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Sleep disturbance and sleep-related impairment in psychotic disorders are related to both positive and negative symptoms

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ABSTRACT

A large literature indicates that sleep disturbances are associated with paranoia and other positive symptoms in psychotic disorders. However, few studies have examined the potential association between sleep disturbances and negative symptoms and the results have been inconsistent. The current study examined the hypothesis that sleep problems would be associated with more severe positive and negative symptoms in a transdiagnostic sample of individuals with psychosis (N = 90). Further, we examined whether sleep would be related to negative symptoms above and beyond the contribution of paranoia, other positive symptoms, and depression-anxiety. Results replicated prior research in finding that both sleep disturbance and sleep-related impairment were related to more severe paranoia, other positive symptoms and depression-anxiety. Consistent with our hypothesis, more severe sleep disturbance and sleep-related impairment were related to greater negative symptoms; this was evident across both motivation-pleasure deficits and diminished expression. Sleep variables remained significantly related to motivation-pleasure deficits even after controlling for other non-negative symptoms. These results indicate the broad symptom impact of sleep disturbances and may suggest a novel treatment target to improve negative symptoms.

1. Introduction

Sleep disturbances, such as insomnia, have been found to be related to a range of mental health problems (Benca et al., 1992; Klingaman et al., 2017); consequently, researchers have proposed that sleep disturbance is a transdiagnostic factor contributing to symptomatology and impairment (Harvey, 2008; Harvey et al., 2011). An accumulation of recent research indicates that sleep may be especially important in psychosis. Sleep disturbances and sleep disorders occur frequently in psychotic disorders (e.g., schizophrenia; Klingaman et al., 2015; Kaskie et al., 2017; Wee et al., 2019) and are evident early in the course of psychosis (Davies et al., 2017; Reeve et al., 2019).

Sleep disturbances have been found to be associated with more severe positive symptoms in psychotic disorders as well as in those at clinical high risk (CHR) for developing psychosis (Ka-Fai et al., 2018; Lunsford-Avery et al., 2015; Mulligan et al., 2016; Poe et al., 2017; Reeve et al., 2019; Xiang et al., 2009; see review by Davies et al., 2017). Reeve et al. (2015) reviewed 66 studies and concluded that there was evidence for the association between positive symptoms and sleep disturbances, especially between insomnia and paranoia. Longitudinal studies suggest that sleep disturbances may contribute to the development of paranoia and its persistence (e.g., Freeman et al., 2011; Sheaves et al., 2016). Consistent with longitudinal studies, research using ecological momentary assessment (EMA) has found that sleep disturbances prospectively predict next-day paranoia and this may be mediated by the impact of sleep disturbances on negative affect (e.g., Kasanova et al., 2019; Mulligan et al., 2016). The relationship between sleep and paranoia extends beyond clinical populations and has been found in non-clinical community samples using a variety of methods (Andorko et al., 2017; Freeman et al., 2011; Hennig and Lincoln, 2018; Koyanagi and Stickle, 2015; Oh et al., 2016; Reeve et al., 2018; Rehman et al., 2018; Sheaves et al., 2016). These later findings are consistent with the view that paranoia and other positive symptoms are dimensional with manifestations varying in severity across community and clinical populations (e.g., Ahmed et al., 2012; Elahi et al., 2017; Taylor et al., 2016).

Despite the accumulating evidence about the role of sleep disturbances in paranoia and other positive symptoms, there has been limited research regarding how sleep may relate to negative symptoms. Negative symptoms (Blanchard et al., 2011; Kring et al., 2013) involve

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diminished motivation and pleasure (anhedonia, amotivation, avolition-apathy) as well as diminished expressivity (flat or blunted affect, alogia). Given that negative symptoms are largely independent of positive symptoms (Blanchard et al., 2011) and that negative symptoms are related to significant functional impairment (Blanchard et al., 2017), it would be highly informative to determine if sleep disturbances have a role in exacerbating negative symptoms. If sleep disturbances were associated with negative symptoms, this finding would improve our understanding of the broad impact of sleep disturbances and potentially identify a treatment target to improve negative symptoms.

There are several lines of evidence to suggest that sleep disturbances may be related to the social, emotional, motivational, and expressive deficits that characterize negative symptoms. Sleep is related to a variety of social processes and interpersonal behavior (see reviews by Beattie et al., 2015 and Gordon et al., 2017). Sleep disturbances may impact social relations through decreases in positive affect, reduced empathy, and poorer emotion recognition (Acheson et al., 2007; Killgore et al., 2008, 2017; van der Helm et al., 2010). Sleep loss in healthy individuals has been shown to lead directly to social withdrawal (Simon and Walker, 2018). In the expressivity domain, sleep deprivation in healthy individuals has been shown to lead to diminished facial expressivity in response to evocative stimuli (Minkel et al., 2011) and diminished speech output (McGlinchey et al., 2011). More broadly, sleep problems may be related to motivational aspects of negative symptoms as sleep-related performance impairments may lead to diminished motivation and effort (Massar et al., 2019a; Massar et al., 2019b).

Only a limited number of studies have examined the potential association between sleep problems and negative symptoms and the results have been inconsistent. Several studies of individuals with schizophrenia have failed to find an association between global measures of negative symptoms and sleep quality (Ristner et al., 2004; Xiang et al., 2009) or with other sleep diary variables or actigraphy (Ka-Fai et al., 2018). On the other hand, studies with CHR individuals have yielded findings indicating that sleep disturbance may be related to more severe negative symptoms. Lunsford-Avery & Mittal (2013) found that in CHR individuals, greater negative symptoms were associated with increased sleep latency, poor sleep quality, and shorter sleep duration. Similarly, Poe et al. (2017) found that within a CHR group greater sleep disturbance was associated with greater negative symptoms. However, Lunsford-Avery et al. (2015) did not find an association between negative symptoms and actigraphy-assessed sleep dysfunction in CHR individuals.

Methodological issues may contribute to the prior inconsistent findings. When negative symptoms have been assessed, studies have relied on potentially problematic clinical assessments (see Blanchard et al., 2017) including the use of a single global score that does not reflect the two major facets of negative symptoms (Blanchard et al., 2017; Kring et al., 2013). This is an important limitation as advances in negative symptom assessment indicate that motivation-pleasure and expressive negative symptoms may have differential correlates with features of the illness such as functioning (Blanchard et al., 2017; Kring et al., 2013). Another concern is that prior studies have not consistently utilized validated measures of sleep disturbance (e.g., Xiang et al., 2009 adopted three yes-no items to classify good and poor sleepers).

The current study examined the hypothesis that sleep problems would be associated with more severe positive and negative symptoms in individuals with a range of psychotic symptoms. Further, we examined whether sleep would be related to negative symptoms above and beyond the contribution of paranoia, other positive symptoms, and depression-anxiety. Our assessments included validated measures of sleep disturbance and sleep-related impairment as well as well-validated measures of negative and positive symptomatology. Guided by the NIMH research domain criteria (RDoC) framework (Cuthbert, 2014; Insel, 2014; Insel et al., 2010) we adopted a symptom-oriented dimensional approach to examine how sleep disturbance and sleep-related impairment are related to symptomatology within a transdiagnostic sample of individuals with psychosis (N = 90). This sample included individuals with a variety of psychotic disorders (N = 75) along with healthy non-clinical participants (N = 15) to ensure sampling across the full range of symptoms and functioning.

2. Methods

2.1. Participants

Participants were enrolled in a larger grant-funded project examining social affiliative deficits in psychosis from an RDoC perspective. The mixed sample (N = 90) included clinical (n = 75) and non-clinical community (n = 15) participants. Participants diagnosed with a psychotic disorder (e.g., schizophrenia/schizoaffective disorder, delusional disorder, major depression with psychosis) were recruited from outpatient community mental health clinics in the Baltimore and Washington, D.C. metro areas. Inclusion criteria for clinical participants included (1) aged 18–60, (2) lifetime history of a psychotic disorder, (3) clinical stability (i.e., no inpatient hospitalizations for 3 months before enrollment, no changes in psychoactive medication in the 4 weeks before enrollment) as indicated by approval of clinician and medical record review, and (4) fluent in English. Community participants were recruited via online advertisements, and inclusion criteria included (1) aged 18–60, (2) no current clinical disorder or psychiatric medications, (3) no lifetime history of a psychotic or mood disorder, (4) no avoidant, paranoid, schizotypal or schizoid personality disorder, and (5) fluent in English. Exclusion criteria for all participants included (1) current substance use disorder, (2) neurological conditions (e.g., epilepsy, multiple sclerosis), (3) evidence of mental retardation as determined by medical history or cognitive testing, (4) any history of serious head injury, (5) any MRI contraindications (e.g., MR unsafe metal in body, weight that exceeds limitations of MRI machine), and (6) unwillingness to be videotaped during study participation (Table 1).

Table 1
Sample characteristics.

	Mean (*SD*)or *n* (percent)
Age (years)	44.44 (11.66)
Sex	
Male	55 (61.1%)
Female	35 (38.9%)
Race	
African-American	66 (73.3%)
White	19 (21.1%)
Asian	2 (2.2%)
More than one race	3 (3.3%)
Ethnicity	
Non-hispanic or latino	82 (91.1%)
Hispanic or latino	7 (7.8%)
Unknown	1 (1.1%)
Marital status	
Married	6 (6.7%)
Divorced/separated	13 (14.4%)
Never married/single	71 (78.9%)
Education (years)	12.78 (2.32)
Has a paying job	
Yes	29 (32.2%)
No	61 (67.8%)
Diagnosis	
Schizophrenia	34 (37.8%)
Schizoaffective bipolar type	13 (14.4%)
Schizoaffective depressive type	13 (14.4%)
Delusional disorder	1 (1.1%)
BP I w/ psychotic features	8 (8.9%)
MDD w/ psychotic features	6 (6.7%)
No diagnosis (healthy control)	15 (16.7%)

Note: BP, Bipolar; MDD, Major depressive disorder.

2.2. Measures

2.2.1. Diagnostic and symptom measures

Diagnoses were determined with the Structured Clinical Interview for DSM-5 (SCID-5; First et al., 2015). The Clinical Assessment Interview for Negative Symptoms (CAINS; Kring et al., 2013) is a 13-item interview measure of negative symptoms that includes two subscales: motivation and pleasure (9 items) and expression (4 items). The motivation and pleasure subscale measures experiential negative symptoms such as amotivation, asociality, and anhedonia, whereas the expression subscale measures affective flattening and alogia (Kring et al., 2013). The CAINS has been demonstrated to have high inter-rater agreement and good convergent and discriminant validity (Blanchard et al., 2017; Kring et al., 2013).

The Expanded Brief Psychiatric Rating Scale (BPRS; Ventura et al., 1993) is a 24-item interview measure designed to assess current clinical symptomatology as experienced over the previous week. Based on the factor work of (Kopelowicz et al., 2008), we computed three BPRS symptom scores: positive symptoms, depression-anxiety, and agitation. Of note, we excluded the BPRS "suspiciousness" item from the positive symptom score as paranoia was more fully assessed with an independent self-report measure (see below) thus yielding a non-paranoia positive symptom score.

The Green Paranoid Thought Scales (GPTS; Green et al., 2008) is a 32-item self-report measure of paranoid thinking over the past month. The GPTS assesses ideas of reference and ideas of persecution. Higher scores indicate greater levels of paranoid thinking. The GPTS has been recently been described as the most psychometrically sound and valid self-report measure of paranoia (Statham et al., 2019). In the current sample, the GPTS was highly correlated with the clinician-rated item of suspiciousness from the BPRS ($r = 0.63$, $p = 0.001$), supporting the validity of the self-report assessment of paranoia.

2.2.2. Assessment of sleep

Sleep assessments utilized the National Institutes of Health Patient-Reported Outcomes Measurement Information System (PROMIS™) Sleep Disturbance and Sleep-Related Impairment short form scales (Yu et al., 2012). The Sleep Disturbance scale includes items such as "I had difficulty falling asleep" and "I had trouble staying asleep." The Sleep-Related Impairment scale includes items such as "I had a hard time concentrating because of poor sleep" and "I had a hard time getting things done because I was sleepy." These scales were developed using rigorous item-response theory methods as well as clinical judgement from content experts. The PROMIS Sleep Disturbance scale has demonstrated high convergent validity with the Pittsburgh Sleep Quality Index and both the PROMIS Sleep Disturbance and Sleep-Related Impairment scales are capable of differentiating healthy individuals from those with clinically diagnosed sleep disorders (Yu et al., 2012). The PROMIS sleep scales have also been shown to be sensitive to treatment effects of positive airway pressure therapy (Donovan et al., 2017). Although not intended to measure symptoms of specific sleep disorders, the PROMIS scales do tap sleep quality and sleep dissatisfaction and thus are useful in assessing global severity of insomnia (Yu et al., 2012).

2.3. Procedures

Study procedures were approved by the University of Maryland School of Medicine Institutional Review Board. Participants completed a standardized informed consent process with trained recruiters and signed an informed consent document. A brief questionnaire was administered to verify that participants were competent to provide consent and understood the consent document. Study procedures were implemented by trained study staff.

Table 2
Descriptive statistics for sleep and symptom assessments ($N = 90$).

	M (*SD*)	Range
Sleep disturbance	17.74 (7.73)	8.00–40.00
Sleep-related impairment	17.02 (7.21)	8.00–40.00
GPTS-paranoia	52.64 (26.17)	32.00–136.00
BPRS-positive symptoms	10.46 (3.95)	7.00–25.00
BPRS-depression/anxiety	7.66 (3.81)	4.00–19.00
BPRS-agitation	7.61 (2.11)	6.00–15.00
CAINS-motivation & pleasure	11.24 (6.51)	1.00–34.00
CAINS-expression	5.30 (3.44)	0.00–14.00

Note: GPTS, Green paranoid thoughts scale; BPRS, Brief psychiatric rating scale; CAINS, Clinical assessment interview for negative symptoms. To avoid redundancy with the GPTS, the BPRS-Positive Symptoms score excludes the "Suspiciousness" item.

2.4. Data analysis

Descriptive statistics for the sleep and symptom ratings are presented in Table 2. Correlational analyses were conducted to assess the relation between sleep and symptom measures. To examine if relations between sleep problems, positive symptoms and negative symptoms were independent of other symptoms, partial correlations were conducted.

3. Results

Correlations between sleep variables and symptoms are presented in Table 3. Replicating prior research, greater sleep disturbance and sleep-related impairment were related to more severe symptom ratings of paranoia, other positive symptoms, and depression-anxiety. Agitation was not related to sleep disturbance but was correlated with greater sleep-related impairment. Finally, consistent with our hypotheses, greater sleep disturbance and sleep-related impairment were associated with both more severe motivation and pleasure negative symptoms and more severe expressive negative symptoms.

Given that both paranoia and negative symptoms were associated with sleep problems, we examined whether the magnitude of these associations were statistically different. Comparing correlations (Steiger, 1980), the correlation between sleep disturbance and paranoia was no different from the correlations between sleep disturbance and the negative symptoms of motivation and pleasure ($z = 0.596$, $p = 0.551$) or expressivity ($z = 0.937$, $p = 0.348$). Similarly, the correlation between sleep impairment and paranoia was similar in magnitude to that obtained between sleep-related impairment and motivation and pleasure ($z = 0.867$, $p = 0.386$) and expressivity ($z = 0.779$, $p = 0.436$). These results indicate that the strength of the

Table 3
Symptom correlates of sleep disturbance and sleep-related impairment ($N = 90$).

	Sleep disturbance	Sleep-related impairment
GPTS-paranoia	0.39***	0.35**
BPRS-positive symptoms	0.23*	0.33**
BPRS-depression/anxiety	0.48***	0.40***
BPRS-agitation	0.09	0.24*
CAINS-motivation & pleasure	0.31**	0.23*
CAINS-expression	0.26*	0.24*

Note: GPTS, Green paranoid thoughts scale; BPRS, Brief psychiatric rating scale; CAINS, Clinical assessment interview for negative symptoms. To avoid redundancy with the GPTS, the BPRS-Positive Symptoms score excludes the "Suspiciousness" item.

* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

association between sleep problems and negative symptoms is comparable to the association between sleep problems and paranoia.

We sought to determine the unique associations between sleep problems and paranoia and other positive symptoms beyond mood symptoms. After controlling for depression-anxiety, results indicated that sleep disturbance was no longer significantly associated with either paranoia ($pr = 0.206$, $p = 0.053$) or other positive symptoms ($pr = 0.133$, $p = 0.215$). Controlling for depression-anxiety, sleep-related impairment was no longer correlated with paranoia ($r = 0.184$, $p = 0.084$) but retained an association with other positive symptoms ($r = 0.215$, $p = 0.043$). These results suggest that the association between sleep disturbance and symptoms of paranoia and other positive symptoms may be, in part, accounted for by depression-anxiety.

To examine if relations between sleep problems and negative symptoms were independent of other symptoms, partial correlations were conducted controlling for paranoia, other positive symptoms and depression-anxiety. After controlling for these other symptoms, sleep disturbance remained correlated with the negative symptoms of motivation and pleasure ($pr = 0.27, p = 0.011$) and diminished expressivity ($pr = -0.23, p = 0.032$). However, sleep-related impairment was no longer associated with motivation and pleasure ($pr = 0.16, p = 0.138$) or diminished expressivity ($r = 0.19$, $p = 0.077$).

4. Discussion

This study examined the hypothesis that sleep disturbance and sleep-related impairment are associated with more severe positive and negative symptoms in a transdiagnostic sample. Replicating prior research (Freeman et al., 2009; Lunsford-Avery et al., 2015; Mulligan et al., 2016; Poe et al., 2017; Xiang et al., 2009), we found that sleep disturbance and sleep-related impairment were associated with elevations in paranoia and other positive symptoms. Symptom ratings of depression-anxiety were robustly related to sleep variables. After controlling for depression and anxiety, the relation between sleep-related impairment and other positive symptoms persisted, but sleep disturbance was no longer associated with paranoia. This later result suggests that the relation between paranoia, sleep disturbance and sleep-related impairments is at least partially accounted for by depression and anxiety. This interpretation is consistent with prior findings indicating that the association between paranoia and insomnia is in part mediated by negative affect (Freeman et al., 2009, 2010; Kasanova et al., 2019; Mulligan et al., 2016).

Consistent with our hypothesis, more severe sleep disturbance and sleep-related impairment were related to greater negative symptoms and this was evident across both motivation-pleasure deficits and diminished expression. To put this in context, the associations between sleep problems and negative symptoms were similar to the strength of association between sleep problems and paranoia. The relation between sleep disturbance (but not sleep-related impairment) and negative symptoms remained significant even after controlling for depression-anxiety, paranoia and other positive symptoms. This finding indicates that the relationship between sleep disturbance and more severe negative symptoms is not merely secondary to the impact of other clinical symptoms.

This is the first demonstration that we are aware of showing that sleep disturbance and sleep-related impairment are associated with both positive and negative symptoms in a transdiagnostic sample of individuals with psychotic disorders. The current findings suggest directions for future research including an examination of mechanisms that might underlie the connection between sleep problems and negative symptoms. Such mechanisms may include the direct impact of sleep on social processes (Beattie et al., 2015; Gordon et al., 2017) including sleep insufficiency leading to social withdrawal (e.g., Simon and Walker, 2018). Sleep disturbance may also contribute to diminished motivation secondary to sleep-related performance impairment (Massar et al., 2019a; Massar et al., 2019b). Finally, sleep may relate to the hedonic deficits of negative symptoms as sleep insufficiency has been shown to contribute to diminished positive affect (Talbot et al., 2010).

Beyond examining factors that may contribute to the relationship between sleep and negative symptoms, the current findings, if replicated, could suggest a novel target for clinical intervention to improve negative symptoms. Negative symptoms have been frustratingly difficult to improve using pharmacological treatments (Fusar-Poli et al., 2015) or cognitive behavioral therapy (CBT; Velthorst et al., 2015) and the benefits of social skills training, although promising, are somewhat limited (Turner et al., 2018). With regard to treating sleep disturbances, CBT for insomnia has been examined as an intervention in psychiatric disorders (e.g., Harvey et al., 2015; Taylor and Pruiksma, 2014) including as a method to improve paranoia and other positive symptoms (Freeman et al., 2015; Freeman et al., 2017). We are not aware of any study that has specifically sought to utilize CBT for insomnia to improve negative symptoms within individuals with psychotic disorders.

The current study does have several limitations that constrain interpretation of the findings. First, since this is a cross-sectional study it is unclear if sleep disturbance and related impairment give rise to negative symptoms or if negative symptoms lead to sleep problems. Longitudinal studies will be necessary to examine the temporal unfolding of sleep problems and negative symptoms. Second, although we used well-validated and psychometrically sound sleep measures these were limited to self-report scales. Future research should incorporate other objective measures such as sleep actigraphy (e.g., Mulligan et al., 2016) as well as clinical assessments of specific sleep disorders. Third, our study adopted a transdiagnostic symptom-oriented approach and we are not able to explore the potential role of different specific diagnoses. Fourth, clinical participants were receiving medications for the treatment of psychiatric disorders and we are not able to determine the possible contribution of medication side effects to the observed findings. Finally, although our study benefited from the use of a highly diverse sample with good minority representation, we were not able to explore the potential role of gender or ethnicity in our findings – an examination of these participant characteristics will be useful in future studies.

In summary, our study indicates that sleep problems are associated with both positive symptoms and negative symptoms. This finding requires replication but suggests the need to examine potential mechanisms that may connect sleep problems to negative symptoms. Further, this result suggests the potential benefit of considering treatments that target sleep disturbance as a novel approach to improve negative symptoms.

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CRediT authorship contribution statement

Jack J. Blanchard: Funding acquisition, Conceptualization, Methodology, Formal analysis, Writing - original draft, Supervision, Project administration. **Alexandra Andrea:** Investigation, Writing - review & editing, Data curation, Project administration. **Ryan D. Orth:** Investigation, Writing - review & editing, Data curation, Project administration. **Christina Savage:** Investigation, Writing - review & editing, Data curation. **Melanie E. Bennett:** Writing - review & editing, Supervision, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors have no conflicts of interest to report.

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