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Self-reported sleep disturbances associated with procedural learning impairment in adolescents at ultra-high risk for psychosis

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ABSTRACT

Sleep disturbance contributes to impaired procedural learning in schizophrenia, yet little is known about this relationship prior to psychosis onset. Adolescents at ultra high-risk (UHR; N = 62) for psychosis completed the Pittsburgh Sleep Quality Index (PSQI) and a procedural learning task (Pursuit Rotor). Increased self-reported problems with sleep latency, efficiency, and quality were associated with impaired procedural learning rate. Further, within-sample comparisons revealed that UHR youth reporting better sleep displayed a steeper learning curve than those with poorer sleep. Sleep disturbances appear to contribute to cognitive/motor deficits in the UHR period and may play a role in psychosis etiology.

1. Introduction

Cognitive and motor deficits are core features of schizophrenia and significant contributors to functional impairment (Bora et al., 2010; Lepage et al., 2014). Moreover, reduced cognitive and motor function occurs prior to psychosis onset, suggesting potential vulnerability markers (Bora et al., 2014; Dean et al., 2014; Sommer et al., 2016). Clarifying the nature of specific neurocognitive deficits among youth at ultra high-risk (UHR) for psychosis is essential for establishing early identification and prevention/intervention strategies (Bora et al., 2014).

Procedural learning (i.e., gradual skill acquisition through practice; Censor et al., 2012), employs cognitive and movement capabilities and has long been of interest in schizophrenia patients (Huston and Shakow, 1949), who struggle to complete daily routines (Adini et al., 2015). Recent investigations suggest a nuanced picture of procedural learning in this population. Specifically, the degree of impairment depends on individual characteristics (e.g., intelligence; Gomar et al., 2011) and task demands (Siegert et al., 2008). Consistent with broader memory deficits across the psychosis continuum (Bora et al., 2014), procedural learning deficits are also observed in non-clinical psychosis (Mittal et al., 2012) and high risk (Dean et al., 2014) samples. Procedural learning deficits may characterize at least a subset of schizophrenia and at-risk groups; however, biological mechanisms contributing to within-group heterogeneity are unclear.

Sleep is disrupted in many, but not all, individuals with schizophrenia (Cohrs, 2008) and normatively is believed to impact procedural learning (Ackermann and Rasch, 2014; Diekelmann and Born, 2010). Sleep disturbances are also observed in at-risk youth (Castro et al., 2013; Castro et al., 2015; Lunsford-Avery et al., 2015; Lunsford-Avery and Mittal, 2013; Lunsford-Avery et al., 2013; Zanini et al., 2013; Zanini et al., 2015). Normative procedural learning is linked to a distributed series of circuits involving the striatum and cerebellum (Doyon et al., 2003; Hikosaka et al., 1999). Studies indicating structural and functional frontal-striatal and frontal-cerebellar circuit abnormalities may also impact procedural learning in the psychosis spectrum (Dean et al., 2014; Kumari et al., 2002). Because these circuits include key structures that have been implicated in normative and pathological sleep (i.e., thalamus; Espana and Scammell, 2011; Lunsford-Avery et al., 2013), there may be a physiological link between sleep and learning in psychosis. Indeed, sleep abnormalities (e.g., slow-wave sleep, sleep spindles) interfere with procedural learning in schizophrenia, suggesting thalamocortical network dysfunction (Goder et al., 2006; Manoach and Stickgold, 2009; Wamsley et al., 2012).

No studies to date have examined the relationship between sleep disturbances and procedural learning in UHR youth. The current study extends our prior work, which revealed procedural learning (Dean et al., 2014) and sleep (Lunsford-Avery et al., 2013) deficits among UHR adolescents, and investigates associations between self-reported

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sleep disturbances and Pursuit Rotor (PR) task performance, a gold standard measure of procedural learning, in a sample of UHR youth (Raz et al., 2000). We hypothesized that greater sleep disturbances would correlate with impaired procedural learning rate. We also examined how procedural learning trajectories differ among UHR youth reporting greater versus fewer sleep problems.

2. Method

2.1. Participants

Sixty-two UHR adolescents (aged 13–22 years) were recruited via media advertisements and community referrals. See Table 1 for demographic information. Inclusion criteria included moderate levels of attenuated positive symptoms and/or a decline in global functioning over the last year accompanied by schizotypal personality disorder and/or a family history of psychosis (Miller et al., 1999). Exclusion criteria included Axis I psychotic disorder, tic disorder, head injury/neurological disorder, intellectual disability, or substance dependence. The protocol and informed consent procedures were approved by the Institutional Review Board.

2.2. Clinical/intellectual assessment

UHR syndromes were diagnosed using the Structured Interview for Prodromal Symptoms (SIPS; McGlashan et al., 2001; Miller et al., 2003; Rosen et al., 2002). The Structured Clinical Interview for DSM-IV (SCID; First et al., 1995) ruled out psychotic disorders. The SCID is reliable in adolescent populations (Howes et al., 2009; Martin et al., 2000). The Global Assessment of Functioning (GAF) determined current level of psychosocial functioning (Jones et al., 1995). Interrater reliability (kappa) in the current study exceeded 0.80.

General intelligence (IQ) was assessed using the Word Reading subtest of the Wide Range Achievement Test, 4th edition (WRAT-4), a well-validated measure of broad learning ability for adolescents (Wilkinson et al., 2006). Standard scores normed for age were calculated based on the total number of letters (max = 15) and words (max = 55) read accurately.

2.3. Self-reported sleep disturbance

The 19-item Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) assessed sleep latency, efficiency, quality, duration, and disturbances/continuity over the week prior to PR administration. PSQI total scores range from 0 to 21 (sub-domains range 0–3). Higher scores reflect greater impairment. The PSQI is a reliable, valid measure (Buysse et al., 1989) used widely with adolescents (Jones et al., 2006; Kaneita et al., 2009). In addition, specific PSQI indices, including sleep duration and efficiency, have been shown to correlate with actigraph measures assessing the same domains among UHR youth, supporting the validity of using the PSQI with this population (Lunsford-Avery et al., 2015).

2.4. Procedural learning

Procedural learning was assessed using a computerized PR task (Life Science Associates, New York, NY) previously employed with schizophrenia and young adult populations (Gomar et al., 2011; Mittal et al., 2012). Participants completed 4 blocks (3 trials each) with 45-min rest periods after each block. In each trial, participants used a computer mouse to follow a moving target around a rectangular track for 20-s (5-s intervals between trials). Initial proficiency level was calculated during practice trials using a widely-used titration strategy (Gomar et al., 2011) and target stimulus speed was adjusted to ensure each participant met a criterion of 20–25% time on target. Once proficiency was established, target speed was kept constant across testing blocks. Procedural learning rate was calculated by subtracting the mean percent time on target for Block 1 from the mean percent time on target for Block 4.

2.5. Statistical approach

Using SAS software (SAS Institute, Inc., Cary, NC) and two-tailed tests, Pearson correlations controlling for age, gender, and IQ examined relationships between PSQI total and subdomain scores and procedural learning rate. Age, gender, and IQ were selected as covariates given their associations with sleep and/or procedural learning (Colrain and Baker, 2011; Gomar et al., 2011; Zhang et al., 2016).

To assess within-group differences in procedural learning trajectories, the sample was divided into two groups based on the median PSQI total score of the sample: "better sleepers" (PSQI ≤ 8, n = 36) and "poorer sleepers" (PSQI > 8, n = 23). Three participants were dropped from group analyses due to missing data (i.e., a missed PSQI item preventing calculation of a total score). This median-split procedure is consistent with previous studies using the PSQI (e.g., Yang et al., 2003). Group differences in demographic variables were assessed using independent *t*-test and chi-square analyses.

Linear regressions adjusted for age and sex investigated differences in symptom severity, overall cognitive ability, and psychosocial functioning between better sleepers and poorer sleepers. Linear regressions controlling for age, gender, and IQ also examined group differences in procedural learning rate, initial mean percent time on target (Block 1), and final mean percent time on target (Block 4) among better and poorer sleepers.

Table 1
Characteristics of the full sample, better sleepers, and poorer sleepers.

Variable	Full sample (n = 62)	Better sleepers (n = 36)	Poorer sleepers (n = 23)	*F*	*p*
Mean (SD)					
Age, in years	18.93 (1.67)	19.08 (1.59)	18.83 (1.90)	0.31	0.58
Parent education, in years	15.49 (3.05)	15.42 (3.42)	15.43 (2.69)	0.00	0.98
WRAT-4 score	109.08 (14.53)	112.30 (14.03)	104.10 (14.08)	4.55	0.04
SIPS-positive	11.72 (4.97)	12.14 (4.54)	11.61 (4.83)	0.13	0.72
SIPS-negative	9.35 (6.92)	8.33 (6.34)	10.91 (6.88)	2.34	0.13
GAF	62.33 (13.61)	62.03 (12.55)	63.95 (13.18)	0.31	0.58
PSQI total score	8.12 (3.20)	6.03 (1.75)	11.39 (1.95)	102.70	<0.0001
PR learning rate index	8.29 (6.16)	10.90 (5.29)	4.75 (6.00)	23.99	<0.0001
PR time on target, Block 1	30.77 (8.94)	31.06 (8.93)	30.02 (9.18)	0.01	0.91
PR time on target, Block 4	39.32 (9.29)	41.96 (9.62)	34.66 (6.78)	7.50	<0.01
Number (%)				X^2	
Gender, male	37 (60)	21 (58)	14 (61)	0.04	0.85
Anti-psychotic use	7 (11)	5 (14)	1 (4)	1.40	0.24

Abbreviations: SIPS, Structured Interview for Prodromal Symptoms (total symptoms); WRAT-4, Wide Range Achievement Test, 4th edition; GAF, Global Assessment of Functioning; PSQI, Pittsburgh Sleep Quality Index; PR, Pursuit Rotor. Note: Group differences in clinical symptoms (WRAT, SIPS, GAF) and PSQI have been adjusted for age and sex. Group differences in PR (learning rate, time on target) have been adjusted for age, sex, and WRAT score as described in the text.

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