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More Time Awake After Sleep Onset Is Linked to Reduced Ventral Striatum Response to Rewards in Youth with Anxiety

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Abstract

Background: Poor sleep and anxiety disorders are highly comorbid in youth, and each predicts altered ventral striatum (VS) response to rewards, which may impact mental health risk. Contrasting evidence suggests previously reported negative associations between sleep health and VS response may be stronger or weaker in youth with anxiety, indicating sensitivity to win/loss information or blunted reward processing, respectively. We cross-sectionally examined the role of sleep in VS response to rewards among youth with anxiety versus a no-psychiatric-diagnosis comparison (ND) group. We expected a group*sleep interaction on VS response to rewards but did not hypothesize directionality.

Methods: As part of the pretreatment battery for a randomized clinical trial, 74 youth with anxiety and 31 ND youth (ages 9–14 years; n = 55 female) completed a monetary reward task during fMRI. During the same pretreatment window, actigraphy- and diary-estimated sleep were collected over five days, and participants and their parents each reported participants' total sleep problems. We examined group*sleep interactions on VS response to monetary rewards versus losses via three mixed linear models corresponding to actigraphy, diary, and questionnaires, respectively.

Results: Each model indicated group*sleep interactions on VS response to rewards. Actigraphy- and diary-estimated time awake after sleep onset predicted reduced VS response in youth with anxiety but not ND youth. Parent-reported sleep problems similarly interacted with group, but simple slopes were nonsignificant.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Conclusions: Wake after sleep onset was associated with blunted reward response in youth with anxiety. These data suggest a potential pathway through which sleep could contribute to perturbed reward function and reward-related psychopathology (e.g., depression) in youth with anxiety.

Keywords

anxiety; adolescence; sleep; brain imaging

Youth with anxiety or at risk for anxiety demonstrate altered reward functioning (Bar-Haim et al., 2009; Benson, Guyer, Nelson, Pine, & Ernst, 2014; Guyer et al., 2006, 2012; Helfinstein et al., 2011), which may partially account for increased vulnerability for disorders like depression in youth with anxiety (Boland, Goldschmied, Wakschal, Nusslock, & Gehrman, 2020; Silk, Davis, McMakin, Dahl, & Forbes, 2012). One factor that may contribute to altered reward functioning in youth with anxiety is sleep health, defined by sleep duration, efficiency, timing, subjective quality, and alertness during wake (Buysse, 2014). Sleep health is linked to both reward functioning and anxiety. Delineating associations between aspects of sleep health and reward function in youth with anxiety could inform modifiable targets for treatment and intervention.

Research examining reward functioning in youth with or at risk for anxiety has focused on ventral (nucleus accumbens, caudate) and dorsal (caudate, putamen) subregions of the striatum, a brain region linked to salience, learning, reward functioning, and goal-directed behavior (Delgado, 2007). Youth with histories of behavioral inhibition (a trait linked to risk for anxiety disorders) show elevated ventral striatum response during anticipation of behavior-contingent rewards and losses, relative to noninhibited youth (Bar-Haim et al., 2009; Guyer et al., 2006). During reward outcome, behaviorally inhibited youth show elevated dorsal striatum response to losses but not gains, indicating sensitivity to aversive information such as poor performance and loss (Helfinstein et al., 2011).

Sleep health could moderate reward functioning in youth with anxiety, given the high frequency of reported sleep problems in anxiety disorders and depression, and particularly around puberty (Alvaro, Roberts, & Harris, 2013; McMakin & Alfano, 2015). Approximately 90% of youth with anxiety and their parents report elevated sleep onset latency, time awake after sleep onset, bedtime resistance, and other sleep-related concerns, though reports are not consistently supported by actigraphy and polysomnography (Alfano, 2018). Sleep is closely tied to striatal response to rewards (Boland et al., 2020; Gujar, Yoo, Hu, & Walker, 2011; Mullin et al., 2013), but it is unclear how sleep health may impact striatal response to rewards in youth with anxiety. On the one hand, worse sleep health may strengthen striatal response to rewards. This would reflect effects of sleep deprivation on ventral (Mullin et al., 2013) and dorsal (Gujar et al., 2011) striatum response to rewards in non-anxious adults, as well as evidence linking poorer subjective sleep quality to greater risk-taking to receive rewards and altered cortico-striatal functional connectivity during risk-taking in non-anxious adolescents (Telzer, Fuligni, Lieberman, & Galván, 2013). On the other hand, worse sleep health may dampen striatal activation to rewards. Insufficient sleep duration, efficiency, and subjective quality lead to greater generation and impaired regulation of negative emotions (McMakin et al., 2016; Palmer & Alfano, 2017), while sleep

deprivation predicts greater salience of negative emotional stimuli (Yoo, Gujar, Hu, Jolesz, & Walker, 2007). Therefore, worse sleep health may potentiate performance sensitivity in youth with anxiety via heightened aversion to loss (Benson et al., 2014; Guyer et al., 2012; Helfinstein et al., 2011) and/or lead to overregulation of striatal responses to rewards (Sequeira et al., 2021). Given the importance of sleep in healthy functioning of emotional and reward systems, sleep health may be key to understanding mechanisms of reward functioning in youth with anxiety.

The aim of the current study was to cross-sectionally examine the role of sleep health in striatal response to rewards in youth with anxiety versus youth with no clinical diagnosis (ND) at a pre-treatment baseline. Since different effects of sleep health and anxiety on reward response are observed in ventral versus dorsal subregions, our region of interest (ROI) analysis examined the ventral striatum (VS). The VS has close ties to reward valuation, prediction error, and learning (Daw, Gershman, Seymour, Dayan, & Dolan, 2011). Furthermore, youth at risk for anxiety show increased VS response to rewards (Bar-Haim et al., 2009; Guyer et al., 2006), and sleep-deprived ND adults show increased VS response to rewards in the same task used here (Mullin et al., 2013). We used three mixed linear models (MLMs) to examine interactions between group (anxiety vs. ND) and three respective categories of sleep health estimates: 1) actigraphy, 2) diary, and 3) questionnaire-reported sleep problems on VS response to rewards. We expected group*sleep interactions, such that simple main effects linking worse sleep health to increased VS response in ND youth would be altered in youth with anxiety. We did not hypothesize directionality of the interaction due to competing literature reviewed above that could support either heightened or blunted responsiveness to reward.

Methods

Participants

One-hundred sixty-two participants aged 9–14 years completed procedures as part of the baseline pre-assessment protocol for a randomized clinical trial comparing treatments for anxiety disorders in youth (Silk et al., 2018). Soon after the study began, a control condition was added to the behavioral task, so fMRI data for the initial 31 participants were excluded. The remaining sample included 92 youth with anxiety and 39 ND youth group-matched for age and sex. Participants with anxiety met DSM-IV criteria for generalized anxiety disorder, social anxiety disorder, and/or separation anxiety disorder. For all participants, current diagnoses of obsessive-compulsive disorder, post-traumatic stress disorder, major depressive disorder, or attention-deficit/hyperactivity disorder (hyperactive-impulsive or combined type) were exclusionary. Other exclusionary criteria included history of autism spectrum disorder, bipolar disorder, psychosis, or illicit substance use; metal braces or implants; IQ < 70; and current use of psychoactive medications other than stimulants (for which participants were asked to remain abstinent on the day of the fMRI session and the day prior).

Among the participants who completed the fMRI session and behavioral task, data from 11 anxious and 2 ND youth were excluded because of issues with scanner alignment (n = 2), excessive motion in the scanner (n = 3), an incidental finding that impeded analysis (n

= 1), and study withdrawal (n = 7). Of the remaining 81 anxious and 37 ND youth with usable BOLD data, current analyses examined a subsample of 74 anxious (38 Female; age: *M* = 11.04 years, *SD* = 1.55 years; Race: Non-Hispanic White: n = 65, Biracial: n = 5, Non-Hispanic Black: n = 3, Hispanic: n = 1) and 31 ND youth (17 Female, age *M* = 11.69 years, *SD* = 1.66 years; Race: Non-Hispanic White: n = 22, Non-Hispanic Black: n = 6, Hispanic: n = 2, Biracial: n = 1) with both actigraphy and diary estimates of sleep patterns for at least three nights. See Table 1 for participant demographics.

Procedures

All procedures were approved by the University of Pittsburgh's Human Research Protection Office. After obtaining signed parent consent and child assent, BA- and MA-level independent evaluators administered all reported clinical interviews and questionnaires to participant families. After the initial intake assessment but before beginning treatment, anxious participants completed an fMRI session (fMRI date: *M* = 24.85 days after intake, *SD* = 11.17, range = 2–56 days). During the fMRI session, participants completed a series of tasks, including a reward task examining responses to wins versus losses. During the same pretreatment window, participants completed a five-day ecological momentary assessment protocol (Thursday night to Tuesday Morning), in which they wore an actigraph watch nightly and were asked to complete sleep diaries each morning (Thursday start date: *M* = 8.51 days after fMRI, *SD* = 8.14, range = −4 – 46 days). Pretreatment protocols were identical for ND participants, but they did not undergo treatment. Participants were compensated for completing the assessments at an hourly rate approximating minimum wage.

Measures

Clinical interview.—Participants were evaluated for DSM-IV criteria for anxiety disorders via the Kiddie Schedule for Affective Disorders and Schizophrenia – Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997). Ratings were obtained by a single evaluator for each parent/child dyad and reviewed by a psychiatrist, who provided final diagnoses. The K-SADS-PL was used to determine group (anxiety vs. ND) assignment.

Actigraphy estimates of sleep patterns.—The Ambulatory Monitoring Octagonal Basic Motionlogger actigraph watch recorded movement to estimate periods of sleep versus wake. Youth pressed a button on the watch that provided a marker in the actigraph record to indicate the beginning and end of the sleep interval (lights out to morning wake up). When a marker was unavailable, diaries (see below) were used to confirm the actigraph-derived sleep interval. Group consensus meetings resolved uncertain estimates. Sleep was scored using a Sadeh algorithm applied to 60s epochs to estimate activity levels as indicative of sleep or wake (Sadeh, Sharkey, & Carskadon, 1994). The following variables from within the sleep interval were included in analyses to capture key dimensions of sleep health (Buysse, 2014): sleep onset latency (SOL; minutes between evening lights out and sleep onset), sleep duration (total minutes asleep between SOL and morning lights on), wake after sleep onset (WASO; total minutes awake between SOL and morning lights on), and sleep timing variability (*SD* [minutes] of lights-out-to-lights-on interval midpoint across nights). Participants had 5 nights (n = 83), 4 nights (n = 18), or 3 nights (n = 4) of both actigraphy-

and diary estimated sleep (M = 4.76 nights, SD = .53). Sleep estimates were limited to 5 nights for feasibility of the protocol (Silk et al., 2018). See Table 2 for all sleep measures included in analyses.

Diary estimates of sleep patterns.—Daily sleep diaries captured participants' subjectively reported sleep patterns, including estimates of lights out, SOL, WASO, and morning wake time. Lights out, SOL, WASO, and wake time were utilized to compute sleep duration. Additionally, participants placed Xs on two 100mm lines to provide respective measures of sleep quality (0 = worst, 100 = best) and difficulty waking (0 = most difficult, 100 = least difficult). All variables except sleep quality (due to high collinearity with WASO [VIF > 10, Tolerance < .1]) were included in analyses as diary estimates of sleep health.

Questionnaire Estimates of Sleep Problems.—Parent- and child-reported sleep problems were collected at intake via the Child Sleep Habits Questionnaire (CSHQ; Owens, Spirito, & McGuinn, 2000) and the Sleep Self Report (SSR; Owens, Spirito, McGuinn, & Nobile, 2000), respectively. The CSHQ includes 35 items, with subscales for bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, sleep-disordered breathing, and daytime sleepiness. Thirty-three items are used to calculate a Total Score (clinical cutoff: 41 or greater). The SSR's 26 items parallel a subset of those in the CSHQ and are used to calculate a Total Score. CSHQ and SSR Total Scores were included in analyses as estimates of sleep-related problems.

Covariates.—As part of the pretreatment battery, participants completed the Mood and Feelings Questionnaire (MFQ; Angold, Erkanli, Silberg, Eaves, & Costello, 2002) as a child-report measure of depressive symptoms. Participants also completed the Pubertal Development Scale (PDS; Petersen, Crockett, Richards, & Boxer, 1988). PDS score was estimated via an established scoring procedure (Shirtcliff, Dahl, & Pollak, 2009) and coded in a range from 1–5 to capture gonadal and adrenal hormonal signals of physical development. PDS score was used as the primary measure of pubertal status.

fMRI task.—During the fMRI session, participants completed a validated task examining neural responses related to rewards versus losses (Mullin et al., 2013). Participants were told that their compensation after completing the task would be based on their performance. During the task, participants were instructed to press one of two buttons to guess whether a hidden card value was greater or lower than 5. Participants had 3000ms to guess via button press, after which a card value was presented for 500ms, and then appropriate "win"/ "loss" feedback was presented for 500ms. During "win" feedback, a green, upward-pointing arrow was presented, and participants gained $1.00. During "loss" feedback, a red, downward-pointing arrow was presented for 500ms, and participants lost $0.50. After win/loss feedback, a fixation cross was presented for 3000ms, for a total trial length of 7000ms. Trials were presented in six blocks of five trials each. During three "reward" blocks, guess-congruent card values and "win" feedback were presented in 80% of trials. During three "loss" blocks, guess-incongruent card values and "loss" feedback were presented in 80% of trials. The six blocks were presented in a pseudorandomized order along with three control blocks. During the control blocks, participants were instead instructed to press one of the

two buttons in response to the presentation of an X onscreen. They then were presented with an asterisk for 500ms, followed by a yellow circle for 500ms. Each block began with appropriate instructions of either “Guess Number” or “Press Button” presented for 2000ms, for a total block length of 37 seconds and a total task length of 5 minutes, 33 seconds.

fMRI Acquisition and Preprocessing

Neuroimaging data were collected in a Siemens 3T Trio MRI scanner. Blood-oxygen-level-dependent (BOLD) T2*-weighted fMRI data were collected with a reverse echo planar imaging sequence during completion of the win/loss task (TR/TE = 1670/29ms, flip angle = 75°, FOV = 205mm, 32 3.2mm axial slices, matrix = 64 × 64; 3.2mm isotropic voxels). Structural (T1-weighted magnetization-prepared rapid gradient-echo [MP RAGE], TR/TE = 2100/3.31ms, flip angle = 8.0°, FOV = 256 × 208mm, 176 1.0-mm axial slices, matrix = 64 × 64) images were collected at the beginning of the neuroimaging protocol.

SPM12 was used to analyze whole-brain images. Neuroimaging data preprocessing included: correction of functional volumes for slice timing, spatial realignment of the volumes for head motion, removal of linear trends over the run, temporal filtering with a 128 Hz high-pass filter, normalization of realigned images to MNI adult template and resampling of voxels to a size of 2mm × 2mm × 2mm, and spatial smoothing with a 6mm FWHM Gaussian filter. Participants with mean motion across volumes greater than 3mm were excluded from analyses.

BOLD Activation Analysis

At the first level, we modeled effects of task (win, loss, and control blocks), with motion parameters included as nuisance regressors. At the second level, an ROI analysis was conducted for the bilateral VS (Figure 1). A mask isolating regions of the VS that activate reliably to monetary rewards was created using Neurosynth (Neurosynth.org), the Wake Forest University (WFU) PickAtlas toolbox for SPM, and FSL (Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012). The association map for the term “monetary reward” was downloaded from Neurosynth (April 2021, thresholded using a false discovery rate criterion of .01). Anatomic ROIs were created for the bilateral nucleus accumbens and caudate using the IBASPM atlas and the WFU PickAtlas toolbox for SPM. A new region comprising the intersection of the Neurosynth and anatomic ROI maps was created to represent regions of the VS that activate reliably in association with monetary rewards. Mean parameter estimates across this region were extracted for each participant for the contrast of interest (win>loss) using the MarsBar toolbox for SPM12. See Figure 1 for all ROI maps.

Analytic Plan

Missing data.—Of the original 118 participants with useable BOLD data, some were missing data for actigraphy (n = 7), sleep diary (n = 6), depression (MFQ; n = 9), pubertal status (PDS; n = 27), parent-reported sleep problems (CSHQ; n = 4), and child-reported sleep problems (SSR, n = 21). Little’s MCAR test failed to associate missing data with any observed variables ($X^2(269) = 244.14$, $p = .859$). All subsequent analyses examined 105 participants who had at least 3 nights of usable data for both actigraphy and diary estimates

of sleep. Among these 105 participants, all other missing data (PDS, MFQ, CSHQ, SSR) were imputed in SPSS (v. 27.0.0) via an MC Monte Carlo method with data pooled from 5 imputations.

Normality checks.—As is common, Shapiro-Wilk tests of normality indicated skewed distributions for all raw sleep variables ($p < .05$), except difficulty waking and sleep duration (both diary and actigraphy estimates). Natural log (LN) transformations of skewed sleep measures (Shapiro-Wilk tests: $p > .05$) replaced raw measures in all reported models. See Table 2 for LN-transformed sleep measures. All analyses were conducted with VS response outliers (n = 13) brought to the 1.5 interquartile range to reduce their potential impact on findings.

Sleep and ventral striatum response to rewards.—Three MLMs in SPSS (v. 27.0.0) examined respective associations between VS response to rewards and actigraphy-estimated sleep patterns, diary-estimated sleep patterns, and questionnaire-reported sleep problems. The model examining actigraphy-estimated sleep patterns included sleep duration, SOL, WASO, and sleep timing variability as fixed factors. The model examining diary-estimated sleep patterns included sleep duration, SOL, WASO, and difficulty waking as fixed factors. The model examining questionnaire-reported sleep problems included CSHQ Total Score and SSR Total Score as fixed factors. Each model also included group (anxiety vs. ND) main effects and all corresponding group*sleep two-way interactions as fixed factors. Age, sex, depressive symptoms, and pubertal status were included as covariates in all models. Models examining actigraphy and diary estimates of sleep also covaried for number of recorded nights and number of recorded school nights. All fixed factors and covariates were nested within participant ID as a random effect to account for variance within participants across different measures (VC covariance structure). Multiple comparisons between models were controlled for via Benjamini-Hochberg FDR correction. See Table 2 for all models.

Results

Manipulation Checks

Independent samples t-tests and Pearson's chi squared analyses evaluated group (anxiety vs. ND) similarity to account for potential confounds. There were no group differences in sex ($X^2(1) = .107$, $p = .744$), pubertal status ($t(103) = 1.407$, $p = .160$), age ($t(103) = 1.922$, $p = .055$), calendar month of fMRI session ($X^2(11) = 17.346$, $p = .098$), or whether participants were in school when sleep data were collected ($X^2(1) = 2.997$, $p = .083$). Anxious youth ($M = 17.51$, $SD = 10.69$) reported greater depressive symptoms than ND youth ($M = 4.29$, $SD = 5.80$; $t(103) = 7.867$, $p < .001$). See Table 1 for group differences in sleep estimates and covariates.

Sleep and Ventral Striatum Response to Rewards

Three MLMs examined respective associations between VS response to rewards and actigraphy-estimated sleep, diary-estimated sleep, and questionnaire-reported sleep problems. In line with our hypotheses, each model detected group*sleep interactions on VS response. The MLM examining relations between actigraphy-estimated sleep and

VS response revealed a group*WASO interaction ($F(1,105) = 5.146$, standardized β = −.504, 95% CI [−.963, −.045], $p = .031$), where greater WASO was linked to attenuated VS response in anxious (standardized β = −.320, 95% CI [−.546, −.094], $p = .005$) but not ND youth (standardized β = .135, 95% CI [−.234, .503], $p = .474$). The model examining diary-estimated sleep corroborated this group*WASO interaction ($F(1,105) = 14.532$, standardized β = −.851, 95% CI [−1.297, −.406], $p < .001$), where greater WASO was again associated with attenuated VS response in anxious (standardized β = −.386, 95% CI [−.600, −.173], $p < .001$), but not ND youth (standardized β = .354, 95% CI [−.041, .749], $p = .079$). Post-hoc analysis revealed these associations were unchanged after covarying for discrepancies between diary- and actigraphy-estimated WASO. The model examining associations between questionnaire-reported sleep problems and VS response found an interaction between group and parent-reported sleep problems ($F(1,105) = 4.806$, standardized β = −.563, 95% CI [−1.076, −.051], $p = .031$). However, simple slopes did not deviate from zero for anxious (standardized β = −.224, 95% CI [−.498, .050], $p = .109$) or ND youth (standardized β = .327, 95% CI [−.075, .729], $p = .111$). See Table 2 for reported models and Figure 2 for scatterplots of significant interactions. See Tables S1–S3 for MLMs examining main effects of anxiety group and sleep without interactions. See Table S4 for bivariate correlations between sleep and VS response separated by group. After accounting for reported interactions, MLMs found no other associations with VS response. Post-hoc analyses revealed similar trends when VS response outliers were not brought to the 1.5 interquartile range ($p < .1$).

Discussion

Our findings support the hypothesis that different associations between sleep and brain function are observed in youth with anxiety and ND youth. Wake after sleep onset (WASO) and parent-reported sleep problems interacted with group (anxiety vs. ND) to capture variance in VS response to rewards. Actigraphy- and diary-estimated WASO were negatively associated with VS response to wins versus losses in anxious youth, indicating that more objectively-measured WASO and anxious youths' perceptions of WASO were both related to reward response. However, we failed to replicate previously reported effects of sleep health on VS response in ND youth.

One interpretation of these cross-sectional findings is that more time awake after sleep onset may be associated with disrupted enjoyment of pleasant experiences in anxious youth. Worse sleep may heighten biases to attend to threats (e.g., poor performance, loss) via increased negative affect (McMakin et al., 2016), impaired emotion regulation (Palmer & Alfano, 2017), and diminished top-down regulation of amygdala response to negative emotional stimuli (Yoo et al., 2007). Specifically, WASO adversely impacts cognition, mood, subjective sleep quality, and physiological health (Buysse, 2014; Della Monica, Johnsen, Atzori, Groeger, & Dijk, 2018). WASO may heighten tendencies for anxious youth to encode rewards differently from ND youth by attending to losses and/or missing rewards entirely, resulting in difficulties attending to rewarding stimuli, maintaining positive affective states, or managing cognitions that dampen reward responding.

This interpretation is in line with developmental models of adolescent risk for depression in youth with anxiety (Silk et al., 2012). Due to greater attention to threats and diminished responsiveness to rewards, youth with anxiety may be more likely to avoid potentially rewarding but risky activities (e.g., social situations) due to competing fears of consequences (e.g., social evaluation). Such avoidance could lead to isolation and withdrawal, which may suppress striatal response to rewards and inhibit motivation to receive rewards (Silk et al., 2012). This developmental trajectory may be especially strong around puberty, when changes in social context coincide with neuromaturation in social, emotional, and reward-related brain functioning (Casey, Getz, & Galvan, 2008) to make anxious youth particularly susceptible to frustration of social goals (e.g., being popular, having romantic relationships; Silk et al., 2012). Worse sleep may exacerbate these difficulties by impairing one's ability to appropriately guide behavior and put forth effort necessary to obtain rewards (Boland et al., 2020). Sleep-induced alterations in reward response may thus predict anxious youths' vulnerability for depression, even controlling for baseline depressive symptoms (Alvaro et al., 2013; Boland et al., 2020).

Contrary to evidence linking sleep deprivation to increased VS response to rewards (Mullin et al., 2013), we observed no associations between sleep health and VS response in ND youth. The current analyses may capture nuance in the relations between sleep health and VS response not previously examined in youth, but it should be noted that these data were drawn from a larger study comparing treatments for anxiety disorders (Silk et al., 2018), so our small ND sample (n = 31) may have provided insufficient power to detect these effects.

In addition to the limited ND sample, reported findings should be viewed with consideration for other limitations. The current study was underpowered to examine effects of sleep on reward response across specific anxiety diagnoses and sex, each of which impact reward response in youth with anxiety (Dorfman, Rosen, Pine, & Ernst, 2016; Guyer et al., 2012). Secondly, given the short task length (15 "win" trials, 15 "loss" trials), replication with more trials could be useful to estimate effects' true magnitudes. Furthermore, cross-sectionality precludes causal interpretations of current findings. Despite these limitations, the current study benefited from a large sample of well-characterized youth with anxiety and sleep measures ranging in subjectivity and across multiple dimensions of sleep. Through these strengths, the findings provide evidence that WASO and parent-reported sleep problems differentially relate to reward response in youth with anxiety and ND youth.

Conclusion

Though insufficient and poor sleep is prevalent in adolescence, sleep is a modifiable target for intervention. For example, a recent open trial of a clinical intervention focused on savoring positive emotions at bedtime and other behavioral sleep strategies (e.g. stimulus control, regularizing sleep schedules, reducing caffeine intake, etc.) improved subjective sleep quality and reduced parent-reported sleep problems in youth with anxiety, even after CBT for anxiety failed to have a clinically significant impact on sleep (McMakin et al., 2019). However, more work is needed to fully capture the impact of sleep on reward functioning in clinical youth populations. In addition to experimentally replicating the current findings and expanding upon its limitations, future research should closely examine

how sleep interventions impact neural reward function in youth. If sleep interventions can mitigate reward processing perturbations in anxious youth, they may bolster the likelihood of treatment success while also reducing adolescent risk for reward-related psychopathology.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Author McMakin was at the University of Pittsburgh at the time of data collection

Authors Sollenberger and McMakin had access to all data. They confirm integrity of the data and reported analyses.

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Abbreviations:

VS	Ventral Striatum
ND	No psychiatric diagnosis
WASO	Wake after Sleep Onset
SOL	Sleep Onset Latency

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Key points

- Anxiety disorders and poor sleep health are highly comorbid.
- Anxiety and sleep health each separately relate to ventral striatum response to rewards versus losses in monetary reward tasks, but their interaction has not been examined.
- Time awake after sleep onset was associated with blunted ventral striatal response to rewards versus losses in youth with anxiety, but not youth without a psychiatric diagnosis.
- Sleep-related blunting of reward response among youth with anxiety may partially explain risk for reward-related psychopathology (e.g., depression).
- Sleep may be a modifiable prevention target.

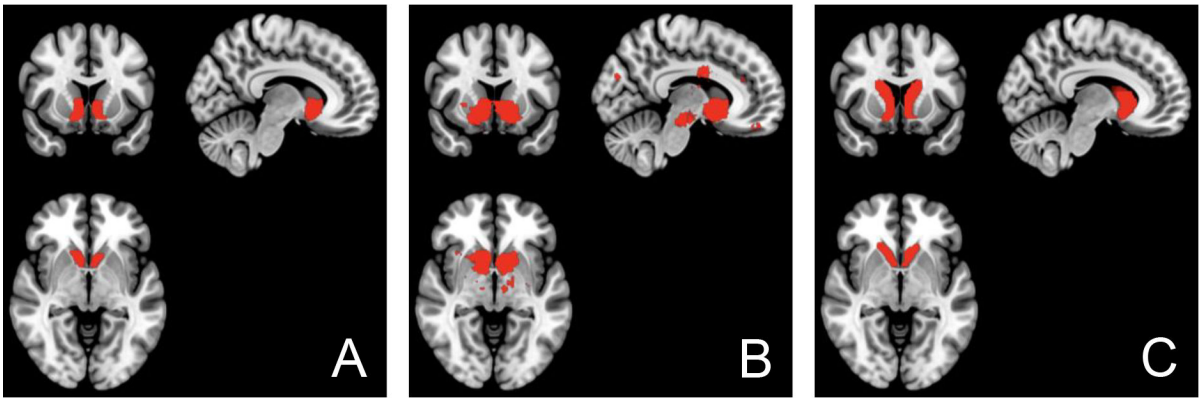

Figure 1. Ventral Striatum Region-of-Interest Mask.

Note. A) Ventral Striatum Mask used in analyses. ROI Mask comprises the intersection of: B) Neurosynth association mask for the term "monetary reward" (obtained April 2021), and C) anatomic mask of the nucleus accumbens and caudate, obtained via the IBASPM atlas and WFU PickAtlas toolbox for SPM.

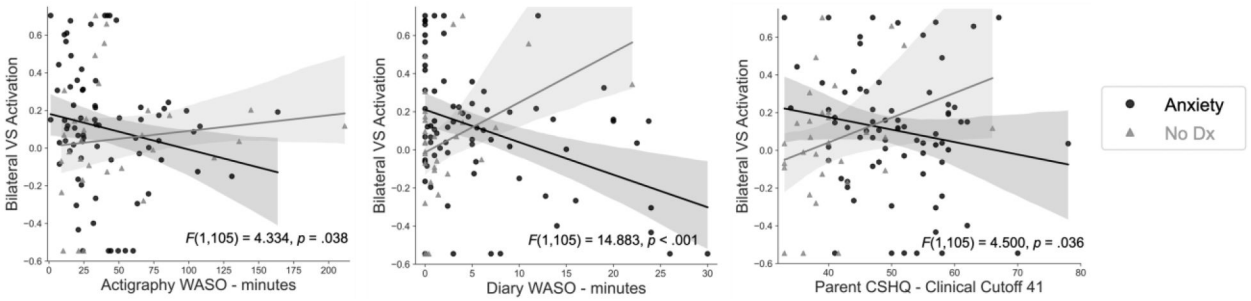

Figure 2. Effects of Actigraphy-Estimated WASO, Diary-Estimated WASO, and Parent-Reported Sleep Problems (CSHQ) on Ventral Striatum Response to Wins Versus Losses in Youth with Anxiety Versus No Diagnosis.

Note. WASO = Wake After Sleep Onset. CSHQ = Child Sleep Habits Questionnaire. Sleep measures were natural log-transformed for analyses (See Table 2). Contrast = wins versus losses; scores above zero indicate greater activation to rewards than losses. Bilateral VS response limited to 1.5 interquartile range. *F*-values for interactions are presented.

Table 1

Descriptive Statistics for Demographic and Sleep Measures in Youth with Anxiety vs. No Diagnosis

Measures[a]	Anxiety (n = 74)	No Dx (n = 31)	*p*
Demographics			
Sex: n Female (% Female)	38 (51.4%)	17 (54.8%)	.744
Age (Years): *M (SD)*	11.04 (1.55)	11.69 (1.66)	.057
Pubertal Status (PDS score, range 1–5[b]): *M (SD)*	2.37 (1.09)	2.72 (1.16)	.160
Depression Symptoms (MFQ Total Score): *M (SD)*	17.51 (10.69)	4.29 (5.80)	<.001*
Actigraphy Estimates of Sleep: *M (SD)*[c]			
Sleep Duration (min.)	482.52 (58.19)	478.29 (52.91)	.729
Sleep Onset Latency (min.)	19.99 (13.47)	18.55 (9.01)	.812
Wake After Sleep Onset (min.)	40.57 (32.27)	49.37 (47.09)	.390
Sleep Midpoint Variability (*SD* [min.] across nights)	48.81 (25.61)	64.40 (51.91)	.123
Diary Estimates of Sleep: *M (SD)*[c]			
Sleep Duration (min.)	526.28 (63.57)	538.44 (53.18)	.351
Sleep Onset Latency (min.)	21.55 (16.60)	16.47 (15.53)	.030*
Wake After Sleep Onset (min.)	6.17 (7.68)	2.38 (4.47)	.002*
Difficulty Waking (%)	59.08 (21.28)	58.20 (18.25)	.840
Reported Sleep Problems: *M (SD)*			
Parent CSHQ (Total Score)	50.71 (8.63)	40.57 (6.90)	<.001*
Child SSR (Total Score)	40.44 (7.73)	32.66 (7.09)	<.001*

Note.

[a]MFQ = Moods and Feelings Questionnaire, CSHQ = Child Sleep Habits Questionnaire, SSR = Sleep Self Report.

[b]Pubertal Development Scale. Recoded range to 1–5 to capture gonadal and adrenal hormonal signals of physical development.

[c]Sleep estimates were averaged across nights.

*Indicates significant group difference, $p < .05$.

Table 2

Mixed Linear Models Examining Group*Sleep Interactions on Ventral Striatum Response to Rewards

Mixed Linear Models[a]	AIC	*F*	df	stand. β	Lower CI	Upper CI	*p*
1. Actigraphy Estimates of Sleep[b]	310.01						
Group (Anxiety vs. No Dx)		2.191	1, 105	.385	−.109	.880	.127
Sleep Duration		.708	1, 105	−.073	−.288	.141	.502
Sleep Onset Latency[LN]		.491	1, 105	−.049	−.231	.132	.593
Wake After Sleep Onset[LN]		.447	1, 105	−.149	−.348	.050	.143
Sleep Timing Variability[LN]		.489	1, 105	−.000	−.191	.190	.997
Group*Sleep Duration		.447	1, 105	−.130	−.564	.304	.559
Group*Sleep Onset Latency		.047	1, 105	−.017	−.450	.416	.940
Group*Wake After Sleep Onset		5.146	1, 105	−.504	−.963	−.045	.031*
Group*Sleep Timing Variability		.007	1, 105	−.004	−.416	.408	.986
2. Diary Estimates of Sleep[b]	297.27						
Group (Anxiety vs. No Dx)		.502	1, 105	.178	−.324	.680	.487
Sleep Duration		4.099	1, 105	−.182	−.386	.022	.081
Sleep Onset Latency[LN]		.263	1, 105	.056	−.141	.252	.580
Wake After Sleep Onset[LN]		2.784	1, 105	−.160	−.351	.032	.102
Difficulty Waking		.112	1, 105	.009	−.174	.193	.920
Group*Sleep Duration		.072	1, 105	−.050	−.504	.404	.828
Group*Sleep Onset Latency		.371	1, 105	.077	−.322	.475	.705
Group*Wake After Sleep Onset		14.532	1, 105	−.851	−1.297	−.406	<.001*
Group*Difficulty Waking		.024	1, 105	.001	−.462	.465	.995
3. Q-Reported Sleep Problems	302.42						
Group (Anxiety vs. No Dx)		.410	1, 105	.197	−.413	.806	.527
Parent CSHQ[LN]		.070	1, 105	−.025	−.252	.202	.829
Child SSR[LN]		.006	1, 105	−.001	−.235	.233	.994
Group*Parent CSHQ		4.806	1, 105	−.563	−1.076	−.051	.031*
Group*Child SSR		.250	1, 105	−.110	−.568	.348	.637

Note.

[a]Covariates: MFQ Total Score, PDS Score (coded range 1–5), age, sex.

[b]Additional Covariates: number of recorded nights, number of recorded school nights.

*LN*Natural log-transformed prior to inclusion.