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RESEARCH ARTICLE

Factors Associated With Sleep Disturbance Amongst Youth With Bipolar Disorder

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Abstract

Background: While sleep disturbances and their impact on functioning are well-established in adults with bipolar disorder (BD), little is known about this topic in youth. **Objective:** This study investigates the prevalence and correlates of sleep disturbance among youth with BD. **Methods:** The study included 103 youth (72 BD, 31 healthy controls [HC]), ages 14-20 years. Study measures included a semi-structured diagnostic interview and the Pittsburgh Sleep Quality Index (PSQI). PSQI yields a global score and 7 subscale scores. Analyses examined between group differences in PSQI scores, and correlates of PSQI within BD. **Results:** BD youth had significantly higher (worse) global sleep scores, and higher scores on 5/7 subscales (quality, latency, disturbance, sleep medication use, daytime dysfunction). In univariate analyses, poorer sleep quality was associated with higher lifetime and current depression severity, mixed mood state, self-reported affective lability, and borderline personality traits. Lifetime lithium treatment and euthymic mood state were associated with better sleep scores. In multivariate analyses, greater current depression severity and self-reported affective lability were most robustly associated with poor sleep quality. **Conclusions:** Converging with data from adults, present findings indicate greater sleep disturbance among youth with BD versus HC. Also convergent with adults with BD, mood disturbance, whether depression severity or emotional lability, comprised the predominant correlates of sleep disturbance among youth with BD. Future research is warranted to better understand the temporal association between sleep disturbance and its correlates in youth with BD. Relatedly, interventions that address both mood and sleep disturbances may help improve overall functioning.

Key Words: *adolescent, youth, mood, bipolar disorder, sleep*

Résumé :

Contexte: Bien que les perturbations du sommeil et leur effet sur le fonctionnement soient bien établies chez les adultes souffrant du trouble bipolaire (TB). Nous en savons peu à ce sujet chez les jeunes. **Objectif:** La présente étude investigue la prévalence et les corrélats de la perturbation du sommeil chez les jeunes souffrant du TB. **Méthodes:** L'étude comprenait 103 jeunes (72 TB, 31 témoins en santé [TS]), âgés de 14 à 20 ans. Les mesures de l'étude étaient

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notamment une entrevue diagnostique semi-structurée et l'Index de Qualité du Sommeil de Pittsburgh (IQSP). L'IQSP donne un score global et 7 scores de sous-échelles. Les analyses ont examiné entre les différences de groupes dans les scores IQSP, et les corrélats d'IQSP dans le TB. **Résultats:** Les jeunes souffrant de TB avaient des scores de sommeil globaux significativement plus élevés (pires), et des scores plus élevés à 5/7 sous-échelles (qualité, latence, perturbation, utilisation de médicament pour dormir, dysfonction diurne). Dans les analyses univariées, la mauvaise qualité du sommeil était associée à la gravité de la dépression de durée de vie et actuelle, à l'état de l'humeur mixte, à la labilité affective auto-déclarée, et aux traits de la personnalité limite. Le traitement au lithium de durée de vie et l'état de l'humeur euthymique étaient associés avec de meilleurs scores de sommeil. Dans les analyses multivariées, une plus grande gravité de la dépression actuelle et de la labilité affective auto-déclarée étaient très robustement associées à une mauvaise qualité du sommeil. **Conclusions:** Convergeant avec les données des adultes, les résultats actuels indiquent une plus grande perturbation du sommeil chez les jeunes souffrant du TB contre les TS. Convergeant également avec les adultes souffrant de TB, la perturbation de l'humeur, que ce soit par la gravité de la dépression ou la labilité émotionnelle, comprenait les corrélats prédominants de la perturbation du sommeil chez les jeunes souffrant de TB. La future recherche est justifiée pour mieux comprendre l'association temporelle entre la perturbation du sommeil et ses corrélats chez les jeunes souffrant du TB. Étant liées, les interventions qui abordent l'humeur et les perturbations du sommeil peuvent aider à améliorer le fonctionnement général.

Mots clés: *adolescent, jeune, humeur, trouble bipolaire, sommeil*

Introduction

Sleep disturbances are among the diagnostic criteria for the depression and manic/hypomanic episodes that characterize bipolar disorder (BD). While sleep disturbance among individuals with BD is especially pronounced during mood episodes, these disturbances are also evident during euthymic intervals [1-3]. The vast majority of adults with BD (70-85%) suffer from some form of clinical sleep impairment [1, 4], contrasting the rate of 20-26% in the general population [5, 6]. Different sleep disturbances are associated with different stages of BD. For example, insomnia, hypersomnia and non-restorative sleep during depressive episodes; insomnia and decreased need for sleep during manic episodes; reduced quality of sleep, reduced sleep duration, decrease of sleep efficiency and greater variability in sleep/wake rhythm during euthymic episodes [7-10]. Studies have reported numerous correlates of sleep impairments among adults with BD, including more severe depression and mania symptoms [9, 11, 12], higher frequency of episodic recurrence [10, 13-15], suicide attempts [2, 16, 17], psychosis [14], comorbid anxiety [2, 14], cigarette smoking, antidepressant treatment [2], medication non-adherence [18], higher neuroticism and impulsivity [19], and neurocognitive deficits [10, 20, 21]. Studies have also reported various other sleep comorbidities such as obstructive sleep apnea and restless legs syndrome [7, 22].

Adults and youth exhibit different sleep patterns. Youth will generally exhibit shorter total sleep time, later sleep and wake-times, and erratic sleep/wake schedules, particularly in terms of weekend to weekday sleep schedules [23-28]. Nonetheless, sleep is crucial during adolescence to promote brain growth and cognitive development [29]. Yet, 76-96% of youth with BD report some form of sleep complaint or disturbance [30-34], rates consistently higher than their psychiatrically healthy peers [35-37]. Relatively little is known regarding clinical correlates of sleep complaints/disturbance in youth with BD. A clinical study of youth with BD (n=70) measuring sleep disturbances through diagnostic interviews found decreased need for sleep was associated with worse current functioning [33]. Two longitudinal studies using self-report questionnaires to measure sleep disturbance among youth with BD found that: worse depression scores predicted worse sleep disturbance at follow-up (n=40) [36]; and worse mania, depression, and psychosocial function predicted worse sleep disturbance at follow-up (n=53) [37]. A number of clinical studies also using self-reports found that among youth with BD: those who had a comorbid nightmare disorder had significantly higher suicidality than those without (n=379) [38]; those who had greater disruption in weekend-sleep schedules scored higher on impulsivity (n=59) [39]; and mood symptoms and self-injurious behavior predicted sleep disturbances (n=61) [40].

Despite the aforementioned studies on sleep among youth with BD, a number of gaps remain: most studies have focused on BD-I subtype, few studies have examined a wide array of clinical correlates, and thus far only one study has used the Pittsburgh Sleep Quality Index (PSQI) [40], a leading self-report sleep measure commonly used in adults with BD [2, 6, 41, 42]. Although polysomnography is the objective physiological gold standard for sleep assessment, it is not always feasible and/or acceptable to patients; importantly, subjective measures of sleep disturbance capture

features relevant to the experience of individuals with mood disorders [43-45]. The PSQI examines seven sleep parameters: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medication, and daytime dysfunction. We therefore set out to add to the existing literature regarding sleep disturbances among youth with BD by using the PSQI and examining a wide range of demographic and clinical correlates of sleep disturbance in a relatively large sample of youth with BD. Based on the current literature, we hypothesized that, compared to psychiatrically healthy controls (HCs; as defined in Methods), BD youth would score significantly worse across all parameters of the PSQI, and that worse depression and mania symptom severity, higher suicidality, and worse global functioning would be associated with worse global sleep scores.

Methods

Subjects

Participants were 103 youth (72 BD, 31 HC), aged 14-20, enrolled in a clinical research registry between 2012-2021. Inclusion criteria for all youth were being between the ages of 13 – 20 years, 11 months of age, able to speak English, and able to give informed consent. Youth with BD-I, -II, or Not Otherwise Specified (NOS; akin to Other Specified Bipolar and Related Disorder) were recruited from a subspecialty clinic at a tertiary academic health sciences centre in Toronto, Canada. Inclusion criteria for BD youth was a diagnosis of BD, probable BD and being evaluated and/or treated at the subspecialty clinic. HCs were recruited from the community. Inclusion criteria for HCs were no lifetime mood or psychotic disorder, substance use disorder, and no first- or second-degree family history of BD or psychotic disorders. The study was approved by the institutional research ethics board, and written informed consent was provided by participants and at least one parent/guardian before study commencement.

Procedure

Assessments were carried out by research staff who had a Bachelor's or Master's degree in a health sciences field and were trained under the supervision of the senior author (B. I. G., a licensed child-adolescent psychiatrist). All instruments were carried out during the one study visit. The Kiddie Schedule for Affective Disorders and Schizophrenia for School Age Children, Present and Lifetime version (K-SADS-PL) [46] was used to determine current and lifetime psychiatric diagnoses, based on interviews with the youth and their parent(s). Diagnoses were based on DSM-IV criteria as this sample was recruited from 2012 through 2021, and the DSM-5 version of the K-SADS-PL was not available until December 2016. The mood sections of the K-SADS-PL were substituted with the extended K-SADS Depression Scale (DRS; clinical significance cut-off score of ≥13), [47] and K-SADS Mania Rating Scale (MRS; clinical significance cut-off score of ≥12) [48]. Criteria for BD-NOS were defined according to criteria used in the Course and Outcome of Bipolar Illness in Youth (COBY) study [49]. Diagnoses were determined using all available information, including youth and parent interviews and any available medical records. Clinical judgment was applied when conflicting information arose. Diagnoses were confirmed by a consensus meeting with a licensed child and adolescent psychiatrist following completion of the K-SADS-PL interview (B.I.G., R.H.B.M.)

Sleep quality over the past month was measured using the PSQI self-report [41]. The PSQI is widely used with evidence of good reliability and validity in adults [50-53] and youth [54-56], as well as high sensitivity (89.6%) and specificity (86.5%) for identifying sleep impairments within general adult populations with a cut-off score of five [41, 57]. The PSQI consists of 19 self-report questions pertaining to sleep quality and disturbance, grouped into seven subscale scores (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction). Subscales are scored on a 0-3 scale, with a score of 3 signifying the worst level of functioning, and then summed to yield a global score. The global score ranges from 0-21, with higher scores indicating worse sleep quality [41].

The four factor Hollingshead Scale was used to determine socioeconomic status (SES) [58]. Global functioning was assessed via the Children's Global Assessment Scale (CGAS).This rated the youth's current, most severe past, and past year of functioning [59]. Higher scores on this scale imply higher levels of global functioning**,** with a clinical cut-off of 60**.** KSADS-PL was used to obtain diagnoses and clinical characteristics, including lifetime physical and/or sexual abuse. "Any Anxiety Disorder(s)" were combined into one variable, which included generalized anxiety disorder, social phobia, separation anxiety disorder, agoraphobia, panic disorder, and anxiety disorder not otherwise specified. Substance use disorder included alcohol or drug abuse or dependence. Lifetime cigarette smoking, also ascertained via the K-SADS-PL, was computed as a "yes" or "no" variable. A Safety Form was used to record any suicidality or non-suicidal self-injury that was not captured during the K-SADS-DRS interview (e.g., occurring outside the context of a depressive interval, such as while intoxicated or situationally dysregulated). The Children's Affective

Lability Scale (CALS) assessed affect regulation and was collected using a youth self-report and parent/guardian-report [60]. The Life Problems Inventory self-report assessed borderline personality disorder (BPD) traits of: identity confusion, impulsivity, emotion dysregulation, and interpersonal problems [61]. The Family History Screen was used to obtain psychiatric history of first- and second-degree relatives from the youth and parent(s) [62].

Study data was collected and managed using REDCap (Research Electronic Data Capture) tools hosted at Sunnybrook Research Institute and the Centre for Addiction and Mental Health, Canada [63, 64].

Data Analysis

Demographic variables and PSQI subscale and global scores were compared between BD and HC groups using t-tests. Within-group analyses were performed for participants with BD to examine correlations between demographic, clinical, and familial characteristics and the global PSQI sleep score. This was done using t-tests and Pearson's correlation for categorical and continuous variables, respectively. Normality was tested using the Shapiro-Wilk Test. Mann–Whitney U Test and Spearman's correlation were used when continuous variables were not normally distributed. False discovery rate (FDR) was used to correct for multiple comparisons [65]. Multiple linear regression was carried out with any variables associated with PSQI global score at $p<0.1$ after FDR correction.

Further exploratory analyses were carried out to compare PSQI subscale and global scores within sex for between BD youth and HCs, and between sex for BD youth. This was carried out to elucidate whether sleep disturbances present differently within the two sexes. All statistical analyses were conducted using Statistical Package for the Social Sciences, version 25.0.

Results

Descriptive results

Demographic characteristics for both BD and HC groups are listed in Table 1.

Between-group analysis of sleep impairments

Sleep impairment scores for BD youth and HCs are presented in Table 1. Overall global sleep scores were significantly worse for BD youth than HCs. Youth with BD also reported significantly worse subjective sleep quality, sleep latency, sleep disturbance, and daytime dysfunction, as well as a higher use of sleep medication. Differences in sleep duration scores ($p=0.16$) and habitual sleeping efficiency scores ($p=0.39$) were non-significant.

Within-group analysis of sleep impairment

Associations between demographic, clinical, and familial characteristics and PSQI global scores for BD youth are reported in Table 2. Worse global sleep scores were significantly associated with more severe lifetime and current depression scores, as well as current mixed mood state. Similarly, higher self-reported affective lability and BPD traits (measured by the Life Problems Inventory) were significantly associated with worse global sleep scores. Better sleep scores were significantly associated with current euthymic mood state, and lifetime lithium use. Associations of worse current global functioning scores and lower SES scores with worse global sleep scores were not significant after FDR correction.

Linear regression analyses

Linear regression was used to determine the unique contributions to variance in PSQI global scores by including demographic and clinical characteristics with $p<0.1$ after FDR correction in the univariate analyses. Variables examined included: current and lifetime depression scores, current euthymic and mixed mood states**,** lifetime lithium treatment, self-reported affective lability, Life Problems Inventory total score, and family history of attention-deficit/hyperactivity disorder (ADHD). When controlling for age and sex, self-reported affective lability ($R^2=0.22$; $F(3, 65)=6.03$, $p=0.001$) and current depression severity score ($R^2=0.29$; $F(4, 64)=6.62$, $p<0.001$) independently significantly predicted PSQI global score.

Exploratory analyses within sex

Compared to HCs, PSQI global scores were significantly worse for both males ($t=2.25$, $p=0.03$) and females ($t=5.08$, $p<0.001$) with BD. Both male and females with BD reported worse subjective sleep quality ($t=2.62$, $p=0.03$; $t=2.95$, $p=0.004$) and daytime dysfunction ($t=2.19$, $p=0.04$; $t=3.96$, $p<0.001$), as well as higher use of sleep medication ($t=2.51$, $p=0.02$; $t=3.23$, $p=0.002$). Females with BD also reported worse sleep latency ($t= 4.30$, $p<0.001$) and sleep disturbance ($t=3.39$, $p=0.001$). There were no sex differences between males and females within the BD group.

Discussion

This study found that, relative to HCs, youth with BD reported worse PSQI global scores and worse scores on the following PSQI subscales: subjective sleep quality, sleep

Table 1. Demographic and sleep characteristics of adolescents with bipolar disorder and healthy controls

	Overall (n = 103)	Bipolar Disorder (n = 72)	Healthy Controls (n = 31)	Statistics		
				$t/\chi^2/U$	p	Effect Size
Demographics						
Age, years [b]	16.63±1.66	16.76±1.68	16.32±1.62	924.50	0.21	0.25
Socio-economic status [b]	4.15±9.30	4.18±0.94	4.16±0.86	1074.50	0.96	0.11
Sex (% female)	77 (74.04%)	55 (75.34%)	21 (67.74%)	0.91	0.34	0.94
Race (% Caucasian)	69 (66.35%)	50 (68.49%)	19 (61.29%)	0.51	0.48	0.70
Living with both natural parents	59 (56.73%)	38 (52.79%)	21 (67.74%)	1.98	0.16	0.14
Pittsburgh Sleep Quality Index (PSQI) Scores						
Subjective Sleep Quality [b]	1.07±0.71	1.23±0.70	0.71±0.59	684.00	.001	0.72
Sleep Latency [b]	2.62±2.11	3.15±1.96	1.39±1.94	540.50	<.001	0.84
Sleep Duration [a b]	0.38±0.65	0.43±0.70	0.26±0.51	944.50	0.16	0.34
Habitual Sleeping Efficiency [b]	1.47±1.40	1.64±1.40	1.13±1.36	827.00	0.10	0.18
Sleep Disturbance [a b]	1.51±0.65	1.62±0.68	1.17±0.38	546.00	<.001	0.95
Use of Sleep Medication [a b]	0.87±1.27	1.14±1.36	0.26±0.77	732.50	<.001	0.86
Daytime Dysfunction [a b]	1.37±0.88	1.60±0.87	0.72±0.54	395.00	<.001	1.43
Summary Score [b]	8.99±5.04	10.61±4.65	5.23±3.79	419.00	<.001	0.99

Values for all continuous variables are written as mean ± SD, categorical variables are written as n (% within group).
Effect Size = Cohen's d or Cramer's V. [a] Homogeneity of Variance not met, Welch's test used. [b] Mann-Whitney U reported

latency, sleep disturbance and daytime dysfunction, and higher use of sleep medication. The two subscales that were not associated (sleep duration and habitual sleeping efficiency) may be particularly influenced by the development of the PSQI in an adult population. A more liberal scoring criteria may yield abnormalities relevant to a youth population. For example, sleep duration of more than 7 hours yields a "0" for this subscale, yet most youth would be expected to have much more sleep [66]. Similarly, a sleep efficiency of 85% yields a "0" for this subscale, yet sleep efficiency is age dependent and most youth would have a much higher sleep efficiency [67]. Therefore, the lack of differences in the aforementioned sleep subscale findings between BD and HC may be an artefact of a ceiling effect of these measures and minimize the effect noted in the global scale as well.

Our findings of worse PSQI global and subscale scores among youth with BD align with prior studies of adults [6, 13, 19] and youth [40] with BD. Prior studies in youth with BD using sleep measures other than the PSQI similarly found evidence of difficulty initiating sleep, frequent awakenings, and more variable sleep durations [36, 39, 43]. In addition, our findings of adverse clinical correlates of poor sleep quality largely aligned with prior studies in youth with BD. Worse current and lifetime depression severity scores were associated with worse PSQI global scores, of which current depression remained significant in multivariable analyses. This aligns with the literature, which similarly supports a dimensional association between depression and sleep [33, 36, 37]. The lack of association of global PSQI scores with current and/or lifetime manic symptom severity may relate to the fact that hypo/manic intervals are shorter than depressive intervals, and the fact that sleep disturbance related to manic symptoms is characterized by reduced need for sleep rather than the aspects of sleep disturbance. Relatedly, we did not find an association between PSQI score and BD subtype. However, we did find that current euthymic mood state was associated with better PSQI global scores, and current mixed mood state was associated with worse PSQI global scores. Similar findings have been previously reported in youth with BD [33, 34], whereas findings in adult studies are mixed [3, 9, 12, 14].

In terms of dimensional scales, higher self-reported affective lability and BPD traits were associated with worse PSQI global scores, with self-reported affective lability remaining a significant predictor of PSQI global score in multivariable analyses. Among the adult BD population, studies have found that sleep disturbances are associated with

Table 2. Clinical characteristics, treatment history and dimensional traits associated with sleep quality (PSQI global score) among 72 youth with bipolar disorder

		Test statistic [a]	p	Effect size
Demographics				
Age, years	16.76±1.68	-0.09	0.47	-
Socio-economic status [b]	4.18±0.94	-0.24	0.047	-
Sex (% female)	55 (75.34%)	-0.26	0.80	0.06
Race (% Caucasian)	50 (68.49%)	-1.35	0.18	0.32
Living with both natural parents	38 (52.79%)	0.39	0.70	0.09
Bipolar Subtype				
BD-I	23 (31.51%)	0.48	0.62	0.66
BD-II	17 (23.29%)			
BD not otherwise specified	32 (43.84%)			
Mood Symptom Severity and Functioning				
Mania – most severe past	30.38±9.04	-0.04	0.72	-
Mania – past month [c]	16.75±14.18	0.20	0.09	-
Depression – most severe past	31.00±11.35	0.32	0.007	-
Depression – past month	19.61±11.94	0.44	<0.001	-
CGAS – most severe past	42.60±9.76	0.03	0.82	-
CGAS – past year	69.35±11.36	-0.08	0.50	-
CGAS – current	54.33±13.70	-0.23	0.049	-
Current Mood State				
Euthymic	9 (12.50%)	-2.25	0.03	0.54
Depressed	17 (23.61%)	0.80	0.43	0.19
Hypo/manic	13 (18.06%)	0.52	0.60	0.12
Mixed	33 (45.83%)	2.64	0.01	0.63
Lifetime Comorbid Diagnoses				
ADHD	31 (42.47%)	-1.03	0.31	0.25
Anxiety disorders	64 (87.67%)	-1.21	0.23	0.29
SUD	26 (35.62%)	-0.30	0.76	0.09
ODD	16 (21.92%)	-1.18	0.24	0.28
Conduct Disorder	3 (4.11%)	0.36	0.72	0.09
Other Characteristics				
Suicide attempt	19 (26.03%)	0.21	0.84	0.06
Suicidal ideation	46 (63.01%)	-0.14	0.89	0.04
Self-injurious behaviour	42 (57.53%)	-1.18	0.24	0.30
Cigarette smoking (ever)	30 (41.10%)	-0.34	0.97	0.08
Lifetime sexual abuse	6 (8.22%)	0.61	0.54	0.15
Lifetime physical abuse	8 (10.96%)	-1.31	0.20	-0.31
Lifetime psychosis	19 (26.03%)	0.72	0.47	0.17
Current Medication Use				
SGA	17 (23.61%)	0.69	0.50	0.17
Lithium	4 (5.56%)	1.50	0.12	0.36
SSRI Antidepressants	10 (13.89%)	-0.7	0.95	0.17
Non-SSRI Antidepressants	1 (1.39%)	-0.95	0.35	0.23
Stimulants	3 (4.17%)	-0.91	0.37	0.22

continued

Table 2. continued

		Test statistic [a]	p	Effect size
Lifetime Treatment History				
SGA	41 (56.16%)	1.34	0.18	0.32
Lithium	13 (18.06%)	-2.83	0.006	0.68
SSRI Antidepressants	38 (51.35%)	0.16	0.87	0.04
Non-SSRI Antidepressants	17 (23.61%)	-0.69	0.49	0.17
Stimulants	12 (16.44%)	0.16	0.88	0.04
Psychiatric hospitalization [c]	14 (19.18%)	0.16	0.87	0.04
Dimensional Traits				
CALS Adolescent report [c]	31.55±15.88	0.46	<0.001	-
CALS Parent report [c]	23.61±17.35	0.09	0.44	-
Life Problems Inventory	149.43±47.18	0.42	<0.001	-
First and second-degree family history				
Mania/hypomania	29 (39.73%)	-1.86	0.07	-0.44
Depression	60 (82.19%)	-0.16	0.88	-0.04
Anxiety	46 (63.01%)	-1.0	0.92	-0.24
ADHD	27 (36.99%)	-2.41	0.019*	-2.41

Values for all continuous variables are written as mean ± SD, categorical variables are written as n (% within group). Effect Size = Cohen's d
[a] F, t or Pearson's correlation. [b] Homogeneity of Variance not met, Welch's test used. [c] Spearman's Correlation reported, *Not significant after FDR correction. BD = Bipolar disorder; CGAS = Children's Global Assessment Scale; ADHD = Attention deficit-hyperactivity disorder; SUD = Substance use disorder; ODD = Oppositional defiant disorder; SGA = Second Generation Antipsychotic; SSRI = Selective Serotonin Reuptake Inhibitor; CALS = Children's Affective Lability Scale. SGA = risperidone, olanzapine, aripiprazole, ziprasidone, quetiapine. SSRI antidepressants = sertraline, paroxetine, fluoxetine, fluvoxamine, citalopram, escitalopram. Non-SSRI antidepressants = bupropion, mirtazapine, venlafaxine, duloxetine. Stimulants = methylphenidate, amphetamine-dextroamphetamine, dextroamphetamine

Table 3. Correlates of sleep disturbance amongst youth with BD analyzed through multiple linear regression

	ß (95% CI)	B, SE	p-value
Depression – past month	0.32 (0.03, 0.22)	0.12, 0.05	0.011
CALS Adolescent report	0.34 (0.03, 0.17)	0.09, 0.04	0.007

Age and sex were included as covariates. Lifetime depression score, current euthymic and mixed mood states, lifetime lithium treatment, life problems inventory total score, and family history of attention-deficit/hyperactivity disorder did not meet significance criteria for forward entry (p entry<0.05). Abbreviations: CALS: Children's Affective Lability Scale. ß= standardized regression coefficient, CI= confidence interval, B= unstandardized regression coefficient, SE= standard error.

higher levels of emotional reactivity and dysregulation [68, 69], as well as impulsivity [70]. While these associations have not been examined among youth with BD, dysregulated emotional, depressive, and labile temperaments among youth with BPD traits have been associated with sleep disturbances [71-73]. However, it is also noteworthy that while self-reported affective lability was significantly associated with global PSQI scores, parent-reported affective lability was not. We examined this association in HCs to follow up on this finding, and found a similar pattern whereby PSQI global scores were associated with self-reported, but not parent-reported, affective lability in HCs ($r = 0.42$, $p = 0.02$). While this pattern may relate to high self-reporting as an intra-individual characteristic, it could equally be due to more accurate reporting of lability and sleep

Lifetime lithium treatment was associated with better PSQI global scores. While this has not been investigated within youth populations, an adult study using the PSQI found that patients who were undergoing lithium treatment

experienced better sleep efficiency and longer sleep duration, with females further experiencing better sleep quality, longer sleep duration, and less use of sleep medication [74]. One study found that lithium treatment did not cause a significant change across any subscales of the PSQI [75]. A study comparing depressed patients and HCs found that lithium had an ameliorative effect on sleep for depressed patients, but no effect for HCs [76]. Use of SGAs was common in this sample, however the current study did not collect information about reasons for treatment, as such it is not clear how many participants may have been taking antipsychotics primarily as sleep aids.

Interestingly, despite the vast literature showing an established association between sleep disturbances and increased risk of suicidality among both adults [2, 16, 17, 77] and youth [38, 78], we did not find an association between suicidality and PSQI global score. This is particularly noteworthy in the context of our observed associations between higher depression severity and emotional lability/dysregulation in relation to poor sleep, as these variables are associated with higher risk of suicidality [79, 80].

The paucity of findings regarding family psychiatric history (with the exception of familial ADHD which was not significant after FDR correction) contradicts with prior findings that there is increased prevalence of sleep disturbances in offspring of adults with BD [81-83]. While this topic has been studied among offspring of parents with BD, this is yet to be studied in youth with BD, and studies among adults with BD are mixed [84, 85].

Lastly, our exploratory within-sex subgroup analyses revealed that sleep disturbances were evident among both males and females, with more consistent and statistically significant findings among females. In contrast, within BD, there were no significant sex differences in sleep. Adult studies have found that the association between sleep disturbances and mood episodes appears to be stronger in females as compared to males with BD [15, 86-88]. Perhaps relatedly, females with BD have been found to score worse on subjective measures of sleep disturbance, but better on objective sleep measures, than males with BD [89]. The same pattern has been found in the general population [90].

The current study has several limitations which should be considered. First, the design was cross-sectional and retrospective, precluding any inferences regarding directionality and/or causality. Second, despite the relatively large sample size there was limited power for within-group analyses for youth with BD. Third, findings were taken from a clinical population at a tertiary outpatient setting, meaning that they may not be representative of the broader youth BD population. Lastly the main outcome (PSQI global score) was measured through self-report only, which has meaningful limitations, including the potential for under- and/or over-reporting of symptoms. Discrepancies between subjective and objective sleep quality have been reported in youth with mood and anxiety disorders [45]. In addition, the one-month timeframe of the PSQI is subject to recall bias [91]. Thus, having objective sleep measures may provide different insights [57]. Nonetheless, the PSQI is established as a valid tool for measuring subjective sleep disturbances within BD populations [43-45].

Despite the acknowledged limitations, our study addresses a gap in the literature by investigating the prevalence of sleep disturbances among youth with BD, and looking at a wide range of correlates of sleep disturbances. The pattern of findings overall converges with prior literature, with youth with BD experiencing more sleep disturbance than their psychiatrically healthy peers, and a number of mood symptoms having a substantial impact on sleep disturbance. Noteworthy exceptions included the lack of global sleep scores with suicidality and/or family history of psychiatric illness. The study revealed some novel correlates not yet examined in the youth BD literature, including the youth BD depression severity, as well as trait emotional and affective lability. Future research is warranted to better understand distal and proximal antecedents of sleep disturbances, prospective associations with other clinical characteristics, and to investigate related neurobiological correlates. In the interim, present findings confirm the importance of evaluating sleep disturbance and its correlates in youth with BD.

Conflicts of Interest

The authors have no conflicts to declare.

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