, and subjective sleep quality. These data are intended to support the scoring of actigraphy data [74]. Sleep diaries are sent to the participant's email address via REDCap each morning and night at predetermined times and are checked regularly for completion. Sleep-wake states are estimated on the Actigpatch record using the Sadeh algorithm [57] and sleep-periods are scored vis-a-vis the sleep diary according to our established procedures and best recommendations [58, 59, 75]. Actigraphy is used in combination with sleep diaries to estimate sleep-wake patterns. Variables of interest include mean total sleep time, sleep efficiency (total sleep time / sleep period time), wake after sleep onset, number of awakenings, and the sleep regularity index (i.e. a measure of consistency of sleep-wake cycles across nights) [63].

Wearable sleep EEG recordings

To measure EEG in this treatment-seeking clinical sample without the prohibitive burden of polysomnography, we use a wearable dual channel electroencephalograph: "ZMax" (Hypnodyne, Inc.), which provides high-quality EEG signals using disposable Ag/AgCl electrodes. The ZMax (see figure 3) is worn like a headband. A demo is provided to all participants prior to being given the device. Participants are asked to attach the electrode to the headband and place it on their forehead just above the eyebrows. ZMax records (256 Hz) left (F7) and right (F8) frontal EEG on a MicroSD card. After preprocessing the raw, overnight sleep EEG data through the Hypnodyne HDREcorder software, deidentified data are processed through an open-source auto scoring algorithm, dubbed DreamentoScorer [76]. Visual quality-control of raw EEG data as well as whole-recording spectrograms generated from DreamentoScorer serve to audit EEG data for signal quality. Only sleep stages estimated from intact whole-night EEG are considered for future sleep architecture analyses. In such recordings, sleep stages are tabulated and reported through our group's open-source Hume software. Outcomes of interest are the quantities of REM sleep and Slow Wave Sleep (as percentages of total sleep time), as well as their ultradian hour-by-hour distribution across the sleep period.

Laboratory-based assessment

On day 8 (fear conditioning), 9 (extinction learning), and 10 (fear recall) of the study Adolescents participate in a computer-based fear extinction learning paradigm. The paradigm is administered using E-Prime software 3.0 (Psychology Software Tools, Pittsburgh, PA). The paradigm is modeled after previously validated work investigating fear extinction learning in youths and it's dubbed the "bell task" [77]. The unconditioned stimulus (US) is an image of a bell ringing co-occurring with the sounds of a bell at 90 dB. Conditioned stimuli (CS) are pictures of a blue bell and yellow bell. During the habituation phase the blue and yellow bell images are presented eight times each in pseudorandom order. During the fear acquisition phase, one of the shapes (CS+) is followed by presentations of the US along with interspersed presentations of the other shape (CS-) all in pseudorandom order for a total of 20 trials. The CS+ is followed by the US according to an 80%

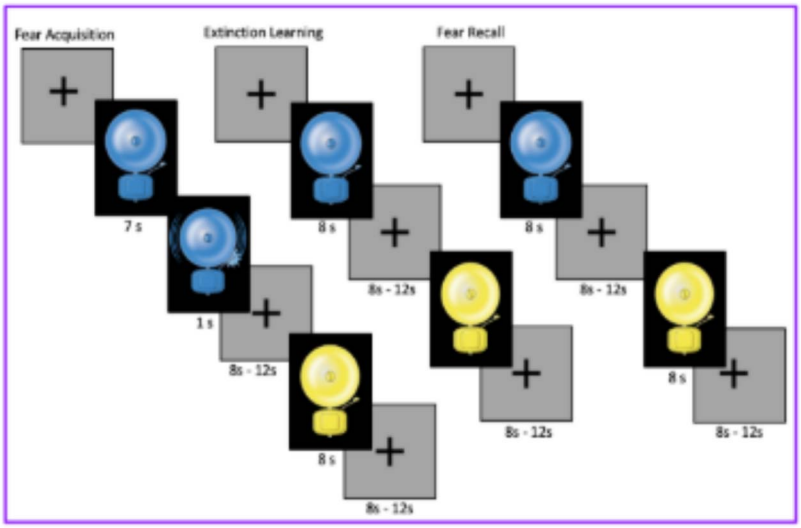

Figure 4. Schematic of fear extinction learning task.

reinforcement schedule. During the extinction learning phase the CS+ is presented unaccompanied by the US for 12 trials, pseudorandomly interspersed with the CS-. During the fear recall phase, the CS+ unaccompanied by the US and CS- are presented in pseudorandom order for 12 trials each. Each trial lasts 8 seconds. Inter trial intervals vary between 8 and 12 seconds across all presentations. The color of the stimuli used for the CS+ and CS- is counterbalanced across participants. See Figure 4 for a schematic of the paradigm.

Variables of interest include skin conductance responses, contingency awareness and state anxiety. Skin conductance level is recorded using a Biopac MP150 wireless system (BIPAC Systems, Inc., Goleta, CA). Data is acquired at a sampling rate of 1 kHz using the GSR module of the Biopac system. Two 5 mm Ag/AgCl disposable electrodes filled with isotonic paste are attached to middle phalanges of the second and third finger of the non-dominant hand. A skin conductance response (SCR) for each trial is estimated by taking the difference between baseline skin conductance (defined as the average skin conductance level 2s before CS onset) and the peak skin conductance value observed anywhere within the seven-second window containing the stimulus presentation.

To assess subject awareness of conditioning, after the fear conditioning phase, the extinction phase, and the recall phase participants are asked whether one of the presented shapes was paired with a sound, and if they respond YES, they are asked to specify which of the bells was paired with the sound. These responses are collected on a computer keyboard with single button presses. To assess subjective anxiety at the end of each experimental phase, participants respond with a 10-point Likert scale rating how anxious they feel. These responses are collected on a computer keyboard with a single button press.

Compensation

Participants enrolled in the study receive up to $325 for study participation. Both participant and parent, if the participant is a minor, are paid $50 each for the initial assessment consisting of clinical and self-report measures. For completion of the 10-day sleep data collection the participant is paid $100. Participation in the fear paradigm task is compensated with $50. Completion of the final assessments, including the week of actigraphy, is compensated with $75. The compensation is provided in cash after each phase of the study is completed.

Data analysis plan

Data management and confidentiality. All staff with access to participant data and identifying information are registered with the institutional review board (IRB) at Brown University Health. Data are stored on secure servers, which undergo daily backups. Participant identifying information is stored separately in a password-protected database. Any paper records are stored in a locked cabinet within a locked office. There is no personally identifiable information stored on any of the devices. If a device were to be lost or stolen, the data on the device would be inaccessible without the appropriate software and hardware.

Sample size justification and statistical power. The study is powered to the hypothesis tests for Aims 1-3. Power analyses were run using G*Power 3.1.9.7 and assumed alpha of .05. With 84 participants this study is powered at .80 to detect a small effect size (Cohen's d>.35) for Aim 1. The multiple regression analyses assume five predictors and are powered to detect medium effect sizes (R^2>.15).

Data analyses

To evaluate aim 1 (multi-methods examination of sleep problems in adolescents with anxiety and/or OCD), we will compute quantitative measures to describe the characteristics of sleep problems in these youths and the patterns observed via direct sleep assessments. We will compare estimates in our sample with normative data with same-age peers [78] using independent samples t-tests. We will use latent profile analysis models to further explore the patterns of sleep in our sample.

To evaluate aims 2 (examine the relationship between adolescents' sleep and fear extinction learning) and 3 (examine the relationship between adolescents' sleep and fear extinction recall), we will use multiple regression to estimate the strengths of association between skin conductance response (SCR) as a measure of fear conditioning, and sleep variables extracted from the night before the administration of the task. SCR will be the dependent variable with sleep duration and number of sleep disruptions as independent variables. Participants' symptom severity, gender, and age will be included as covariates. We will

use the same analytical methods to estimate the strength of association between REM sleep and slow wave sleep duration during the night preceding the learning phase and fear extinction learning as characterized by SCR. Exploratory analysis will use regularized regression to examine the contributions of additional sleep variables (e.g. sleep regularity, actigraphy based circadian timing) to fear extinction learning as measured by SCR.

To evaluate aim 4 (assess changes in sleep problems at the end of intensive treatment), we will use within subjects t-test to examine differences in self and parent reported sleep problems pre- and post-treatment and the end of the stay in the intensive program. We will also divide our sample into youths who responded to treatment as evidenced by significant symptom reduction and those who did not, and then utilize between subject t-tests to compare sleep problems in these two groups at the outset of treatment. Finally, we will again use regularized regression to identify predictors of pre-post treatment change in symptoms.

Based on available data we estimate that up to 80% of participants might be prescribed psychotropic medication during their partial hospital stay [28]. While some of the medications used in treatment (e.g. SSRI, Clonidine) are known to impact sleep, it is necessary to include participants on medications to accurately study youth with more severe symptoms–a group that has largely been absent from prior studies. Active psychiatric medications and all relevant medication changes are documented, and we will consider the impact of medication changes in sensitivity analyses (e.g., rerunning analyses with only those receiving particular classes of medications) or including medication information (dose and class) as covariates in our modeling.

Discussion

Anxiety disorders are prevalent and impairing. Exposure-based CBT is the gold standard treatment, but a significant subset of youth who receive this intervention will not experience symptom improvements. In this study, we aim to characterize sleep in adolescents with anxiety disorders broadly specified and examine how it relates to fear extinction learning, a central mechanism of exposure-based CBT. This study will be the largest dataset to date of multi-night multi-modal sleep phenotyping (actigraphy and sleep EEG) in such a severely impacted sample of treatment seeking youth, providing novel phenotyping data in addition to linking these sleep phenotypes to mechanisms of exposure-based therapy. The results of this study will enhance our understanding of sleep problems in relation to fear extinction learning among adolescents with severe or refractory symptoms. Doing so in a treatment-seeking population complements and expands upon prior experimental studies of sleep-dependent emotion processing relying on healthy control populations. Thus, these data will provide a first-step in using multi-method sleep assessments in an adolescent partial hospital setting as well as inform the future development and evaluation of interventions targeting sleep to improve treatment outcomes.

Acknowledgements

The authors would like to thank the research staff who are helping with the data organization and collection (Michaela Maron, Ella Diab, Alexander Markowitz, Mitchell Jackson) and the administrators offering support to this project (Cristal Meideros, Deidre Walton).

Author contributions

Kathrin Renschler (Writing - original draft [equal]), Giulia Righi (Conceptualization [lead], Writing - original draft [equal]), Kristen G Benito (Conceptualization [supporting], Writing - original draft [supporting]), David H Barker (Conceptualization [supporting], Writing - original draft [supporting]), Mary A Carskadon (Conceptualization [supporting], Writing - original draft [supporting]), Jared M Saletin (Conceptualization [supporting], Writing - original draft [supporting]). KR and GR drafted the initial manuscript. JS, KB, MC and DB reviewed and revised the manuscript.

Funding

This work is funded by an award (P20GM139743) to MAC from the National Institute of General Medical Sciences.

Disclosure statement

Financial disclosure: The authors have no disclosures to report.

Non-financial disclosure: The authors have no disclosures to report.

Data availability

No new data were generated or analyzed in support of this manuscript.

Research ethics and protocol amendments

All study procedures were approved by the Brown University Health IRB.

References

1. Merikangas KR, He JP, Burstein M, *et al*. Lifetime prevalence of mental disorders in U.S. adolescents: results from the National Comorbidity Survey Replication–Adolescent Supplement (NCS-A). *J Am Acad Child Adolesc Psychiatry*. 2010;**49**(10):980–989.
2. Mancebo MC, Boisseau CL, Garnaat SL, *et al*. Long-term course of pediatric obsessive-compulsive disorder: 3 years of prospective follow-up. *Compr Psychiatry*. 2014;**55**(7):1498–1504.
3. Walitza S, Melfsen S, Jans T, Zellmann H, Wewetzer C, Warnke A. Obsessive-compulsive disorder in children and adolescents. *Dtsch Arztebl Int*. 2011;**108**(11):173–179.
4. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;**62**(6):617–627.
5. Ramsawh HJ, Chavira DA, Stein MB. Burden of anxiety disorders in Pediatric medical settings: prevalence, phenomenology, and a research agenda. *Arch Pediatr Adolesc Med*. 2010;**164**(10):965–972.
6. Alfano CA, Zakem AH, Costa NM, Taylor LK, Weems CF. Sleep problems and their relation to cognitive factors, anxiety, and depressive symptoms in children and adolescents. *Depress Anxiety*. 2009;**26**(6):503–512.
7. Storch EA, Murphy TK, Lack CW, Geffken GR, Jacob ML, Goodman WK. Sleep-related problems in pediatric obsessive-compulsive disorder. *J Anxiety Disord*. 2008;**22**(5):877–885.
8. Reynolds KC, Gradisar M, Alfano CA. Sleep in children and adolescents with obsessive-compulsive disorder. *Sleep Med Clin*. 2015;**10**(2):133–141.

9. Ivarsson T, Skarphedinsson G. Sleep problems and cognitive behavior therapy in pediatric obsessive-compulsive disorder have bidirectional effects. *J Anxiety Disord*. 2015;**30**:28–33.
10. Bai S, Ricketts EJ, Thamrin H, *et al.* Longitudinal study of sleep and internalizing problems in youth treated for Pediatric anxiety disorders. *J Abnorm Child Psychol*. 2020;**48**(1):67–77.
11. Poznanski B, Cornacchio D, Coxe S, Pincus DB, McMakin DL, Comer JS. The link between anxiety severity and irritability among anxious youth: evaluating the mediating role of sleep problems. *Child Psychiatry Hum Dev*. 2018;**49**(3):352–359.
12. Narmandakh A, Roest AM, Jonge P de, Oldehinkel AJ. The bidirectional association between sleep problems and anxiety symptoms in adolescents: a TRAILS report. *Sleep Med* 2020;**67**:39-46.
13. Alfano CA, Ginsburg GS, Kingery JN. Sleep-related problems among children and adolescents with anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2007;**46**(2):224–232.
14. McMakin DL, Alfano CA. Sleep and anxiety in late childhood and early adolescence. *Curr Opin Psychiatry*. 2015;**28**(6):483–489.
15. Alfano CA, Kim KL. Objective sleep patterns and severity of symptoms in Pediatric obsessive compulsive disorder: a pilot investigation. *J Anxiety Disord*. 2011;**25**(6):835–839.
16. Cousins JC, Whalen DJ, Dahl RE, *et al.* The bidirectional association between daytime affect and nighttime sleep in youth with anxiety and depression. *J Pediatr Psychol*. 2011;**36**(9):969–979.
17. Fletcher FE, Conduit R, Foster-Owens MD, Rinehart NJ, Rajaratnam SMW, Cornish KM. The association between anxiety symptoms and sleep in school-aged children: a combined insight from the Children's sleep habits questionnaire and actigraphy. *Behav Sleep Med*. 2018;**16**(2):169–184.
18. Mullin BC, Pyle L, Haraden D, *et al.* A preliminary multimethod comparison of sleep among adolescents with and without generalized anxiety disorder. *J Clin Child Adolesc Psychol*. 2017;**46**(2):198–210.
19. Alfano CA, Patriquin MA, De Los RA. Subjective - objective sleep comparisons and discrepancies among clinically-anxious and healthy children. *J Abnorm Child Psychol*. 2015;**43**(7):1343–1353.
20. Mesa F, Beidel DC, Bunnell BE. An examination of psychopathology and daily impairment in adolescents with social anxiety disorder. *PloS One*. 2014;**9**(4):e93668
21. Patriquin MA, Mellman TA, Glaze DG, Alfano CA. Polysomnographic sleep characteristics of generally-anxious and healthy children assessed in the home environment. *J Affect Disord*. 2014;**161**:79–83.
22. Alfano CA, Reynolds K, Scott N, Dahl RE, Mellman TA. Polysomnographic sleep patterns of non-depressed, non-medicated children with generalized anxiety disorder. *J Affect Disord*. 2013;**147**(1-3):379–384.
23. Kendall PC, Robin JA, Hedtke KA, Suveg C, Flannery-Schroeder E, Gosch E. Considering CBT with anxious youth? *Think exposures Cogn Behav Pract*. 2005;**12**(1):136–148.
24. Bloch MH, Storch EA. Assessment and management of treatment-refractory obsessive-compulsive disorder in children. *J Am Acad Child Adolesc Psychiatry*. 2015;**54**(4):251–262.
25. Storch EA, Wilhelm S, Sprich S, *et al.* Efficacy of augmentation of cognitive behavior therapy with weight-adjusted d-cycloserine vs placebo in pediatric obsessive-compulsive disorder: a randomized clinical trial. *JAMA Psychiatry*. 2016;**73**(8):779–788.
26. Seligman LD, Ollendick TH. Cognitive Behavioral therapy for anxiety disorders in youth overview and clinical presentation. *Child Adolesc Psychiatr Clin N Am*. 2011;**20**(2):217–238.
27. Ginsburg GS, Kendall PC, Sakolsky D, *et al.* Remission after acute treatment in children and adolescents with anxiety disorders: findings from the CAMS. *J Consult Clin Psychol*. 2011;**79**(6):806–813.
28. Garcia AM, Case B, Freeman JB, *et al.* Predictors of treatment outcome and length of stay in a partial Hospital program for Pediatric obsessive-compulsive disorder. *Evidence-Based Practice in Child and Adolescent Mental Health*. 2023;1–14.
29. Bouton ME. Conditioning, remembering, and forgetting. *J Exp Psychol Anim Behav Process*. 1994;**20**(3):219–231.
30. Bouton ME. Context and behavioral processes in extinction. *Learning and Memory*. 2004;**11**(5):485–494.
31. Goldstein AN, Walker MP. The role of sleep in emotional brain function. *Annu Rev Clin Psychol*. 2014;**10**(1):679–708.
32. Craske MG, Kircanski K, Zelikowsky M, Mystkowski J, Chowdhury N, Baker A. Optimizing inhibitory learning during exposure therapy. *Behav Res Ther*. 2008;**46**(1):5–27.
33. Ryan KM, Zimmer-Gembeck MJ, Neumann DL, Waters AM. The need for standards in the design of differential fear conditioning and extinction experiments in youth: a systematic review and recommendations for research on anxiety. *Behav Res Ther*. 2019;**112**:42–62.
34. Davidson P, Pace-Schott E. The role of sleep in fear learning and memory. *Curr Opin Psychol*. 2020;**34**:32–36.
35. Yoo SS, Hu PT, Gujar N, Jolesz FA, Walker MP. A deficit in the ability to form new human memories without sleep. *Nat Neurosci*. 2007;**10**(3):385–392.
36. Walker MP, Stickgold R. Sleep-dependent learning and memory consolidation. *Neuron*. 2004;**44**(1):121–133.
37. Abel M, Bäuml KHT. Sleep can eliminate list-method directed forgetting. *J Exp Psychol Learn Mem Cogn*. 2013;**39**(3):946–952.
38. Diekelmann S, Born J. The memory function of sleep. *Nat Rev Neurosci*. 2010;**11**:114–126.
39. Rasch B, Born J. About sleep's role in memory. *Physiol Rev*. 2013;**93**(2):681–766.
40. Dutcher CD, Dowd SM, Zalta AK, *et al.* Sleep quality and outcome of exposure therapy in adults with social anxiety disorder. *Depress Anxiety*. 2020;**2021**. https://doi.org/10.1002/da.23167
41. Zalta AK, Dowd S, Rosenfield D, *et al.* Sleep quality predicts treatment outcome in CBT for social anxiety disorder. *Depress Anxiety*. 2013;**30**(11):1114–1120.
42. Harvey AG, Lee J, Williams J, *et al.* Improving outcome of psychosocial treatments by enhancing memory and learning. *Perspect Psychol Sci*. 2014;**9**(2):161–179.
43. Kredlow MA, Eichenbaum H, Otto MW. Memory creation and modification: enhancing the treatment of psychological disorders. *Am Psychol*. 2018;**73**(3):269–285.
44. Pace-Schott EF, Milad MR, Orr SP, Rauch SL, Stickgold R, Pitman RK. Sleep promotes generalization of extinction of conditioned fear. *Sleep*. 2009;**32**(1):19–26.
45. Pace-schott EF, Germain A, Milad MR, Hospital MG. Effects of sleep on memory for conditioned fear and fear extinction. *Psychol Bull*. 2015;**141**(4):835–857.
46. Spoormaker VI, Sturm A, Andrade KC, *et al.* The neural correlates and temporal sequence of the relationship between shock exposure, disturbed sleep and impaired consolidation of fear extinction. *J Psychiatr Res*. 2010;**44**(16):1121–1128.
47. Spoormaker VI, Schröter MS, Andrade KC, *et al.* Effects of rapid eye movement sleep deprivation on fear extinction recall and prediction error signaling. *Hum Brain Mapp*. 2012;**33**(10):2362–2376.
48. Straus LD, Acheson DT, Risbrough VB, Drummond SPA. Sleep deprivation disrupts recall of conditioned fear extinction. *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2017;**2**(2):123–129.

49. Pace-Schott EF, Verga PW, Bennett TS, Spencer RMC. Sleep promotes consolidation and generalization of extinction learning in simulated exposure therapy for spider fear. *J Psychiatr Res*. 2012;**46**(8):1036–1044.
50. Bottary R, Seo J, Daffre C, *et al.* Fear extinction memory is negatively associated with REM sleep in insomnia disorder. *Sleep*. 2020;**43**(7). https://doi.org/10.1093/sleep/zsaa007
51. Richards A, Inslicht SS, Yack LM, *et al.* The relationship of fear-potentiated startle and polysomnography-measured sleep in trauma-exposed men and women with and without PTSD: testing REM sleep effects and exploring the roles of an integrative measure of sleep, PTSD symptoms, and biological sex. *Sleep*. 2022;**45**(1):zsab271
52. Straus LD, Norman SB, Risbrough VB, Acheson DT, Drummond SPA. REM sleep and safety signal learning in posttraumatic stress disorder: a preliminary study in military veterans. *Neurobiol Stress*. 2018;**9**:22–28.
53. Wallace ML, McMakin DL, Tan PZ, *et al.* The role of day-to-day emotions, sleep, and social interactions in pediatric anxiety treatment. *Behav Res Ther*. 2017;**90**:87–95.
54. Difrancesco S, Lamers F, Riese H, *et al.* Sleep, circadian rhythm, and physical activity patterns in depressive and anxiety disorders: a 2-week ambulatory assessment study. *Depress Anxiety*. 2019;**36**(10):975–986.
55. Meltzer LJ, Walsh CM, Peightal AA. Comparison of actigraphy immobility rules with polysomnographic sleep onset latency in children and adolescents. *Sleep Breath*. 2015;**19**(4):1415–1423.
56. Ancoli-Israel S, Martin JL, Blackwell T, *et al.* The SBSM guide to actigraphy monitoring: clinical and research applications. *Behav Sleep Med*. 2015;**13**(Suppl 1):S4–S38
57. Sadeh A, Sharkey KM, Carskadon MA. Activity-based sleep-wake identification: an empirical test of methodological issues. *Sleep*. 1994;**17**(3):201–207.
58. Meltzer LJ, Montgomery-Downs HE, Insana SP, Walsh CM. Use of actigraphy for assessment in pediatric sleep research. *Sleep Med Rev*. 2012;**16**(5):463–475.
59. Meltzer LJ, Westin AML. A comparison of actigraphy scoring rules used in pediatric research. *Sleep Med*. 2011;**12**(8):793–796.
60. Wong PM, Barker D, Roane BM, Van Reen E, Carskadon MA. Sleep regularity and body mass index: findings from a prospective study of first-year college students. *Sleep Adv*. 2022;**3**(1):zpac004.
61. Burke TA, Hamilton JL, Seigel D, *et al.* Sleep irregularity and nonsuicidal self-injurious urges and behaviors. *Sleep*. 2022;**45**(6). https://doi.org/10.1093/sleep/zsac084
62. Carskadon MA, Chappell KR, Barker DH, *et al.* A pilot prospective study of sleep patterns and DNA methylation-characterized epigenetic aging in young adults. *BMC Res Notes*. 2019;**12**(1):583.
63. Phillips AJK, Clerx WM, O'Brien CS, *et al.* Irregular sleep/wake patterns are associated with poorer academic performance and delayed circadian and sleep/wake timing. *Sci Rep*. 2017;**7**(1):3216.
64. Sheehan DV, Sheehan KH, Shytle RD, *et al.* Reliability and validity of the Mini international neuropsychiatric interview for children and adolescents (MINI-KID). *J Clin Psychiatry*. 2010;**71**(3):313–326.
65. Scahill L, Riddle MA, McSwiggin-Hardin M, *et al.* Children's Yale-Brown obsessive compulsive scale: reliability and validity. *J Am Acad Child Adolesc Psychiatry*. 1997;**36**(6):844–852.
66. T H E Research Units O N Pediatric Psychopharmacology Anxiety Study. The Pediatric anxiety rating scale (PARS): development and psychometric properties. *J Am Acad Child Adolesc Psychiatry*. 2002;**41**(9):1061–1069.
67. Guy W, National Institute of Mental Health (U.S.). *Psychopharmacology Research Branch, Early Clinical Drug Evaluation Program. ECDEU Assessment Manual for Psychopharmacology. U.S. Dept. of Health, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, National Institute of Mental Health, Psychopharmacology Research Branch, Division of Extramural Research Programs*; 1976.
68. Forrest CB, Meltzer LJ, Marcus CL, *et al.* Development and validation of the PROMIS Pediatric sleep disturbance and sleep-related impairment item banks. *Sleep*. 2018;**41**(6). https://doi.org/10.1093/sleep/zsy054
69. Werner H, Lebourgeois MK, Geiger A, Jenni OG. Assessment of chronotype in four- to eleven-year-old children: reliability and validity of the Children's chronotype questionnaire (CCTQ). *Chronobiol Int*. 2009;**26**(5):992–1014.
70. Chervin RD, Hedger K, Dillon JE, Pituch KJ. Pediatric sleep questionnaire (PSQ): validity and reliability of scales for sleep-disordered breathing, snoring, sleepiness, and behavioral problems. *Sleep Med*. 2000;**1**(1):21–32.
71. Cella D, Riley W, Stone A, *et al.* The patient-reported outcomes measurement information system (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. *J Clin Epidemiol*. 2010;**63**(11):1179–1194.
72. Victor SE, Klonsky ED. Validation of a brief version of the difficulties in emotion regulation scale (DERS-18) in five samples. *J Psychopathol Behav Assess*. 2016;**38**(4):582–589.
73. Markowitz A, Barker DH, Saletin J, Gredvig-Ardito C, McGeary J, Carskadon M. 0262 comparing wrist actigraphy to a novel wearable (Actigpatch): nonparametric activity estimation. *Sleep*. 2023;**46**(Supplement_1):A117–A117
74. Short MA, Arora T, Gradisar M, Taheri S, Carskadon MA. How many sleep diary entries are needed to reliably estimate adolescent sleep? *Sleep*. 2017;**40**(3). https://doi.org/10.1093/sleep/zsx006
75. Acebo C, Sadeh A, Seifer R, *et al.* Estimating sleep patterns with activity monitoring in children and adolescents: how many nights are necessary for reliable measures? *Sleep*. 1999;**22**(1):95–103.
76. Jafarzadeh Esfahani M, Daraie AH, Zerr P, Weber FD, Dresler M. Dreamento: an open-source dream engineering toolbox for sleep EEG wearables. *SoftwareX*. 2023;**24**:101595
77. Shechner T, Britton JC, Ronkin EG, *et al.* Fear conditioning and extinction in anxious and nonanxious youth and adults: examining a novel developmentally appropriate fear-conditioning task. *Depress Anxiety*. 2015;**32**(4):277–288.
78. Wolfson AR, Carskadon MA. Sleep schedules and daytime functioning in adolescents. *Child Dev*. 1998;**69**(4):875–887.

SLEEP Advances, 2025, **6**, 1–9
https://doi.org/10.1093/sleepadvances/zpaf072
Protocol Papers