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Actigraphic-measured sleep disturbance predicts increased positive symptoms in adolescents at ultra high-risk for psychosis: A longitudinal study

Jessica R. Lunsford-Avery [a,*], Monique K. LeBourgeois [b], Tina Gupta [c], Vijay A. Mittal [c,d]

[a] Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC, USA
[b] Department of Integrative Physiology, University of Colorado Boulder, Boulder, CO, USA
[c] Department of Psychology and Neuroscience, University of Colorado Boulder, Boulder, CO, USA
[d] Center for Neuroscience, University of Colorado Boulder, Boulder, CO, USA

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ABSTRACT

Background: Sleep disturbance is prevalent among patients with psychosis, yet little is known about sleep health during the ultra high-risk (UHR) period. This study used actigraphy to evaluate sleep in healthy control (HC) and UHR adolescents to examine the relationship between sleep disturbance and psychosis symptoms at baseline and 12-month follow-up, as well as comparisons between objective and subjective measurements of sleep functioning in UHR youth.
Method: Thirty-six UHR and 31 HC youth participated in a baseline evaluation including 5 nights of actigraphy, subjective measurement of sleep health (Pittsburgh Sleep Quality Index; PSQI), and clinical interviews. Clinical measures were repeated with UHR youth (N = 23) at a 12-month follow-up.
Results: The actigraphy data indicated that UHR youth displayed increased wake time after onset (WASO), increased movements during sleep, and decreased efficiency compared to HC, and several markers of sleep disturbance including decreased efficiency, increased WASO, number of awakenings, and increased movements were associated with symptomatology in the UHR group. Interestingly, there were associations between actigraph and self-report indices of sleep duration and efficiency (at the trend level) but not awakenings. Several objective measures of sleep disturbance and one self-reported measure (disrupted continuity) predicted the longitudinal course of symptoms over 12 months in the UHR group.
Conclusions: Taken together, the results suggest a potential role for sleep problems in the etiology of schizophrenia, and highlight sleep health as a possible target for prevention/intervention efforts. Additionally, actigraphy represents an inexpensive, sensitive measurement providing unique information not captured by self-report, and may be an informative adjunct to UHR assessments.

1. Introduction

Sleep disturbance is a prevalent symptom among individuals with psychosis, including deficits in duration, efficiency, and continuity. Among individuals with schizophrenia, sleep problems are associated with greater distress and reduced quality of life (Cohrs, 2008; Waters and Manoach, 2012) and occur regardless of medication status (Chouinard et al., 2004) or mood state (Wulff et al., 2012). Additionally, sleep disturbance is associated with increased illness severity (Cohrs, 2008), often precedes relapse (Benson, 2008), and when targeted in treatment, improves sleep and psychosis symptoms (Kantrowitz et al., 2010). Taken together, converging evidence suggests that poor sleep may play an important role in schizophrenia pathophysiology (Keshavan and Tandon, 1993; Monti and Monti, 2005).

Despite the pervasiveness of sleep disturbance in psychosis populations, few studies have investigated its prevalence before schizophrenia onset or how it relates to the emergence and course of symptoms over time among at-risk adolescents. At present, it is unclear whether objectively-measured sleep disturbance (e.g., deficits in duration, efficiency, continuity) precedes psychosis onset, emerges secondary to exposure to schizophrenia, or reflects comorbid mood disorders. To the extent that sleep problems precede illness onset and predict increased symptoms over time, it may represent an important target for early identification, prevention, and treatment strategies for at-risk youth.

Although few studies have examined sleep in the prodromal period, retrospective data from schizophrenia samples suggest that impairments in sleep duration and continuity precede psychosis onset (Yung and McGorry, 1996; Lunsford-Avery and Mittal, 2013). Three studies

* Corresponding author at: Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, 2608 Erwin Road Suite 300, Durham, NC 27705, USA. Tel.: +1 919 681 0035; fax: +1 919 681 0016.

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have investigated sleep in at-risk populations. Our recent investigation of *self-reported* sleep disturbance in the prodrome examined relationships between sleep deficits and psychosis symptoms at a single time point (Lunsford-Avery et al., 2013). Results revealed increased sleep latency and nocturnal awakenings among UHR youth compared to healthy controls (HC), with significant associations between poor sleep quality and increased negative symptoms. Two additional studies have observed sleep physiology abnormalities in at-risk samples (Keshavan et al., 2004; Castro et al., 2012). Overall, these results suggest sleep difficulty in the prodromal period and point to its possible role in the etiology and pathophysiology of psychosis.

Although existing data have increased the understanding of sleep disturbance in at-risk samples, they are limited for several reasons. First, cross-sectional studies have not permitted determination of the temporal order of increases in sleep disturbance versus symptom severity. Second, prior studies have utilized either self-report or polysomnography. Self-reports are vulnerable to recall biases, particularly among adolescents at risk for psychosis (Granö et al., 2011). Whole-night polysomnography is widely viewed as the gold-standard of sleep measurement. It is, however, expensive, infeasible in many UHR youth-based clinics, and often implemented in laboratory settings, which may not accurately reflect sleep in natural settings (Meltzer et al., 2012).

In the current study, we extended our initial investigation (Lunsford-Avery et al., 2013) by including actigraphic assessment of sleep and a follow-up clinical time point. Our first aim evaluated whether objectively-measured sleep (duration, efficiency, wake time after onset (WASO), total movements) is disrupted in UHR youth compared to HC using a novel measurement approach (actigraphy), and if present, how sleep deficits relate to symptom severity in UHR adolescents. Actigraphy has established reliability and validity, is relatively inexpensive, provides an objective measure of sleep in the natural environment, and supplies data over longer periods of time than polysomnographic studies (Sadeh, 2011; Meltzer et al., 2012).

A second aim evaluated the relationship between actigraphic measures of sleep duration, efficiency, and continuity with self-reports of corresponding constructs from the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989). To the degree that actigraphy provides important information over and above subjective assessments of sleep, it may represent an informative supplement to current UHR assessments. Finally, the current study employed a longitudinal design to assess the extent to which sleep health at clinical intake predicts increased symptom severity over a 12-month period. If specific areas of disturbed sleep predict worsened illness over time, elucidating these deficits may improve our understanding of the etiology of psychosis and highlight potential biomarkers.

2. Method

2.1. Participants

Thirty-eight UHR and 31 HC adolescents (12–21 years) participated in the baseline assessment (time 1; T1); two UHR participants were excluded due to insufficient sleep data (as described below), such that 36 UHR and 31 HC youth were included in the T1 analyses. Participants were self- or physician-referred and recruited as part of an ongoing longitudinal study at the Adolescent Development and Preventative Treatment (ADAPT) program at the University of Colorado Boulder. UHR inclusion criteria included moderate levels of positive symptoms on the SIPS and/or a decline in global functioning in the presence of schizotypal personality disorder and/or a family history of psychosis (Miller et al., 1999). Exclusion criteria for all participants included lactation, tic disorder, history of significant head injury or neurological disorder, mental retardation, or substance dependence in the preceding 6 months. Additionally, UHR exclusion criteria included psychotic disorder diagnosis and HC exclusion criteria included any Axis I disorder and history of psychosis in a first-degree relative. At the time of analysis, 23 of the 36 UHR participants and 21 of the 31 HC youth had returned for a 12-month follow-up (time 2; T2), all of whom provided sufficient data for inclusion in the longitudinal analyses.

2.2. Clinical measures

UHR syndromes were diagnosed at T1 using the Structured Interview for Prodromal Symptoms (SIPS), which includes the Scale of Prodromal Symptoms (SOPS; positive and negative symptoms) (McGlashan et al., 2001; Rosen et al., 2002; Miller et al., 2003), and Axis I disorders were diagnosed using the Structured Clinical Interview for DSM-IV (SCID, Research Version; First et al., 2005). Given the prevalence of depression in high-risk populations (Svirskis et al., 2005; Rosen et al., 2006; Shioiri et al., 2007; Salokangas et al., 2012) and the relationship between sleep dysfunction and depression in adolescents (Lunsford-Avery et al., 2012), depression symptoms were controlled for using the 21-item Beck Depression Inventory-II (BDI-II; Beck et al., 1996). All clinical measures were repeated at T2.

2.3. Actigraphy and sleep/activity diary

At T1, participants wore an ActiSleep monitor (ActiGraph; Pensacola, FL) on their non-dominant wrist for 5 consecutive days. The ActiSleep monitor measures total sleep time (TST; minutes from sleep start to sleep end), number of awakenings between sleep start and sleep end, WASO (number of minutes awake between sleep start and sleep end), sleep efficiency (% of sleep epochs between sleep start and sleep end), and total movement counts during the sleep period. The ActiSleep monitor recorded epoch lengths in 60-second intervals. In accordance with best practice parameters for actigraphy (Ancoli-Israel et al., 2003; Acebo and LeBourgeois, 2006), a sleep/activity diary accompanied the actigraph and required participants to record lights-out time, wake time, school attendance, naps, physical illness, and participation in activities daily.

The sleep/activity diary was used to determine the sleep period for the actigraphy analyses. Target sleep variables for the analyses were calculated using Sadeh algorithms (Sadeh et al., 1994) in the ActiLife version 5.10.0 scoring program. The sleep/activity diary also recorded the times the watch was removed (e.g., during showers), which was verified by validation data (i.e., measurements of activity) within the ActiLife scoring program.

Following automatic scoring, data were hand-checked for accuracy by the first author (Lunsford-Avery). Using the sleep/activity diary to determine the sleep period, the experimenter ensured accurate sleep onset time (first sleep epoch of three successive sleep epochs following a wake epoch) and offset time (last sleep epoch of five sleep epochs, prior to an awake epoch). To address incidents of ambiguous data, consensus meetings including at least three authors (Lunsford-Avery, Mittal, LeBourgeois, Gupta) determined whether nights with an anomaly (e.g., high nighttime waking activity) were appropriate for inclusion. Participants with at least 3 out of the 5 nights with accurate actigraph data were included in the analyses; 2 UHR and 0 HC participants were excluded at T1 due to insufficient number of nights of data.

2.4. Subjective sleep measure

The 19-item, self-report Pittsburgh Sleep Quality Index (PSQI) assesses multiple domains of sleep disturbance, including difficulties with sleep duration, efficiency, and disturbances (i.e., frequency of awakenings due to environmental/physiological factors) (Buysse et al., 1989). PSQI total scores range from 0 to 21 (sub-domains range from 0 to 3), with higher scores reflecting greater impairment. The PSQI displays sound validity and reliability and is commonly used with adolescent (Jones et al., 2006; Kaneita et al., 2009) and psychosis (Ritsner et al., 2004; Hofstetter et al., 2005; Afonso et al., 2011) populations.

Given the focus on the PSQI in our previous study (Lunsford-Avery et al., 2013), the current study focused only on variables that overlapped between the PSQI and actigraph (i.e., duration, efficiency, disturbances/awakenings) to assess if 1) the overlapping items are related and 2) the actigraph is better at predicting course than the PSQI.

2.5. Statistical analyses

For each participant, aggregated means for each actigraphy variable (TST, efficiency, WASO, number awakenings, total movements) were calculated. Stepwise linear regressions covarying for age (step 1) and depressive symptoms (step 2) assessed group differences in T1 actigraphy scores. Stepwise linear regressions covarying for age (step 1) and depressive symptoms (step 2) tested the associations between actigraphy variables and T1 attenuated positive and negative symptoms among UHR and HC samples separately.

Linear regressions tested the associations between subjective and objective measures of sleep disturbance (i.e., PSQI duration (minutes) with TST, PSQI efficiency with actigraph efficiency, PSQI disturbances with WASO and number awakenings) among UHR and HC groups separately. Finally, stepwise linear regressions covarying for T1 SIPS symptoms (positive, negative), age, and depressive symptoms evaluated the predictive association between T1 sleep disturbance (actigraph, PSQI) and worsening of T2 SIPS symptoms among UHR and HC samples.

Due to the relatively small sample size, all regression analyses were also completed without the covariates. This process yielded comparable results in terms of significance and direction of findings, and highlights the robustness of the current findings. Thus, all reported findings are based on regressions including the covariates, as these variables have been shown to have an important impact on sleep health.

3. Results

3.1. Demographics

Participants at T1 included 36 UHR and 31 HC adolescents. See Table 1 for demographic information. Of note, UHR youth were slightly older than HC at the trend level; thus, age was controlled for in the primary analyses. UHR adolescents displayed significantly higher levels of T1 positive ($F(1, 64) = 160.76$, $p < .01$), negative ($F(1, 64) = 48.12$, $p < .01$), and depressive symptoms ($F(1, 64) = 28.81$, $p < .01$) compared to HC. The majority of UHR (94%) and HC (100%) adolescents were not taking anti-psychotic medication at T1. Due to low base rate, there were no group differences in anti-psychotic use ($X^2(1) = 1.72$, $p = .19$). At T2, 4 UHR youth were prescribed anti-psychotic medication (17% of the 23 presenting for follow-up): 1 individual continued medication from T1, 3 individuals were newly prescribed anti-psychotics before T2, and 1 individual medicated at T1 had discontinued anti-psychotic use at T2.

Table 1
Demographic characteristics of the samples at time 1.

Variable	UHR sample (n = 36)	HC sample (n = 31)	*p* value
Mean (SD)			
Age in years	18.73 (1.89)	17.85 (2.62)	.07
Parent education	15.63 (2.55)	16.19 (2.09)	.33
SIPS-positive	11.81 (4.67)	.67 (1.27)	.00
SIPS-negative	9.28 (6.72)	.63 (1.27)	.00
BDI	16.89 (12.58)	3.71 (5.65)	.00
Number (%)			
Gender (male)	19 (53%)	16 (52%)	.92
Anti-psychotic medication use	2 (6%)	0 (0%)	.19

Abbreviations: UHR, ultra high-risk; HC, healthy control; SIPS, Structured Interview for Prodromal Symptoms (total symptoms); BDI, Beck Depression Inventory.

Table 2
Group differences in actigraphic measures of sleep at time 1.

	UHR mean (SD)	HC mean (SD)	R^2	*F*	*p*
TST	401.48 (74.45)	412.48 (62.54)	.00	0.02	.45
Efficiency	84.78 (8.82)	87.99 (4.20)	.06	4.33	.02
WASO	72.05 (52.11)	55.78 (23.07)	.07	5.03	.01
Total movements	28,690.31 (14,356.17)	20,144.73 (8815.99)	.08	5.75	.01
# awakenings	20.67 (8.37)	20.63 (5.42)	.01	0.77	.19

Abbreviations: UHR, ultra high-risk; HC, healthy control; TST, total sleep time; WASO, wake after sleep onset.

3.2. Group differences in actigraph variables at T1

As shown in Table 2, controlling for age and depressive symptoms, UHR adolescents displayed significantly reduced sleep efficiency ($F(3, 62) = 4.33$, $p < .05$), increased total movements during sleep ($F(3, 62) = 5.75$, $p = .01$), and increased WASO ($F(3, 62) = 5.03$, $p = .01$) compared to HC at T1. Controlling for age and depressive symptoms, groups did not differ on TST or number of awakenings.

3.3. Relationships of sleep disturbance to psychosis symptoms at T1

Controlling for age and depressive symptoms, decreased sleep efficiency ($F(3, 31) = 8.19$, $p < .01$), increased WASO ($F(3, 31) = 12.50$, $p < .01$), greater number of awakenings ($F(3, 31) = 2.81$, $p = .05$), and increased movements ($F(3, 31) = 7.26$, $p < .01$) were significantly associated with increased positive symptoms in the UHR sample at T1 (see Table 3). Specifically, efficiency reductions accounted for a significant proportion of the variance in positive symptoms (19%), as did increased WASO (26%), greater number of awakenings (8%), and total movements (17%). TST was not correlated with positive symptoms. Negative symptom level was not associated with any actigraph variables among UHR youth. There were no significant relationships between actigraph variables and positive or negative symptoms among HC youth, likely due to a low base rate of symptoms.

3.4. Relationships of actigraph variables to PSQI

As shown in Table 4, self-reported PSQI duration was positively related to actigraphic estimates of TST among UHR ($F(1, 22) = 3.46$, $p < .05$) and HC ($F(1, 19) = 5.55$, $p = .01$) at T1. Among UHR youth, self-reported PSQI efficiency was associated with actigraph-measured efficiency at the trend level ($F(1, 22) = 2.78$, $p = .06$). No correlation between self-reported and actigraphically-estimated efficiency was observed among HC ($F(1, 19) = 0.25$, $p = .31$). Self-reported sleep

Table 3
Relationship of actigraphic measures of sleep and psychosis symptoms in the UHR sample at time 1.

	Beta	R^2	df	*F*	*p*
SIPS positive					
TST	−.057	.00	3, 31	0.11	.37
Efficiency	−.507**	.19	3, 31	8.19	<.01
WASO	.622**	.26	3, 31	12.50	<.01
Total movements	.494**	.17	3, 31	7.26	<.01
# awakenings	.289*	.08	3, 31	2.81	.05
SIPS negative					
TST	−.127	.02	3, 31	0.62	.22
Efficiency	−.217	.04	3, 31	1.41	.12
WASO	.181	.02	3, 31	0.88	.18
Total movements	.159	.02	3, 31	0.71	.20
# awakenings	.088	.01	3, 31	0.27	.30

Abbreviations: TST, total sleep time; WASO, wake after sleep onset.
** Indicates $p < .01$.
* Indicates $p < .05$.

Table 4
Relationship of subjective and objective measures of sleep at time 1.

	PSQI sleep duration (min)	PSQI efficiency	PSQI disturbances
UHR			
Actigraphy TST	.369*	–	–
Actigraphy efficiency	–	.335+	–
Actigraphy WASO	–	–	.218
Actigraphy # awakenings	–	–	.023
HC			
Actigraphy TST	.475*	–	–
Actigraphy efficiency	–	.113	–
Actigraphy WASO	–	–	.256
Actigraphy # awakenings	–	–	.234

Note: Relationships indicated as beta values. For ease of interpretation, PSQI efficiency was reverse-coded.
Abbreviations: UHR, ultra high-risk; HC, healthy control; PSQI, Pittsburgh Sleep Quality Index; TST, total sleep time; WASO, wake after sleep onset.
* Indicates $p < .05$.
+ Indicates $p < .10$.

disturbances were not associated with WASO among UHR ($F(1, 22) = 1.10$, $p = .15$) or HC ($F(1, 19) = 1.33$, $p = .13$). Similarly, PSQI sleep disturbances were not related to actigraph-measured number of awakenings for UHR ($F(1, 22) = 0.01$, $p = .46$) or HC ($F(1, 19) = 1.10$, $p = .15$) groups.

3.5. T1 sleep disturbance predicts the longitudinal course of symptoms over 12 months

As depicted in Table 5, after controlling for T1 positive symptoms, age, and depressive symptoms, decreased T1 efficiency ($F(4, 18) = 8.27$, $p < .01$), reduced TST ($F(4, 18) = 4.39$, $p < .05$), and increased WASO ($F(4, 18) = 4.94$, $p < .05$) were significantly associated with increased T2 positive symptoms among UHR youth. Specifically, reduced efficiency accounted for a significant proportion of the variance (12%) in predicting an increase in positive symptoms at 12 months, as did increased WASO (9%) and reduced TST (8%). After controlling for T1 positive symptoms, age, and depressive symptoms, T1 total movements and number of awakenings were not significantly related to T2 positive symptoms among UHR youth. After controlling for T1 negative symptoms, age, and depressive symptoms, no actigraphic variables were correlated with T2 negative symptoms for UHR adolescents. There were no significant findings for the HC group. When we utilized the same statistical strategy using the baseline PSQI variables, disturbances ($F(4, 11) = 5.46$, $p < .05$) significantly predicted T2 positive symptoms among UHR youth. PSQI variables were not predictive of T2 negative symptoms among UHR youth, and there were no significant findings for any of the PSQI variables in the HC group.

Table 5
Relationships of time 1 actigraphic sleep measures to 12-month follow-up psychosis symptoms among UHR youth.

Predicting 12 month variable	Positive symptoms at T2			Negative symptoms at T2		
	R^2	*F* statistic	*p* value	R^2	*F* statistic	*p* value
T1 actigraph						
TST	.08*	4.39	.03	.01	0.26	.31
Efficiency	.12**	8.27	<.01	.03	1.15	.15
WASO	.09*	4.94	.02	.02	0.62	.22
Total movements	.03	0.37	.13	.04	1.44	.12
# awakenings	.04	1.74	.10	.02	0.54	.24
T1 PSQI						
Duration	.11	2.80	.07	.00	0.01	.48
Disturbances	.17*	5.46	.03	.12	2.25	.09
Efficiency	.01	0.12	.37	.04	.593	.23

Abbreviations: TST, total sleep time; WASO, wake after sleep onset.
** Indicates $p < .01$.
* Indicates $p < .05$.

4. Discussion

A first aim of the current study evaluated whether objectively-measured sleep is disrupted in UHR youth compared to HC, and if present, how sleep deficits relate to symptom severity in UHR adolescents. Results indicated that UHR adolescents displayed reduced efficiency, disrupted continuity, and increased movements during sleep compared to HC, and these sleep behaviors were significantly associated with increased positive symptoms at baseline. In addition, controlling for baseline psychosis symptoms, actigraph-measured sleep disturbance at intake (reduced duration and efficiency, increased WASO) was predictive of worsened positive symptoms at a 12-month follow-up, suggesting that UHR youth also experiencing problematic sleep may be vulnerable to increased illness severity and at-risk for conversion to psychosis. These results support the hypothesis that sleep disturbance may play an important role in the pathogenesis of schizophrenia. Additionally, results highlight the potential utility of targeting specific sleep difficulties (i.e., increased WASO, decreased efficiency) in aiding early identification, prevention, and intervention with UHR youth.

A second aim assessed the utility of an inexpensive, objective sleep measure (actigraphy) with UHR adolescents and evaluated the extent to which it provides additional information over self-reports. Comparisons between actigraphy and PSQI reports revealed that UHR adolescents are accurate reporters of duration and fairly good reporters of efficiency, but poor reporters of continuity, a domain commonly disrupted in UHR youth. HC youth were similarly accurate reporters of duration, but not efficiency or continuity; notably, the absence of a correlation between PSQI and actigraphically-measured efficiency in HC may be attributable to low variability of efficiency disruptions in this group. Secondly, several actigraph-measured sleep indices were predictive of worsened symptoms over time; indeed, one actigraph variable (efficiency) was predictive of increased symptoms while the PSQI equivalent was not. Overall, these findings suggest that actigraphy may reveal sleep difficulties not subjectively observed by adolescents. Additionally, it appears uniquely sensitive to determining which youth may be displaying specific sleep problems (reduced efficiency) that predict poorer outcomes over time. Consequently, actigraphy may represent a useful adjunct measurement of sleep functioning for use in research and clinical settings.

In a previous review (Lunsford-Avery and Mittal, 2013), we postulated a developmental diathesis-stress model in which disturbed sleep reflects an underlying psychosis vulnerability, which is aggravated during adolescence due to biological/psychological/social stressors and neuromaturational factors. In turn, sleep problems may drive psychosis onset through contributions to increased stress (e.g., cortisol response; Buckley and Schatzberg, 2005), cognitive problems (e.g., memory consolidation; Kopasz et al., 2010), and neural development abnormalities (e.g., thalamus; Lunsford-Avery et al., 2013). The current findings that sleep disturbance is present prior to onset and predicts worsened symptoms over time support this model and suggest a role of insufficient sleep in schizophrenia etiology. However, longitudinal research utilizing neuroimaging, polysomnography, and actigraphy is necessary to clarify the contribution of sleep disturbance to conversion to psychosis. To be optimally informative, these studies should investigate the potential mechanisms by which sleep dysfunction may drive onset of psychosis (e.g., changes in cortisol response, neurodevelopmental abnormalities in brain structure and function such as the thalamus, cognitive deficits such as memory consolidation).

Although it is not presently clear if sleep disturbances represent a biomarker or are directly involved in the pathogenesis of psychosis, the present findings provide preliminary support for the notion that prevention and intervention protocols supporting optimal sleep health may have the potential to not only alleviate current symptoms, but

also affect the course of illness in UHR adolescents. Cognitive Behavioral Therapy — Insomnia (CBT-I) targets the specific deficits observed in UHR youth (e.g., disrupted continuity, efficiency) and is efficacious with adolescent samples (Gradisar et al., 2011). Future studies should examine whether incorporation of CBT-I into UHR treatments is effective in reducing problematic sleep and psychosis symptoms in affected youth.

This study should be considered in the context of limitations. First, actigraphy does not measure sleep physiology. REM sleep and NREM sleep are disrupted in schizophrenia (Monti and Monti, 2005; Benson, 2008; Cohrs, 2008) and may be impaired in at-risk youth (Keshavan et al., 2004; Castro et al., 2012); thus, in-home polysomnographic recordings represent a potential future strategy for evaluating sleep functioning in UHR youth (e.g., Marcus et al., 2014). In addition, prolonged sleep latency is a common finding in the schizophrenia literature (Cohrs, 2008), but was not examined in the current study. Future studies should investigate this important sleep parameter in UHR youth as well. Second, our longitudinal data were collected at only two time points, and due to the small number of conversions within this short window (N = 2 at T2), the current study focused on the relationships between sleep disturbance and symptom course rather than sleep problems and conversion. As between 10 and 35% of UHR adolescents subsequently develop psychosis (Cannon et al., 2008), the assessment of risk factors for conversion remains a research priority. Although the investigation of the relationship between sleep and symptom course represents an important preliminary step in this effort, future studies utilizing larger sample sizes, multiple time points, and following UHR past the typical window for conversion will be better powered to investigate this transitional period and are essential for clarifying the role of sleep in the etiology and pathophysiology of schizophrenia.

Third, the current study utilized a self-report measure of depression as a covariate in our analyses. Although the BDI-II is a commonly utilized assessment of depression with established validity and reliability (Beck et al., 1996), an assessment using a clinician-rated scale (e.g., HAM-D; Hedlund and Vieweg, 1979) may yield a fuller picture of depression in UHR youth and future studies would benefit from inclusion of this measure. Finally, evidence suggests that sleep disturbances may represent symptom *states* contributing to daily variations in psychosis symptoms among individuals with schizophrenia (Waters et al., 2011) as well as *traits* potentially contributing to vulnerability in youth at-risk for conversion to psychosis (Lunsford-Avery and Mittal, 2013). This study did not examine the possible interacting and/or independent mechanisms by which specific sleep disturbances contribute to the course of schizophrenia as state-related versus trait-related processes. Future investigations should examine this important question.

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Contributors

Drs. Lunsford-Avery, Mittal, and LeBourgeois conceptualized the study. Dr. Lunsford-Avery conducted the analyses and drafted the initial manuscript. Dr. Mittal obtained funding, helped to conduct the analyses, and aided in drafting the manuscript. Dr. LeBourgeois contributed to the design of the study and helped with the interpretation of results and manuscript drafting. Ms. Gupta helped to collect and interpret the data and draft the manuscript.

Conflict of interest

There are no conflicts of interest to report.

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