# CONTRIBUTIONS OF SLEEP QUALITY AND DISSOCIATION TO ATTENUATED POSITIVE PSYCHOTIC SYMPTOM SEVERITY

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## ABSTRACT

Sleep disturbances have been observed across the entire psychosis spectrum. Research has begun to focus on the clinical high risk (CHR) period for psychosis, as the presence of sleep disturbance can be examined separately from the effects of antipsychotic medication and is potentially a risk factor for later psychosis. Several studies have demonstrated a link between sleep disturbance and worsened positive symptoms in CHR individuals. However, sleep disturbance is not unique to the psychosis-spectrum and is well documented in individuals experiencing dissociation. Transdiagnostically, dissociation has been associated with poorer outcomes and reduced treatment response. Despite the established associations between these variables, their respective contributions to positive symptom severity in the CHR period has not yet been characterized. This study examined the separate and combined contributions of sleep quality and dissociation on positive symptom severity in a cross-sectional sample of individuals identified as being at CHR for psychosis. Hierarchical linear regression was conducted to examine the independent and additive influence of sleep quality and dissociation on unusual thought content, suspiciousness, and perceptual abnormalities. Finally, logistic regression was used to determine if sleep quality and dissociation increase odds of a CHR diagnosis. Analyses of indirect effects revealed a significant indirect effect of sleep disturbance on perceptual abnormalities through dissociation in the CHR group. In addition, both sleep disturbance and dissociation significantly contributed to a model predicting to perceptual abnormalities, also in the CHR group. In the total sample, both sleep quality and dissociation significantly increased the odds of a CHR diagnosis. These results suggest that dissociation plays a significant role in the sleep-attenuated positive psychotic symptom relationship in the CHR period, and as a result, could be a modifiable treatment target in these individuals.

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# CHAPTER ONE

# MANUSCRIPT IN JOURNAL ARTICLE FORM


## Abstract

Sleep disturbances have been observed across the entire psychosis spectrum. Research has begun to focus on the clinical high risk (CHR) period for psychosis, as the presence of sleep disturbance can be examined separately from the effects of antipsychotic medication and is potentially a risk factor for later psychosis. Several studies have demonstrated a link between sleep disturbance and worsened positive symptoms in CHR individuals. However, sleep disturbance is not unique to the psychosis-spectrum and is well documented in individuals experiencing dissociation. Transdiagnostically, dissociation has been associated with poorer outcomes and reduced treatment response. Despite the established associations between these variables, their respective contributions to positive symptom severity in the CHR period has not yet been characterized. This study examined the separate and combined contributions of sleep quality and dissociation on positive symptom severity in a cross-sectional sample of individuals identified as being at CHR for psychosis. Hierarchical linear regression was conducted to examine the independent and additive influence of sleep quality and dissociation on unusual thought content, suspiciousness, and perceptual abnormalities. Finally, logistic regression was used to determine if sleep quality and dissociation increase odds of a CHR diagnosis. Analyses of indirect effects revealed a significant indirect effect of sleep disturbance on perceptual abnormalities through dissociation in the CHR group. In addition, both sleep disturbance and dissociation significantly contributed to a model predicting to perceptual abnormalities, also in the CHR group. In the total sample, both sleep quality and dissociation significantly increased the odds of a CHR diagnosis. These results suggest that dissociation plays a significant role in

the sleep-attenuated positive psychotic symptom relationship in the CHR period, and as a result, could be a modifiable treatment target in these individuals.

## Introduction

### *Sleep Quality in the Psychosis-Spectrum*

Sleep disturbances have been reliably documented in schizophrenia patients, who experience decreased total sleep time, decreased sleep efficiency, increased sleep latency, and increased REM latency compared to healthy controls (Cohrs, 2008). Whereas these aspects of sleep disturbance are present in other psychiatric disorders, certain alterations appear to be more specific to psychosis, such as reduced sleep spindles (Ferrarelli et al., 2007; Manoach et al., 2016). Furthermore, these sleep deficits have been observed in antipsychotic-naïve early course schizophrenia, as well as non-psychotic first degree relatives (Manoach et al., 2014). Sleep quality disturbances often begin prior to the onset of a first psychotic episode, in individuals identified to be at clinical high risk (CHR) for psychosis, and in non-help seeking members of the general population who report subthreshold psychotic experiences, called psychotic-like experiences (PLEs) (Clarke et al., 2020). Sleep disturbances are important to consider prior to the onset of a threshold psychotic disorder because this offers the opportunity to examine them separately from the effects of antipsychotic medication, as well as their contributions to the development of a full psychotic disorder. Examining sleep quality in CHR individuals also provides the opportunity to understand how early in the development of a psychotic disorder sleep disturbance develops, and as a result, when sleep interventions might become necessary.

The CHR period is defined by clinically significant and distressing subthreshold versions of the positive psychotic symptoms experienced in schizophrenia, called attenuated positive psychotic symptoms (APPS), and these individuals are considered to be at increased risk of developing a fully psychotic disorder (McGlashan, Walsh, & Woods, 2010). CHR status has been associated with increased sleep latency, daytime sleepiness, increased wake time after sleep

onset, increased REM latency, and nighttime movements (Clarke et al., 2020). In addition to general sleep quality disturbances, CHR individuals also experience circadian rhythm disruptions, as evidenced by greater circadian rhythm fragmentation and day/night reversal compared to nonclinical controls (Castro et al., 2015; Poe et al., 2017). Finally, CHR status has also been linked to parasomnias, including nightmares (Sheaves et al., 2015). CHR individuals experience more frequent nightmares and recall dreams at a greater frequency compared to controls and nonpsychotic individuals with a first degree relative with a psychotic disorder (Michels et al., 2014). It is possible that a more specific mechanism is responsible for the relationship between parasomnias and psychosis, as studies have suggested that although sleep disturbance is ubiquitous across different types of mental illness, parasomnias are more specifically related to psychotic disorders and dissociative disorders (Sheaves et al., 2015).

Although these disturbances of sleep are a cause for concern on their own, they do not exist without consequence. Sleep disturbance has been associated with increased severity of APPS in CHR individuals, such as unusual thought content, perceptual abnormalities, and paranoid ideation (Goines et al., 2019; Reeve et al., 2019). Circadian rhythm disruptions have been associated with APPS severity and have predicted severity of APPS at one-year follow up (Lunsford-Avery et al., 2017). Whereas studies attempting to link sleep disturbances to negative symptoms in the CHR period have been mixed, negative symptoms have been associated with increased sleep latency, decreased sleep quality, and general sleep disturbance, although which negative symptoms are specifically driving this relationship has not been made clear (Lunsford-Avery et al., 2013a; Poe et al., 2017). Taken together, this prior research suggests a strong relationship between sleep disturbance and worsening of the full spectrum of psychotic

experiences, and a need to fully understand additional contributors and consequences of this relationship.

### *Sleep Quality and Dissociation*

Sleep disturbances are not unique to the psychosis-spectrum—sleep alterations occur across many psychiatric disorders and are even part of the diagnostic criteria for major depressive disorder, bipolar disorder, generalized anxiety disorder, and post-traumatic stress disorder (APA, 2013; Krystal, 2012). One category of psychiatric disorders of interest is dissociative disorders. Dissociation is characterized as a disruption in the integration or continuity of consciousness, memory, identity, emotion, perception, body representation, motor control, and behavior (APA, 2013). Although much of the focus on dissociation outside of dissociative disorders focuses on trauma-related disorders, dissociation occurs transdiagnostically, and has been associated with worsened treatment outcomes, higher rates of comorbidity, poorer functional outcomes, and greater illness severity (McKinnon et al., 2016). Sleep disruption has co-occurred with dissociation often enough that a model has been developed of dissociation as occurring within the context of a fragmented sleep-wake cycle where sleep phenomena intrude into wakefulness (van der Kloet et al., 2012). In a study of patients with dissociative identity disorder (DID), individuals with DID scored higher on measures of general sleep disturbance compared to nonclinical controls but not PTSD patients; however, higher scores on a measure of unusual sleep experiences better predicted participants belonging to the DID group than the PTSD group (van Heugten–van der Kloet et al., 2014). Polysomnography has revealed that individuals with insomnia disorder experience elevated levels of dissociative experiences, that these experiences correlate with poor sleep quality and unusual sleep experiences, but not traumatic experiences, and that longer REM periods were predictive of dissociation (Van Der Kloet et al., 2013). A

longitudinal inpatient sample of patients with varied diagnoses found that improving sleep was associated with general reduction in psychopathology, including dissociation (Van Der Kloet et al., 2012). In nonclinical general population studies, associations have been found between dissociative symptoms and insomnia, nightmare frequency, and parasomnias generally (Levin & Fireman, 2002; Van Heugten-van der Kloet et al., 2014; Van Heugten-Van Der Kloet et al., 2015). Sleep deprivation studies in healthy volunteers have observed significant increases in dissociation after one night of sleep loss (Giesbrecht et al., 2007). As a result of this body of work, some researchers have even suggested sleep normalization as a treatment target for individuals struggling with dissociation (Van Heugten-Van Der Kloet et al., 2015).

***Dissociation in the Psychosis-Spectrum***

Dissociation is commonly experienced in individuals with psychosis spectrum disorders, with studies showing that individuals with schizophrenia score higher on measures of dissociation than non-psychiatric controls (Renard et al., 2017). A study of first-episode psychosis individuals found that 36.4% of participants had clinical levels of dissociation, and 13.6% met diagnostic criteria for a lifetime dissociative disorder (Sun et al., 2019). In non-clinical samples, studies of undergraduates have found significant overlap between measures of positive and disorganized symptoms of schizotypy and dissociation (Giesbrecht et al., 2007; Pope et al., 2000). Building on this relationship, several studies have found dissociation to be a mediator of the relationship between psychological symptoms and psychosis. In patients with schizophrenia, participants endorsing hallucinations experienced more dissociative symptoms than controls and non-hallucinating clinical controls, and dissociation was found to mediate the effect of childhood trauma on hallucination-proneness (Varese, Barkus, et al., 2012). In a multiple mediation study, dissociative symptoms were the only mediator that remained

significant for the relationship between traumatic life experiences and PLEs when controlling for other forms of psychopathology (Gibson et al., 2018). The strength of this mediating role appears to differ across ethnicities, as another study found that dissociation fully mediated the effect of traumatic life events on PLEs for Black participants, partial mediation occurred for Hispanic participants, and dissociation was not a significant mediator for Asian participants (Anglin et al., 2015).

The common inter-relationship between sleep disturbance, dissociation, and psychosis has led some to believe that these experiences belong to a common domain (Koffel & Watson, 2009). Prior work from our lab has demonstrated that dissociation has a significant, indirect effect on the relationship between sleep quality and PLEs in an undergraduate sample (Creatura et al., 2022). Despite this, the ways in which dissociation and sleep disturbance contribute to APPS in CHR populations has not been well characterized. Given that individuals who are at CHR for psychosis need to express distress about their symptoms to meet criteria for an APSS diagnosis, it is even more critical to better understand within this population what could be exacerbating symptoms, and more importantly, how to improve them. Achieving better understanding of the pathways that lead to distressing APPS can lead to more comprehensive treatment plans that healthcare providers can adapt to a given patient based on their unique presentation. The current study is the first to examine the combined and independent contributions of sleep disturbance and dissociation to specific APPS within a sample of individuals meeting for CHR for psychosis, as well as how these variables together predict to the presence or absence of a CHR diagnosis.

### *Aims and Hypotheses*

*Aim 1:* **To examine the indirect effect of dissociation on the relationship between sleep quality and attenuated positive psychotic symptoms.** Sleep disturbance has been consistently

associated with APPS in CHR individuals, with the most evidence supporting the link between disrupted sleep and paranoid ideation (P2), perceptual abnormalities (P4), and unusual thought content (P1). Dissociation similarly has been associated with these domains of APPS, in both clinical and nonclinical samples. Dissociation has been linked to impaired sleep quality, has been associated with a more severe course of psychiatric illness, and has been found in the CHR period. We hypothesize that dissociative symptoms will significantly mediate the relationship between sleep quality and unusual thought content, paranoid ideation, and perceptual abnormalities rated on the Structured Interview for Psychosis Risk Syndromes (SIPS).

*Aim 2:* **To examine the additive contributions of sleep quality and dissociation to attenuated positive psychotic symptoms.** Whereas sleep disturbance has been linked consistently with subthreshold psychosis symptoms, previous research has demonstrated that there are other psychological symptoms, such as dissociation, that account for a significant portion of the relationship between the two. Therefore, we predict that dissociation will significantly predict unusual thought content, persecutory ideation, and perceptual abnormalities in CHR individuals, above sleep quality alone.

*Aim 3:* **To examine how sleep quality and dissociative symptoms influence CHR status.** Sleep disturbance and dissociative symptoms have been shown to be increased in CHR individuals compared to the general population. Because of this, we aim to explore how accurately a model containing sleep quality and dissociation predicts CHR status.

## Method

### *Participants*

A total of 767 participants were recruited from a community sample of 16 – 30-year-olds from the greater Philadelphia, Chicago, Irvine, and Baltimore areas as a part of a multi-site

psychosis-risk screening study entitled “The Multi-site Assessment of Psychosis-risk (MAP) study” (Ellman, Schiffman, & Mittal, 2020). Of these participants, 140 met criteria for CHR status. Participants completed an initial battery of questionnaires via Qualtrics (n=5,944), and a subset of these individuals (n=767) returned to complete clinical interviews based on cutoff criteria for two psychosis risk questionnaires. All individuals meeting for questionnaire high risk (participants endorsing 8 items and/or higher on the Prodromal Questionnaire, or 2 items or higher on the PRIME screen) were invited to return for additional assessments, including clinical interviews to determine CHR status. Community controls were randomly selected below cut-point on both questionnaires (Ellman, Schiffman, & Mittal, 2020).

***Inclusion Criteria for Current Analyses***

The current study included only the participants who were invited for clinical interviews (n=767) and for Aims 1 and 2, participants had to meet criteria for a CHR diagnosis assessed by the Structured Interview for Psychosis Risk Syndromes (SIPS), such as attenuated positive symptom syndrome, psychosis-risk syndrome, genetic risk and functional decline syndrome, and/or DSM-5 attenuated psychosis syndrome (n=140).

***Exclusion Criteria for the Current Study***

Because the focus of this study was on the CHR period, individuals were excluded from analysis based on the presence of a psychotic disorder. The presence of a psychotic disorder was determined by any diagnosis of a psychotic disorder on the Structured Clinical Interview for DSM-5.

***Recruitment and Informed Consent***

For all four catchment areas, participants were recruited through flyers placed in public spaces, such as coffee shops, community centers, and other public spaces where flyers are

allowed. Ads were placed on a variety of websites, such as Craigslist and Facebook. Interested participants were provided with a link to complete the initial informed consent and online surveys. For participants under 18, the link was sent to the parents or legal guardian of the participant to provide consent, and then the participant completed the online surveys. Participants received a gift card for completion of this part of the study. Following this study portion, individuals were selected to participate in the interview portion of the study, for which they completed a second informed consent process and received a monetary payment or gift card for this portion of the study.

### *Measures*

**Self-Report.** PRIME screen: The PRIME screen (Miller et al., 2004) is a self-report measure that was designed to be similar in both content and structure to the Structured Interview for Psychosis-Risk Syndromes. The recommended screening threshold (≥2 endorsements of "somewhat" or "definitely agree,") has yielded sensitivity of .90 and specificity of 1.00 in identifying a possible CHR diagnosis with the Structured Interview for the Psychosis-Risk Syndromes in a sample of 36 adolescents and young adults referred for CHR evaluation, and a sensitivity of .80, specificity of .48, and positive predictive value of .52 in a sample of adolescents and young adults receiving mental health services (Kline et al., 2012; Miller et al., 2004). This questionnaire is one of the two questionnaires used to determine whether a participant meets for questionnaire high risk based on the stated cutoff.

Prodromal Questionnaire: The Prodromal Questionnaire (Loewy et al., 2005) is a 92-item measure that assesses the presence of PLEs over the previous month while not under the influence of drugs or alcohol. For this study, we used the 45-item positive scale to determine whether a participant meets for questionnaire high risk prior to the interview study. Prior

research has demonstrated that endorsement of 8 or more distressing PLEs on the positive symptom scale has 90% sensitivity and 49% specificity in predicting psychosis risk syndromes (Loewy et al., 2005, 2007).

Dissociative Experiences Scale (DES): The Dissociative Experiences Scale (DES; (Carlson & Putnam, 1993) was used to examine dissociative experiences. The DES is a 28-item self-report questionnaire that asks participants to report on a range of dissociative experiences and is considered to be the gold standard for evaluating dissociation. Each question asks about a different dissociative symptom, to which the participant must indicate what percentage of the time they have that experience on an 11-point scale (0% to 100%). We modified this scale into a 14-item version for brevity, removing items that were redundant or solely associated with dissociative identity disorders (a rare diagnosis; see appendix for table of items removed). The mean score was used for the analysis.

Pittsburgh Sleep Quality Index (PSQI): The Pittsburgh Sleep Quality Index (PSQI; (Buysse et al., 1989) is a 19-item self-report measure of sleep quality over the previous month. Components of sleep quality assessed include sleep latency, sleep efficiency, sleep duration, sleep disturbance, use of sleep medication, and daytime dysfunction. The PSQI has shown 89.6% sensitivity and 86.5% specificity in distinguishing between good and poor sleepers (participants with and without a diagnosis of a sleep disorder) and has shown convergent validity with physiological measures of sleep, such as home polysomnography (Buysse et al., 1989). The PSQI global score was used in the analysis.

Demographic characteristics: Age, sex assigned at birth, race, and ethnicity were collected from all participants through self-report questionnaires.

**Clinical Interviews.** Structured Interview for Psychosis-risk Syndromes (SIPS) version 5.6: The Structured Interview for Psychosis-Risk Syndromes (SIPS; (Miller et al., 2003; Woods et al., 2019) is the most commonly used interview for assessing psychosis-risk syndromes within the United States. The SIPS has established predictive validity of conversion to psychosis, specificity, and interrater reliability (Woods et al., 2019). The SIPS was used to determine CHR for psychosis, based on the presence of one or more psychosis-risk syndrome. In addition, SIPS P item scores were used to examine APPS, specifically Unusual Thought Content/Delusional Ideas (P1), Suspiciousness/Persecutory Ideas (P2), Grandiose Ideas (P3), Perceptual Abnormalities/Hallucinations (P4), and Disorganized Communication (P5). Each item is scored 0-6, with higher scores indicating greater symptom severity.

Structured Clinical Interview for DSM-5 (SCID): Presence of any DSM-5 psychiatric diagnoses was assessed using the Structured Clinical Interview for DSM-5 (SCID; (First et al., 2017). The SCID is considered to be the "gold standard" clinical diagnostic tool and demonstrates moderate-to-strong reliability.

**Training and Reliability.** All clinicians conducting clinical interviewing were advanced level graduate students, postdoctoral fellows, or research assistants with bachelor's degrees and at least 2-3 years of experience working with clinical populations. All study clinicians were SIPS certified by an official SIPS certifier. Interviewers were blind to whether participants exceeded the cutoffs for questionnaire high risk on the PRIME screen or Prodromal Questionnaire. Each interviewer wrote a narrative following the interview, which was then reviewed by an advanced interviewer. More complex cases (including all potential CHR cases) were further reviewed by a consensus group of advanced interviewers, and if no consensus could be made the decision was ultimately made by the 3 PIs (majority rules).

### *Analytic Strategy*

**Power Analysis.** Power analyses for this study were based on similar analyses conducted in the lab which yielded a small effect (Creatura et al., 2022). A power analysis was conducted in Gpower on a 2-level cross-sectional MLM with 3 predictors and 2 control variables. Results indicated that a sample of 89-123 participants would be needed to achieve power within the range of .7-.9 with a small effect size (ES=.18) at an alpha level of .05.

For the logistic regression, a power analysis was conducted to determine the number of participants needed to detect a small effect (ES=.15) in an analysis predicting to a binary dependent variable using three continuous, normally distributed variables, and an alpha level of .05. To achieve power of .8, a sample size of 252 is needed to detect a significant effect.

Given that the sample size of the CHR group exceeds the upper bounds of 123 required for Aims 1 and 2, and the total sample exceeds the cutoff of 252, all analyses conducted were sufficiently powered.

**Analyses.** All variables of interest were first examined visually/statistically for normality, multicollinearity, and homoscedasticity. DES scores were determined to not be normally distributed, and therefore, the log transformed DES scores were used for the analyses (DES kurtosis= 2.76, skewness= 1.52; post-log transformation kurtosis= -.12, skewness= -.55).

To account for the possibility of the impact the COVID-19 pandemic may have had on study variables, analyses were conducted to determine if there were differences in the data pre- and post-COVID-19 pandemic. Participants were grouped by date, with all participants having initiated study assessments prior to March 16$^{th}$, 2020 being sorted into the "pre-COVID-19" group, and all participants having initiated study assessments after March 16$^{th}$, 2020 being sorted into the "post-COVID-19" group. This date was selected due to it being the date all sites

involved in the study had transitioned to fully remote assessments. Analyses were performed for both the entire sample and the CHR group only for each variable of interest. In the whole sample, there were significant differences in non-transformed scores of grandiose ideas, log-transformed grandiose ideas, and perceptual abnormalities between pre and post-COVID-19 groups, with the pre-COVID-19 group reporting higher scores for each variable [$t$ (765) = 2.297, $p$ = .022; $t$(765) = 2.611, $p$ = .009; $t$(764) = 2.343, $p$ = .019]. In the CHR group, participants recruited post-COVID reported higher PSQI scores compared to those recruited pre-COVID [$t$ (128) = -2.113, $p$ = .037]. Because of this, a sensitivity analysis was performed excluding the post-COVID group for all analyses using the CHR only group.

Age and gender were examined as potential covariates in the whole sample as well as the CHR only group, because previous studies in the lab have demonstrated a relationship between age and gender and the variables of interest in this analysis (Ered et al., 2018). In the total sample, there were gender differences for the PSQI, with female participants reporting worse sleep [$t$ (705) = -2.238, $p$ = .026]. In addition, age was determined to be significantly correlated with log-transformed DES scores ($r$ = -.088, p = .015). Because of this, age and gender were included as covariates in the logistic regression analysis. In the CHR group, age was determined to be significantly associated with P4 scores ($r$ = -.194, $p$ =.022). Because of this, age was included as a covariate in analyses of indirect effects and hierarchical linear regression.

Analyses to detect the indirect effect of dissociation on the relationship between sleep quality and perceptual abnormalities in the CHR group was conducted using Hayes' PROCESS macro for SPSS (Hayes, 2012). The indirect effect of sleep quality on perceptual abnormalities, accounting for the effects of dissociation was tested using a bootstrap estimation approach with 5000 samples. Significance was determined for bivariate analyses by $p$<.05 (two tailed), and

significant mediation was determined by a 95% confidence interval of the effect size not including zero (Hayes, 2013).

Hierarchical linear regression was conducted in SPSS to further explore contributions of dissociative symptoms and sleep quality to APSS, in a subsample including only CHR participants. As with the analysis of indirect effects, log-transformed DES scores were used in these analyses due to these scores being positively skewed. The regression model was constructed with age entered in the first block as a covariate, sleep quality (as measured by the PSQI) entered in the second block, and dissociative symptoms (as measured by the DES) entered in the third block, predicting to one of five APPS domains.

The logistic regression analysis was conducted in SPSS to determine whether sleep quality and dissociative symptoms increase the odds that a participant meets criteria for a SIPS assessed CHR diagnosis. Bivariate correlations were conducted to check for multicollinearity among the independent variables. For this analysis, all participants with complete data on the PSQI, DES, and SIPS were included. Participants possessing any psychosis-risk syndrome diagnosis on the SIPS were coded as meeting for CHR status (yes=1; n=140) and participants with none of these diagnoses were coded as not meeting for CHR status (no=0; n=647)). Gender was included in the analysis as a covariate.

**Results**

Demographic characteristics are displayed in Table 1. In the CHR group, bivariate correlations revealed a significant relationship between PSQI scores and log-transformed DES scores ($r$ = .292, $p$ <.001), PSQI scores and P4 scores ($r$ = .184, $p$ =.036), and log-transformed DES scores and perceptual abnormalities scores ($r$ = .286, $p$ <.001). Because perceptual

abnormalities was the only SIPS symptom domain that was significantly correlated with both PSQI and log-transformed DES scores, indirect effects only were examined for perceptual abnormalities. Bivariate correlations are listed in Table 2 for the CHR group, and Table 3 for the overall sample.

**Table 1. Demographics and clinical characteristics**

| | Overall sample (*n*=767) | CHR Sample (*n*=140) |
|---|---|---|
| Male, *n* (%) | 184 (24.2%) | 40 (28.6%) |
| Age (years), mean (SD) [range] | 20.79 (2.83) [16-30] | 20.49 (2.32) [16-30] |
| Ethnicity, Hispanic *n* (%) | 104 (13.5%) | 13 (9.3%) |
| Race n (%) | | |
| American Indian/Alaska Native | 3 (.4%) | 0 (0%) |
| Asian | 182 (23.7%) | 26 (18.6%) |
| Native Hawaiian/Other Pacific Islander | | |
| Black/African American | 2 (.3%) | 0 (0%) |
| White | 108 (14.1%) | 21 (15%) |
| More Than One Race | 394 (51.3%) | 81 (57.9%) |
| Unknown | 49 (6.4%) | 8 (5.7%) |
| | 30 (3.9%) | 4 (2.9%) |
| Total PSQI score, mean (SD) [range] | 7.29 (3.38) [.00-18] | 8.44 (3.52) [1-18] |
| Total DES score, mean (SD) [range] | 15.62 (14.17) [.00-83.57] | 21.43 (14.99) [.00-82.86] |
| Log transformed DES score, mean (SD) [range] | 2.41 (.98) [.00-4.44] | 2.86 (.80) [.00-4.43] |
| CHR, *n* (%) | 140 (18.3%) | -- |
| SIPS P item scores, mean (SD) [range] | | |
| P1 | 1.23 (1.15) [0-6] | 2.56 (1.20) [0-5] |
| P2 | 1.06 (1.13) [0-6] | 2.14 (1.28) [0-5] |
| P3 | .33 (.73) [0-5] | .76 (1.07) [0-4] |
| P4 | .94 (1.18) [0-6] | 2.17 (1.36) [0-5] |
| P5 | .84 (.90) [0-5] | 1.42 (1.11) [0-5] |

**Table 2. Bivariate correlations for CHR group.**

| Variables | Age | PSQI | DES | lnDES | P1 | P2 | P3 | lnP3 | P4 | P5 |
|---|---|---|---|---|---|---|---|---|---|---|
| Age | -- | .041 | -.043 | -.119 | -.057 | .079 | .051 | .068 | -.194* | .008 |
| PSQI | .041 | -- | .295** | .292** | .038 | -.180* | -.044 | -.013 | .184* | .088 |
| DES | -.043 | .295** | -- | -- | .102 | .153 | .250** | .263** | .286** | .200* |
| lnDES | -.119 | .292** | -- | -- | .080 | .052 | .223** | .229** | .319** | .250** |
| P1 | -.057 | .038 | .102 | .080 | -- | -- | -- | -- | -- | -- |
| P2 | .079 | -.180* | .153 | .052 | -- | -- | -- | -- | -- | -- |
| P3 | .051 | -.044 | .250** | .223** | -- | -- | -- | -- | -- | -- |
| lnP3 | .068 | -.013 | .263** | .229** | -- | -- | -- | -- | -- | -- |
| P4 | -.194* | .184* | .286** | .319** | -- | -- | -- | -- | -- | -- |
| P5 | .008 | .088 | .200* | .250** | -- | -- | -- | -- | -- | -- |

* = correlation significant at the .05 level; ** = correlation significant at the .01 level

**Table 3. Bivariate correlations for overall sample.**

| Variables | Age | PSQI | DES | lnDES | CHR status | P1 | P2 | P3 | lnP3 | P4 | P5 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Age | -- | .045 | -.057 | -.088* | -.050 | -.053 | .023 | -.008 | -.003 | -.067 | -.020 |
| PSQI | .045 | -- | .272** | .325** | .161** | .236** | .225** | .086* | .082* | .261** | .226** |
| DES | -.057 | .272** | -- | -- | .194** | .317** | .295** | .225** | .216** | .340** | .281** |
| lnDES | -.088* | .325** | -- | -- | .213** | .325** | .290** | .197** | .191** | .368** | .308** |
| CHR status | -.050 | .161** | .194** | .213** | -- | .548** | .451** | .281** | .277** | .495** | .304** |
| P1 | -.053 | .236** | .317** | .325** | .548** | -- | -- | -- | -- | -- | -- |
| P2 | .023 | .225** | .295** | .290** | .451** | -- | -- | -- | -- | -- | -- |
| P3 | -.008 | .086* | .225** | .197** | .281** | -- | -- | -- | -- | -- | -- |
| lnP3 | -.003 | .082* | .216** | .191** | .277** | -- | -- | -- | -- | -- | -- |
| P4 | -.067 | .261** | .340** | .368** | .495** | -- | -- | -- | -- | -- | -- |
| P5 | -.02 | .226** | .281** | .308** | .304** | -- | -- | -- | -- | -- | -- |

* = correlation significant at the .05 level; ** = correlation significant at the .01 level

As indicated in Table 4, indirect bootstrapping results demonstrated a significant indirect effect of dissociation on the relationship between sleep quality and perceptual abnormalities among CHR participants [95% CI= .0039, .0550]. Results from alternative models examining indirect effects are detailed in Table 5. Results revealed a significant indirect effect of dissociation on the effect of perceptual abnormalities on sleep quality [95% CI= .0408, .3993], as well as a significant indirect effect of perceptual abnormalities on the effect of sleep quality on dissociation [95% CI= .0006, .0228].

**Table 4. Indirect, direct, and total effect of perceptual abnormalities and sleep quality through dissociative experiences in the CHR sample.**

| Perceptual abnormalities (n=130) | | | | | | |
|---|---|---|---|---|---|---|
| *IV* | *Mediator* | *Total Effect* | *Indirect Effect* | *SE* | *95% CI* | $R^2$ |
| Sleep Quality | Dissociative experiences | .0731 | .0260 | .0132 | .0039, .0550 | .114 |
| | | -- | *Direct Effect* | *SE* | *95% CI* | -- |
| | | -- | .0471 | .0335 | -.0193, .1135 | -- |

**Table 5. Alternative mediation models in the CHR sample.**

| *IV* | *Mediator* | *DV* | *Total Effect* | *Indirect Effect* | *SE* | *95% CI* | $R^2$ |
|---|---|---|---|---|---|---|---|
| Perceptual Abnormalities | Dissociative experiences | Sleep Quality | 0.5177 | 0.1904 | 0.0919 | 0.0408, 0.3993 | 0.1052 |
| | | | | *Direct Effect* | *SE* | *95% CI* | -- |
| | | | | 0.3273 | 0.2330 | -.1338, .7885 | -- |
| Sleep Quality | Perceptual Abnormalities | Dissociative Experiences | 0.0657 | 0.0093 | 0.0057 | 0.0006, 0.0228 | 0.1492 |
| | | | | *Direct Effect* | *SE* | *95% CI* | -- |
| | | | | 0.0564 | 0.0185 | .0197, .00197 | -- |

As indicated in Table 6, PSQI and DES scores significantly predicted to perceptual abnormalities among CHR participants ($F$ (3, 129) = 5.113, $p$ = .002), and accounted for 10.9% of the variance in perceptual abnormalities. Adding the PSQI to the model explained an additional 3.7% of variance in perceptual abnormalities above age alone, and this $R^2$ change was significant, $F$ (1, 127) = 4.997, $p$ = .027). Adding DES scores to the model explained an additional 4.2% of variance in perceptual abnormalities above age and PSQI scores alone, and this $R^2$ change was also significant, $F$ (1, 126) = 5.897, $p$ = .017).

**Table 6. Hierarchical linear regression model predicting to perceptual abnormalities in the CHR group.**

| Variables | β | *t* | *R* | $R^2$ | $\Delta R^2$ |
|---|---|---|---|---|---|
| Step 1 | | | 0.173 | 0.030 | 0.030 |
| Age | -0.173 | -1.992 | | | |
| Step 2 | | | 0.258 | 0.067 | 0.037 |
| Age | -0.181 | -2.113 | | | |
| Sleep quality | 0.192 | 2.235 | | | |
| Step 3 | | | 0.329 | 0.109 | 0.042 |
| Age | -0.150 | -1.767 | | | |
| Sleep quality | 0.124 | 1.405 | | | |
| Dissociation | 0.229 | 2.591 | | | |

Details of logistic regression analyses are listed in Table 7. PSQI scores, log-transformed DES scores, gender, and age all were added to the same model predicting to CHR status. Logistic regression analyses revealed that poor sleep quality was associated with a 1.094 increase in the odds of having a CHR diagnosis ($p$= .003), controlling for the other variables in the model. In addition, it was determined that dissociative symptoms

also significantly increased the odds of CHR diagnosis by 1.839 ($p$<.001), controlling for the other variables in the model.

**Table 7. Logistic regression predicting to CHR status.**

| Variable | OR | 95% CI | *p*-value |
|---|---|---|---|
| Gender | 1.537 | .977-2.419 | 0.063 |
| Age | 0.956 | .885-1.033 | 0.252 |
| PSQI | 1.094 | 1.031-1.161 | 0.003 |
| DES | 1.839 | 1.428-2.367 | <.001 |

Results of the sensitivity analysis are presented in Tables 8 and 9. The indirect effect of dissociation on the association of sleep with perceptual abnormalities remained significant in the pre-COVID group [95% CI=.0051, .0599]. In addition, both alternative models examining the effect of dissociation on the relationship between perceptual abnormalities and sleep quality [95% CI= .0113, .3290] and the effect of perceptual abnormalities on the relationship between sleep quality and dissociation [95% CI= .0026, .0372] remained significant. Similarly, in this analysis, PSQI and DES significantly predicted to perceptual abnormalities ($F$ (3, 108) = 6.884, $p$ < .001). Adding both sleep quality and dissociation to the model continued to result in significant $R^2$ change ($F$ (1, 106) = 8.770, $p$ = .004; $F$ (1, 105) = 7.783, $p$ = .006) with sleep quality accounting for an additional 7.4% of variance and dissociation accounting for an additional 6.2% of variance.

**Table 8. Indirect, direct, and total effect of perceptual abnormalities and sleep quality through dissociative experiences for participants recruited prior to COVID-19 lockdowns.**

| Perceptual abnormalities (n=109) | | | | | | |
|---|---|---|---|---|---|---|
| *IV* | *Mediator* | *Total Effect* | *Indirect Effect* | *SE* | *95% CI* | $R^2$ |
| Sleep Quality | Dissociative experiences | .112 | .0284 | .0139 | .0051 - .0580 | .1644 |
| | | -- | *Direct Effect* | *SE* | *95% CI* | -- |
| | | -- | .0836 | .0380 | .0082 - .1589 | -- |

**Table 9. Hierarchical linear regression model predicting to perceptual abnormalities for participants recruited before COVID-19 lockdowns.**

| Variables | Unstandardized B | *t* | *R* | $R^2$ | $\Delta R^2$ |
|---|---|---|---|---|---|
| Step 1 | | | 0.168 | 0.028 | 0.028 |
| Age | -0.111 | -1.760 | | | |
| Step 2 | | | 0.320 | 0.102 | 0.074 |
| Age | -0.120 | -1.980 | | | |
| Sleep quality | 0.112 | 2.961 | | | |
| Step 3 | | | 0.406 | 0.165 | 0.062 |
| Age | -0.108 | -1.836 | | | |
| Sleep quality | 0.091 | 2.440 | | | |
| Dissociation | 0.026 | 2.795 | | | |

## Discussion

This study is the first to examine the combined contributions of sleep quality and dissociation to individual APSS symptom categories among those at CHR, as well as CHR status. Specifically, our results indicated that poorer sleep quality and increased dissociative symptoms are associated with more severe perceptual abnormalities in CHR individuals, and that there is a significant indirect effect of dissociative symptoms on the relationship between sleep quality and perceptual abnormalities, specifically in CHR individuals. Furthermore, adding sleep quality to a model that predicts to perceptual abnormalities significantly improved the percentage of variance accounted for (3.7%), and the addition of dissociative symptoms to that model further improved the percentage of variance that was accounted for (4.2%). Finally, when predicting to the presence or absence of a SIPS CHR diagnosis, sleep quality and dissociative symptoms both significantly increased the odds of a diagnosis when added to the same model. A sensitivity analysis revealed that although individuals recruited after the beginning of the COVID-19 pandemic reported worsened sleep compared to the pre-COVID-19 cohort, the main analyses remained significant when this group was removed from the analyses, suggesting that sleep quality worsened by the pandemic does not influence these results. Unusual thought content, suspiciousness/persecutory ideation, grandiose ideas, and disorganized communication did not have significant associations with both sleep quality and dissociation.

These results suggest that the significant relationship between CHR status, dissociation, and sleep disturbance may be specific to perceptual abnormalities and not other APPS symptoms. This is not surprising, as perceptual abnormalities have been

associated with sleep disturbance in CHR individuals and non-clinical controls with PLEs, and sleep deprivation studies have demonstrated causal links between sleep loss and perceptual abnormalities (Goines et al., 2019b; Reeve et al., 2017; Taylor et al., 2015). In addition, perceptual abnormalities have been linked strongly to dissociation. A meta-analysis of both clinical and nonclinical positive psychotic symptoms found that compared to other positive symptoms, the most robust association was between dissociation and hallucinations (Longden et al., 2020). Pharmacological studies administering ketamine, a non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, have reliably induced perceptual abnormalities and dissociative symptoms in nonclinical volunteers, which suggests that NMDA receptor dysfunction could explain the common co-occurrence of perceptual abnormalities and dissociation (Krystal et al., 1994).

However, other positive symptoms, such as unusual thought content and persecutory ideation, similarly have been linked to both sleep disturbance and dissociation, and these associations were not found in this study (Freeman et al., 2009; Pope et al., 2000; Reeve et al., 2015). It remains a possibility that there is a link between sleep quality, dissociation, and other positive psychotic symptoms that simply were not captured by the current study. One explanation for this could be the use of the SIPS items to measure positive symptoms in the current sample. Although the SIPS was used due to the benefit of having rater-assessed symptoms, other studies that have reported associations between sleep quality, dissociation, and positive symptom have used other assessments such as the Positive and Negative Symptom Scale (PANSS), the PQ, or the Comprehensive Assessment of At-Risk Mental States (CAARMS) (Pope et al., 2000;

Reeve et al., 2015)). In addition, the range of scores on the SIPS for the CHR group was 0-5, leaving out the highest score of 6, likely due to individuals with a psychotic disorder being removed from the sample (a score of 6 on any one SIPS item does not necessarily result in a diagnosis of a psychotic disorder). This slightly restricted range could potentially explain the weakened associations. A recent systematic review has demonstrated stronger effect sizes for the association between sleep deprivation and hallucinations than sleep deprivation and both paranoia or delusions broadly, and the association between insomnia and hallucinations was stronger than delusions (Barton et al., 2018). Finally, significant associations were found for both unusual thought content and paranoid ideation with dissociation and sleep disturbance, but not in the CHR only sample. It is possible that this could be driven by other diagnoses that can register under unusual thought content or paranoid ideation, such as PTSD or other anxiety disorders, which would then not meet criteria for a CHR diagnosis.

This study presents interesting implications for the diathesis-stress model of psychotic disorders, which posits that psychotic disorders are a result of the combination of underlying genetic vulnerability and environmental insults (Jones & Fernyhough, 2007). One explanation for how these variables lead to APPS could be that in individuals with increased vulnerability for psychosis, sleep disruption leads to dissociative symptoms, and the combination of sleep disturbance and distressing dissociative symptoms pushes these individuals over the threshold for disruptive psychotic experiences. Insomnia has been shown to have a significant impact on an individual's functioning and quality of life, and has been associated with increases in suicidal ideation independent of depression symptoms (Drake et al., 2003; Simmons et al., 2020).

Furthermore, dissociation has been associated with poorer quality of life, poorer social relationships, increased suicidal ideation, and poorer treatment outcomes (Brokke et al., 2022; Hoeboer et al., 2020; Polizzi et al., 2022). The impact of these distressing symptoms, as well as their interference with psychotherapy outcomes, could lead to exacerbations of many types of psychiatric symptoms, including psychosis.

There are several notable strengths of this project. One includes the multisite dataset that was collected from large, ethnically and socioeconomically diverse cities. This allows us to generalize these findings to a broader number of individuals. In addition, this study did not specifically recruit help-seeking individuals, which allowed for the collection of a broad spectrum of severity on SIPS scores. Finally, this project utilized semi-structured interviews for APPS symptoms based on the SIPS, which is conducted and scored by individuals who are required to meet a specific standard of competency to administer it and all CHR cases were reviewed in consensus calls, enhancing the reliability and validity of our symptom data versus self-report questionnaires of PLEs (often which includes overreporting) (Capizzi et al., 2022).

This project is not without its limitations. One notable limitation is the cross-sectional design of the study, which prohibits the ability to make causal claims about the directionality of the relationships between variables. As a result, the present study demonstrates statistical mediation, rather than true theoretical mediation. To address this further, alternative models were tested when examining indirect effects between variables. Specifically, we tested whether dissociation mediated the direct effect of perceptual abnormalities on sleep quality, and whether perceptual abnormalities mediated the direct effect of sleep quality on dissociation. Because the indirect effects of these

alternative models were also significant, the evidence most likely points to a strong interrelationship between these three variables in which any of the three could serve as the independent, dependent, or mediating variable. In addition, this project focused specifically on dissociation and how it interacts with both sleep disturbance and APPS. It has been well documented that other psychological symptoms have been associated with sleep quality and APPS, such as depression, anxiety, and experiences of trauma (Ered et al., 2018; Freeman et al., 2012; Goines et al., 2019b). However, this study was the first to examine the relationship between sleep disturbance, dissociation, and APPS specifically in a CHR sample, which should be followed up by future examinations exploring these additional variables. Future studies should examine dissociation within the context of a multiple mediation model to determine the unique and combined contributions of each mediator to the relationship between sleep disturbance and APPS symptoms.

The project further clarifies the relationship of sleep quality and dissociation with the severity of APPS in CHR individuals, as well as their contributions to CHR diagnoses. Identifying symptoms that occur during the CHR period can improve our understanding of which individuals are at the highest risk for developing a psychotic disorder, and identifying risk factors ultimately can increase prevention efforts. Additionally, determining variables that increase severity of specific APPS can inform intervention strategies (e.g., cognitive behavioral therapy for insomnia, imagery rehearsal therapy, mindfulness-based approaches) in help-seeking individuals. Given the common co-occurrence of sleep disturbance and dissociation with APPS, routinely assessing for these symptoms prior to treatment could inform whether to include interventions for sleep and dissociation as part of a comprehensive treatment plan for CHR individuals.

# CHAPTER TWO

## EXPANDED ANALYSES

**Table 10. Bivariate correlations between Nightmare Distress Questionnaire and other study variables.**

| Variables | NDQ |
|---|---|
| Age | -.043 |
| PSQI | .028 |
| DES | -1.93 |
| lnDES | -.102 |
| P1 | .171 |
| P2 | .060 |
| P3 | .454 |
| lnP3 | .440 |
| P4 | .187 |
| P5 | .256 |

**Table 11. Logistic regression predicting to CHR status, including Nightmare Distress Questionnaire.**

| Variable | OR | 95% CI | *p*-value |
|---|---|---|---|
| Gender | 0 | .000-.000 | 0.998 |
| Age | 0.938 | .725-1.214 | 0.627 |
| PSQI | 0.974 | .763-1.244 | 0.836 |
| DES | 3.561 | 1.149-11.038 | 0.028 |
| NDQ | 0.998 | .924 | 1.079 |

**Table 12. Items excluded from the Dissociative Experiences Scale.**

| DES Excluded Items | |
|---|---|
| 1 | Some people have the experience of driving a car and suddenly realizing that they don't remember what has happened during all or part of the trip. |
| 5 | Some people have the experience of finding new things among their belongings that they do not remember buying. |
| 6 | Some people find that they are approached by people that they do not know who call them by another name or insist that they have met them before. |
| 8 | Some people are told that they sometimes do not recognize friends or family members. |
| 9 | Some people find that they have no memory for some important events in their lives (for example, a wedding or graduation). |
| 10 | Some people have the experience of being accused of lying when they do not think that they have lied. |
| 15 | Some people have the experience of not being sure whether things that they remember happening really did happen or whether they just dreamed them. |
| 18 | Some people sometimes find that they become so involved in a fantasy or daydream that it feels as though it were really happening to them. |
| 19 | Some people find that they are sometimes able to ignore pain. |
| 22 | Some people find that in one situation they may act so differently compared with another situation that they feel almost as if they were different people. |
| 23 | Some people sometimes find that in certain situations they are able to do things with amazing ease and spontaneity that would usually be difficult for them (for example, sports, work, social situations, etc.). |
| 24 | Some people sometimes find that they cannot remember whether they have done something or have just thought about doing that thing (for example, not knowing whether they have just mailed a letter or have just thought about mailing it). |
| 25 | Some people find evidence that they have done things that they do not remember doing. |
| 27 | Some people find that they sometimes hear voices inside their head that tell them to do things or comment on things that they are doing. |

# CHAPTER THREE

# EXPANDED LITERATURE REVIEW

## Introduction

Sleep disturbances have been observed across the entire psychosis-spectrum. In patients with schizophrenia, disruptions have been documented in sleep quality domains such as total sleep time, sleep efficiency, sleep latency, and sleep continuity (Cohrs, 2008). Circadian rhythm disturbances, alterations in sleep architecture and neural rhythms as measured by polysomnography, and increased nightmares are also commonly experienced in schizophrenia (Cosgrave, Wulff, & Gehrman, 2018; Sheaves, Onwumere, Keen, Stahl, & Kuipers, 2015; Wamsley et al., 2012). There has been significant interest in characterizing the extent of sleep quality disruptions in the clinical high risk (CHR) group for psychosis, as well as in people with psychotic-like experiences (PLEs). The CHR period is defined by clinically significant and distressing subthreshold versions of the positive psychotic symptoms experienced in schizophrenia, called attenuated positive psychotic symptoms (APPS), and these individuals are considered to be at increased risk of developing a fully psychotic disorder (McGlashan, T; Walsh, B; Woods, 2010). PLEs are subthreshold psychotic symptoms that occur in non-help seeking individuals, and are common in the general population (Yung et al., 2009). The purpose of this effort to characterize sleep disturbance in the CHR period and PLEs is largely to examine sleep separately from the sedating effects of antipsychotics, and determine how early in the course of development of a psychotic disorder this sleep difficulty might begin.

Self-report measures are common in sleep research on psychosis spectrum disorders, likely because they are easy to administer and score, as well as fast, cost-effective, and non-invasive. However, they are not without cons—very few sleep questionnaires that claim to

measure general sleep disturbance include an exhaustive evaluation of all that could go wrong with sleep, and individuals are not always accurate in reporting their sleep (Lauderdale, Knutson, Yan, Liu, & Rathouz, 2008). Interview measures, such as the Sleep Disturbance scale of the Structured Interview for Psychosis-Risk Syndromes (SIPS; (Woods, Walsh, Powers, & McGlashan, 2019), suffer from a similar issue—the SIPS scale uses only two semi-structured questions to assess sleep disturbance, and rely on the participant's memory and best estimate of what is happening. Concerns about reliability and validity drive certain researchers to use more objective measures of sleep, such as wrist actigraphy—a wristwatch-like device that is worn 24 hours per day that records movements, and polysomnography (PSG)—the gold standard of sleep measurement, which is a device that individuals wear on their scalp and body during sleep that integrates EEG, EMG, eye movements, heart rate, and breathing. In addition to providing more accurate readings of sleep parameters such as sleep latency, wake time after sleep onset (WASO), and total sleep time, wrist actigraphy and PSG can provide information on how much time is spent in each sleep stage, and PSG can provide information about sleep disorders and allow for analysis of specific brain rhythms during sleep (Van De Water et al., 2011). While all of this information is beneficial, these objective measures have their own pitfalls, such as significant cost, specialized training required to use the equipment and analyze results, and are generally more uncomfortable to participants (Van De Water et al., 2011).

**Sleep Disturbance and CHR**

In CHR individuals, self-report measures of sleep quality have demonstrated increased sleep latency, daytime sleepiness, and greater general sleep disturbance compared to nonclinical controls (Clarke et al., 2020). Sleep disturbances have also been measured in the CHR period using wrist actigraphy, which has revealed increases in sleep latency, WASO, daytime naps, and

nighttime movements (Clarke et al., 2020). Polysomnography studies, while less common, have demonstrated increased sleep latency and REM latency in CHR individuals, with no differences in sleep efficiency, WASO, or total sleep time compared to controls (Zanini et al., 2015). Beyond general sleep disturbance, circadian rhythm disruptions have also been documented in the CHR period. Actigraphy studies have demonstrated greater circadian rhythm fragmentation in CHR youth, and self-report assessments have indicated that CHR youth are more likely to experience day/night reversal (Castro et al., 2015; Poe et al., 2017). Nightmares and other parasomnias have also been associated with psychosis (Sheaves et al., 2015). Notably, parasomnias such as nightmares, vivid dreams, and other unusual sleep behaviors show specificity to schizotypy, whereas overall sleep quality disturbance generalizes to mood and anxiety disorders (Koffel & Watson, 2009). Compared to controls and individuals with a first degree relative with a psychotic disorder, CHR participants experience more frequent nightmares, and recall dreams at a greater frequency (Michels et al., 2014).

**Sleep Disturbance and PLEs**

Non-help seeking members of the general population with PLEs also report diminished sleep quality on self-report assessments, specifically increased rates of insomnia, fragmented sleep, and night anxiety (Andorko et al., 2017; Sarah Reeve, Sheaves, & Freeman, 2015). In general population studies, actigraphy has shown that shorter sleep time is linked to increases in PLEs (Hennig & Lincoln, 2018). There have been no studies reporting results on circadian rhythm disruption in PLEs, nor have there been any studies using PSG to investigate sleep disturbance in relation to PLEs. Nightmare frequency and distress have both been found to be significantly associated with PLEs, such as paranoid ideation and perceptual disturbances, in non-help seeking general population samples (Sheaves et al., 2016). In university students,

episodes of sleep paralysis have correlated with measures of persecutory ideation, and measures of unusual sleep experiences have correlated with self-report measures of perceptual aberrations and magical thinking (Fukuda, Miyasita, Inugami, & Ishihara, 1987; Knox & Lynn, 2014; Watson, 2001).

In summary, sleep quality disturbances, disruptions in circadian rhythm, and parasomnias have all been observed in both the CHR period and individuals with PLEs. Studies in CHR participants and in individuals with PLEs have demonstrated that the sleep disturbance that occurs across the psychosis-spectrum is not merely a side effect of antipsychotic medication, but is rather a trait of psychosis (Barton, Kyle, Varese, Jones, & Haddock, 2018; Clarke et al., 2020). This has led some researchers to argue that sleep disturbances may in fact be a biomarker of schizophrenia (Manoach, Pan, Purcell, & Stickgold, 2016).

**Sleep Disturbance in Non-Psychotic Disorders**

However, it is necessary to note that sleep disturbance is not unique to the psychosis spectrum. Sleep alterations occur across many psychiatric disorders, and are part of the diagnostic criteria for major depressive disorder, bipolar disorder, generalized anxiety disorder, and post-traumatic stress disorder (PTSD) (Association, 2013; Krystal, 2012). Furthermore, psychosis-spectrum disorders do not exist in a bubble. It is estimated that approximately 50% of schizophrenia patients carry a comorbid depression diagnosis, 47% have a comorbid substance use disorder, 29% suffer from PTSD, and a meta-analysis yielded pooled prevalence rates of 12.1% for anxiety disorders (Achim et al., 2011; Buckley, Miller, Lehrer, & Castle, 2009). Schizophrenia patients without these comorbidities experience a higher quality of life compared to those that do have a comorbid illness (Tsai & Rosenheck, 2013). In addition, these comorbid disorders do not wait to appear until after the first episode of psychosis. A longitudinal study

found that 79% of CHR participants had a comorbid psychiatric diagnosis, with some having as many as two to three comorbidities, most commonly depression or an anxiety disorder (Addington et al., 2017). Another study found that CHR participants had an 80.4% lifetime comorbidity, and 50.3% had a current comorbidity, with the most common comorbidity being depressive disorders, followed by anxiety disorders (Lim et al., 2015). Similar to patients with schizophrenia, CHR individuals with a comorbid mental health diagnosis experience decreased quality of life, poorer functioning, and increased symptom distress (Chang et al., 2020; Lim et al., 2015). The impact of comorbidity on quality of life highlight the importance of characterizing the mechanisms through which this distress is exacerbated, such as through sleep.

There is added value to understanding variables that influence sleep disturbance prior to the onset of a first psychotic episode, as CHR patients with disrupted sleep experience worsened positive symptoms, negative symptoms, and prognosis at follow up (Lunsford-Avery et al., 2013b, 2017). Elucidating the ways in which psychological and behavioral variables contribute to variance in the sleep—early psychosis relationship could provide additional treatment targets, and clarify what sleep disturbance symptoms predict psychosis with greater specificity. The present review will summarize the evidence for several variables that may influence the relationship between sleep disturbance and attenuated psychosis, implications for treatment, and future directions.

**Mood and Anxiety Symptoms**

Mood and anxiety symptoms have been the most thoroughly researched domain of variables associated with sleep in subthreshold psychosis. To date, many studies have examined these associations in the context of the consequences of the presence of sleep disturbance in CHR individuals and PLEs, such as exacerbated positive, negative, and cognitive symptoms

(Clarke et al., 2020). In addition, several studies have examined potential variables that could impact the relationship between sleep, APPS, and PLEs, likely due to the reciprocal relationship between sleep disturbance and psychopathology more generally (Morin & Ware, 1996).

### Mood/Anxiety Symptoms and Sleep in CHR

A study focused on CHR youth aimed to characterize the impact of sleep disturbance in APPS (Goines et al., 2019a). After correcting for multiple comparisons, they found a significant relationship between paranoid ideation and sleep disturbance, as well as perceptual disturbances and sleep disturbance. Mediation analyses found that while depression did not mediate the effect of sleep disturbance on total APPS or perceptual abnormalities, depression did significantly mediate the effect of sleep disturbance on paranoid ideation.

### Mood/Anxiety Symptoms and Sleep in PLEs

(Oh et al., 2016) reported that experiencing sleep disturbances for two weeks or longer over the previous 12 months was associated with significantly increased likelihood of reporting PLEs, specifically after experiencing difficulty falling asleep, waking up during the night, early morning awakenings, and feeling sleepy during the day. However, when controlling for comorbid DSM-5 disorders such as PTSD, mood, anxiety, and substance use disorders, only difficulty falling asleep and early morning awakenings were still significant. A large, multi-country general population study found that sleep disturbances were associated with significantly higher odds of experiencing PLEs, but that these odds were reduced when adjusting for anxiety and depression (Koyanagi & Stickley, 2015). An experimental design by (Sarah Reeve, Emsley, Sheaves, & Freeman, 2017) assessed the causal effects of sleep restriction on PLEs, and included mediation analyses. Nonclinical volunteers in the sleep loss condition, with sleep restriction confirmed by actigraphy, slept an average of five hours and 15 minutes compared to an average

of six hours and 58 minutes in the control condition. Compared to the control condition, the sleep loss condition saw significant increases in paranoid ideation, perceptual abnormalities, and cognitive disorganization, but not grandiose ideas. This group also saw significant increases in negative affect, worry, stress, and negative beliefs about self and others. The effects of sleep restriction on paranoid ideation and cognitive disorganization were significantly mediated by negative affect, negative beliefs, and worry, whereas the effect of sleep restriction on perceptual disturbances was mediated specifically by stress. Working memory impairment was also significantly increased in the sleep loss condition, however it was not a significant mediator for any of the sleep—PLEs relationships. A twin study examining genetic and environmental influences on adolescent vulnerability to developing PLEs and sleep disturbances found significant associations between sleep disturbance and paranoid ideation, perceptual abnormalities, and cognitive disorganization (Taylor, Gregory, Freeman, & Ronald, 2015). These associations remained significant after controlling for negative affect (traits of depression, anxiety sensitivity), however the strength of the associations was reduced.

Mood and anxiety symptoms have been shown to influence the relationship between PLEs and nightmares. A general population study of young adults sought to characterize the relationships between nightmare variables (nightmare distress, nightmare frequency, and nightmare content), PLEs (paranoid ideation, perceptual abnormalities, and negative symptoms), perceived stress, and depression (Kammerer et al., 2020). Stress and depression partially mediated the relationships between nightmare distress and paranoid ideation, as well as the relationship between nightmare distress and perceptual abnormalities.

### Mood and Anxiety in Persecutory Ideation

Several studies have taken a focus on the impact of depression and anxiety symptoms on the relationship between sleep quality and persecutory ideation in particular. One study aimed to characterize the effect of depression and anxiety on the relationship between insomnia and persecutory ideation in a general population sample (Freeman, Pugh, Vorontsova, & Southgate, 2009). A cross-sectional analysis found that adding depression to the regression model significantly reduced the relationship between insomnia and paranoid ideation, and when anxiety was added to the model, the relationship is weakened further to the point of becoming statistically non-significant. (Freeman et al., 2012) aimed to examine predictors of new and persistent paranoid ideation, and found that for participants who reported paranoid ideation at baseline, each one point increase in insomnia led to a 1.2 increase in odds of paranoid ideation at follow up. When insomnia, depression, worry, anxiety, and depressive ideas were entered into a multiple regression model, only worry came out as a significant predictor of paranoid ideation for these subjects. Another study found similar results in a sample of adolescents using actigraphy measured sleep data while attempting to determine directionality of the relationship between paranoid ideation and poor sleep (Hennig & Lincoln, 2018). Results indicated that sleep time and greater frequency of dreaming predicted persecutory ideation symptoms, and that this effect was partially mediated by both positive and negative affect.

Overall, symptoms of depression, anxiety, and related variables have been the most commonly examined psychological symptoms to influence the relationship between sleep disturbance and subthreshold psychosis, particularly in PLEs. Further examination of specific subdomains of PLEs has demonstrated that depression and anxiety have the strongest influence over paranoid ideation and perceptual abnormalities, and appear to be less influential with regard to grandiose ideas, disorganization, and non-paranoid unusual thought content. While the

abovementioned studies suggest a strong influence of depression and anxiety on PLEs, there is evidence that these symptoms do not necessarily make up the whole picture. A study of adolescents in South Korea found that insomnia predicted PLEs independent of depression (Lee, Cho, Cho, Jang, & Kim, 2012). Group differences have been observed between nonclinical controls and CHR individuals on sleep assessments, with CHR participants exhibiting increased sleep latency and greater disruption of continuity of sleep, even when controlling for symptoms of depression and hypomania (Lunsford-Avery et al., 2013b). Finally, the results of a study of clinical trajectory in CHR individuals with sleep disturbance found that depression was not significantly correlated with various domains of sleep disturbance, including self-reported average sleep duration on "bad" nights of sleep, and range of sleep duration (S. Reeve et al., 2019). These results suggest that perhaps mood and anxiety symptoms are less robust mediators in APPS compared to PLEs, and that there are differences in the mechanisms driving sleep disturbance that are associated with help-seeking individuals with clinically significant subthreshold psychotic symptoms, compared to those that are not help-seeking. An alternative explanation could be that there are specific symptom domains in CHR participants that are more vulnerable to influence of low mood and anxiety, such as persecutory ideation, as reported by (Goines et al., 2019).

**Post-Traumatic Stress Disorder**

Despite the fact that several studies have investigated the role that depression and anxiety play in the link between sleep disruption and subthreshold psychosis, there has been little research on the possible influence of trauma and PTSD on sleep disruption in APPS and PLEs. This is surprising, given that sleep disturbances are well-documented in individuals suffering from PTSD, and traumatic life experiences have been linked to increased risk and severity of

psychotic disorders (Koffel, Khawaja, & Germain, 2016; Spauwen, Krabbendam, Lieb, Wittchen, & Van Os, 2006). Additionally, people with psychotic disorders are more likely to report a history of childhood trauma compared to the general population—roughly 2.72 times more likely (Varese, Smeets, et al., 2012).

### PTSD and Sleep in CHR

In a cohort of help-seeking CHR individuals, history of trauma was significantly associated with SIPS interview assessed unusual thought content and perceptual abnormalities, as well as sleep disturbance, however the direct relationship between sleep disturbance and APPS was not investigated in this study (Grivel et al., 2018).

### PTSD and Sleep in PLEs

Ered et al., (2017) examined several psychological symptoms as mediators of the relationship between sleep quality and PLEs, using a multiple mediation approach. Sleep quality, symptoms of depression, PTSD, anxiety, and PLEs were evaluated using self-report measures in a cross-sectional sample of non-help seeking undergraduates. Results revealed that symptoms of depression and PTSD, but not anxiety, mediated the relationship between sleep quality and PLEs when controlling for the effects of gender and age. In non-help seeking undergraduates, endorsing previous traumatic experiences was associated with PLEs and sleep disturbance (Andorko et al., 2018). Trauma significantly predicted total PLEs when entered into the first step of a hierarchical multiple regression model with other demographics characteristics, however it ceased to be a significant predictor once sleep variables were added to the model. Ultimately, when each predictor variable was examined individually, nightmares, fragmented sleep, and depressive symptoms significantly predicted PLEs.

In summary, these preliminary studies suggest significant relationships between sleep quality, trauma, and subthreshold psychotic symptoms in CHR and general population samples. More studies examining PTSD and trauma as potential mediators are needed to better understand this relationship, particularly in CHR samples.

**Emotion Regulation**

Because depression and anxiety have been observed to have mediating effects on the relationship between sleep disturbance and subthreshold psychosis, it comes as no surprise that investigators have also examined the role of emotion regulation in this relationship, as difficulties in regulating emotions have been observed in major depression, anxiety disorders, and PTSD (Gross & Jazaieri, 2014). These transdiagnostic difficulties in emotion regulation could serve as a potential explanation for why sleep disturbance is present in many different psychiatric disorders. To date, there have been no studies that have examined the effect of emotion regulation on the relationship between sleep quality and APPS in the CHR population.

Emotion Regulation and Sleep in PLEs

(Grezellschak, Jansen, & Westermann, 2017) collected questionnaire data in a sample that spanned the psychosis spectrum, from nonclinical controls to patients with a diagnosis of a psychotic disorder to examine the relationship between sleep quality, paranoid ideation, and emotion regulation. In the total sample, the effect of insomnia on paranoid ideation was mediated by frequent use of expressive suppression, and infrequent use of reappraisal. These results remained true when examined in the subsample of psychosis patients, but in the subsample of nonclinical controls, only infrequent use of reappraisal was a significant mediator. Another study conducted in a university student population also sought to characterize the role of emotion regulation in sleep and subclinical psychosis, however, with a specific focus on nightmares

rather than insomnia (Akram et al., 2020). Results indicated a significant association between PLEs and nightmare symptoms, such as nightmare intensity, resulting awakenings, and perceived consequences of nightmares. Regression based multiple mediation modelling was used to examine the indirect effect of these nightmare variables on PLEs through six dimensions of emotion regulation difficulty. Poorer emotion regulation was a significant mediator of the effect of nightmare experience on PLEs.

Results of the abovementioned studies suggest that emotion regulation, especially poor emotion regulation skills, play a role in the relationship between sleep quality, nightmare experiences and PLEs. With the exception of paranoid ideation, no other subdomain of PLEs has been investigated in relationship to both sleep quality and emotion regulation. Overall, these studies suggest that emotional regulation may be a cross-diagnostic phenotype that may contribute to sleep disruptions found in various disorders. Future work in CHR samples as well as studies focusing on PLEs outside of paranoid ideation are needed to fully characterize how sleep quality and emotion regulation combine to influence subthreshold psychotic symptoms.

**Cannabis use**

Few studies have examined the role of illicit drug and alcohol use in the association between sleep and subthreshold psychotic symptoms. Drug use, particularly cannabis use, is common in CHR individuals, and has been associated with increased APPS (Corcoran et al., 2008; Kuepper et al., 2011). In addition, cannabis use has well established effects on sleep in the general population, such as reduced sleep latency and decrease in REM sleep, and in chronic users, abrupt cessation of cannabis use can result in reduced total sleep time, sleep efficiency, percent of time spent in REM sleep, and increased sleep latency, WASO, and periodic limb

movements (Babson et al., 2017). Currently, no studies have investigated cannabis as a mediator of the sleep—APPS relationship in the CHR population.

### Cannabis Use and Sleep in PLEs

A large general population study in Great Britain focused specifically on the effect of insomnia on persecutory ideation assessed several potential mediators in their analysis (Freeman et al., 2010). Insomnia was associated with increases in paranoid ideation, however both paranoid ideation and insomnia were significantly associated with mood symptoms and cannabis use. A path analysis revealed that cannabis use partially mediated the effect of insomnia and persecutory ideation, although negative affect mediated this relationship to a greater degree. To date, no other substances have been examined as potential mediators of the effect of sleep disturbance on subthreshold psychosis, including alcohol.

## Physical Activity

Thus far, one study has examined the relationship between physical activity and sleep quality in individuals with subthreshold psychosis. This is an important relationship to characterize, given the established association between insomnia and exercise in the general population, as well as the reduced physical activity levels in individuals with schizophrenia (Dolezal et al., 2017; Vancampfort et al., 2012). Many studies have demonstrated the beneficial effects of even moderate exercise on sleep, including increased sleep duration, sleep continuity, and sleep efficiency, as well as decreased sleep latency (Dolezal et al., 2017). No studies have reported on the role of physical activity in the relationship between sleep quality and PLEs.

### Physical Activity and Sleep in CHR

A study comparing CHR individuals, first-episode psychosis (FEP) patients, and nonclinical controls found that CHR individuals had poorer overall sleep quality and increased

daytime dysfunction due to sleepiness than both FEP patients and controls (Lederman, Rosenbaum, Maloney, Curtis, & Ward, 2017). In addition, CHR individuals reported decreased physical activity and energy expenditure compared to controls, and did not differ in energy expenditure compared to FEP patients. When observing all groups, there was a significant correlation between energy expenditure and sleep quality, with lower energy expenditure leading to poorer sleep quality. The results suggest that sedentary lifestyles in the CHR period could be a modifiable target to improve physical health outcomes, including poor sleep.

**A Diathesis-Stress Model of Sleep Disturbance in Psychosis**

Because of the cross-sectional nature of many of the studies reviewed, it can be difficult to make sense of what these mediators mean. What is clear is that there is a disturbance in sleep that occurs prior to the onset of a psychotic disorder, and that this sleep disturbance reaches all the way to the mildest ends of the psychosis continuum, affecting even non-help seeking individuals with PLEs. Several researchers have suggested that sleep disturbance might play a causal role in the development of psychosis, citing the presence of sleep disruption prior to the onset of psychosis and psychotic episodes, as well as the increase in PLEs that follows sleep deprivation (Barton et al., 2018). Currently, mood and anxiety disorder symptoms appear to have the most commonly observed mediating effect on the relationship between sleep disturbance and subthreshold psychosis. One possible explanation for this relationship could be that the presence of a major depressive episode, PTSD, or anxiety disorder leads to significant sleep disturbance, which is then a causal factor for the onset of APPS or PLEs. This hypothesis is supported by research that has linked high rates of major depression, anxiety, cannabis use disorder, and history of trauma to the prodrome of psychosis (Rosen et al., 2006; Strakowski et al., 1995; Varese et al., 2012). Alternatively, there is evidence that insomnia can play a causal role in the

development of depression and anxiety symptoms (Khurshid, 2018). This has interesting implications for the diathesis-stress model of psychosis, which suggests that schizophrenia and other psychotic disorders arise from a combination of genetic vulnerability and stressors, or other environmental insults (Jones & Fernyhough, 2007). Chronically disrupted sleep in youth can result in the emergence or worsening of mood and anxiety symptoms, which could pose as a significant enough psychosocial stressor that triggers psychotic symptoms in individuals with genetic vulnerability. Regular practice of adaptive coping strategies, such as exercise and emotion regulation skills (i.e. reappraisal), have long been shown to aid in managing stress and other painful emotional states, such as depression and anxiety (Schäfer et al, 2017; Wegner et al., 2014). The absence of these skills, and increased use of maladaptive coping such as substance use, could significantly impact an individual's ability to cope with stress, and in turn exacerbate any existing subthreshold psychotic symptoms.

**Potential Biological Mechanisms of Sleep Disturbance in Psychosis**

It has been hypothesized that these sleep disturbances may originate as a result of impaired thalamo-cortical communication in the brains of individuals with schizophrenia (Vukadinovic, 2011). Sleep spindles are a sleep rhythm that commonly occurs during stage NREM 2 of sleep and are generated as a result of thalamo-cortical brain circuits, and this rhythm is notably reduced in individuals with schizophrenia compared to both nonclinical controls, and clinical control groups (Ferrarelli et al., 2007; Manoach et al., 2014). Reduced bilateral thalamus volumes have been observed in CHR participants, and this volume reduction was associated with increased sleep disturbance (Lunsford-Avery et al., 2013a). This may be evidence that thalamic abnormalities are present prior to the onset of a first psychotic episode, and could aid in early identification of the disorder.

## Conclusion

Based on the abovementioned studies, it is apparent that there is more to the bidirectional relationship between sleep dysfunction and subclinical psychosis than simply the direct relationship. While there have been a number of studies where this relationship has persevered despite controlling for the effects of negative affect, there is a consistent body of research that has found symptoms of depression and anxiety to significantly mediate the link between sleep disturbance and PLEs in the general population, but this relationship is less clear in CHR. PTSD and experiences of trauma appear to influence the effects of sleep on PLEs, however only two studies have examined this to date, and more research will need to be done in this area before conclusions can be drawn. Finally, cannabis use was found to partially mediate the effects of insomnia on paranoid ideation, and energy expenditure was correlated with sleep quality in a CHR sample. These are interesting results that should similarly be expanded upon in future studies.

There are several significant ways that future studies can build upon this necessary body of research. The majority of the studies mentioned in this review are cross-sectional, and therefore it is not possible to make claims about the directionality of the effects. Future studies should employ longitudinal designs in an effort to further clarify the order in which the effects of sleep disturbance, subthreshold psychosis, and any potential mediator occur. This review focused primarily on mediation, however it is highly likely that many of these variables, if not all, have bidirectional effects—for example, sleep disturbance can lead to an exacerbation of PLEs, and also bothersome PLEs can be present at bedtime, which might impact sleep. Similarly, because of the cross-sectional nature of these studies, an argument can be made to place any of the variables discussed in this review as the antecedent variable. All of these studies built their

models with sleep disturbance as the independent variable, and APPS or PLEs as the dependent variable. However, one could argue that distressing APPS could lead to clinically significant depressive or anxiety symptoms, which lead to sleep disruptions. Therefore, while longitudinal studies can begin to shed light on the relationship between these symptoms, alternative models should also be tested. Finally, many of the studies listed rely upon self-report measures, so there is ample opportunity to gain additional insight through the use of objective sleep measurement techniques.

There are several potential mediator variables of this relationship that have yet to be tested. While physical activity and energy expenditure have been examined in CHR individuals, no study has examined bright light exposure in relationship to sleep in this population. Bright light, particularly sunlight, is one of the most influential factors in circadian rhythm—so much so that well-timed bright light exposure is a primary treatment for delayed phase circadian rhythm disorders (Faulkner, Bee, Meyer, Dijk, & Drake, 2019). For this same reason, use of electronics, or screen time, should also be examined due to the possible influence of blue light emitted from these devices on circadian rhythm (Tosini et al., 2016). Further evidence for the importance of examining light exposure and screen time is that CHR individuals' decreased physical activity, as a result of negative symptoms such as reduced motivation or social withdrawal, could serve as a proxy for decreased bright light exposure, and that CHR youth exhibit increased problematic internet use (internet use that negatively impacts daily life, social interactions, and productivity) compared to their nonclinical peers (Lederman et al., 2017; Pelletier-Baldelli et al., 2015).

In addition, no studies have examined the potential mediating role of substance use besides cannabis on the relationship between sleep disturbance and subthreshold psychosis. Prevalence rates for use of cannabis, alcohol, and tobacco range from 33%-54%, 17%-44%, and

16%-34%, respectively (Addington et al., 2014). All of these substances can have deleterious effects on sleep as a result of both acute and chronic use, especially when used close to bedtime (Angarita et al., 2016; Wetter & Young, 1994).

Furthermore, taking a more dimensional approach to examining mediators could provide useful information regarding which symptoms of depression, or which presentations of anxiety, seem to account for the most variance. Finally, treatment studies could potentially evaluate whether targeting mood and anxiety symptoms results in improvements to sleep quality or PLEs in CHR individuals.

Characterizing the roles of sleep disturbance, other psychological symptoms, and behavior in the formation of APPS and PLEs can aid in the development of comprehensive treatment or prevention strategies for psychosis-spectrum disorders. While clinical trials have demonstrated success in targeting psychosis symptoms directly with cognitive behavioral therapy, CBT for insomnia (CBT-I) has recently been adapted for individuals with psychosis, and has resulted in improvements in quality of life and psychological wellbeing (Freeman, Waite, et al., 2015; Wood et al., 2015). A study of non-help seeking undergraduates found that compared to a "usual care" condition, CBT-I reduced symptoms of insomnia, persecutory ideation, and perceptual abnormalities (Freeman et al., 2017). A different study from this same research group focused instead on targeting worry in schizophrenia patients, and found that a CBT intervention targeting worry significantly reduced worry and persecutory delusions, with a mediation analysis revealing that change in worry was a significant mediator of change in delusions (Freeman, Dunn, et al., 2015). These studies suggest that targeting sleep quality and mediating variables can be an effective strategy for alleviating both fully psychotic and subthreshold psychosis symptoms. Due to the interrelated nature of these variables, it is highly

likely that targeting any one piece—whether it be mood symptoms, sleep, exercise, or emotion regulation—will have beneficial effects on APPS and distressing psychological symptoms more broadly. Therefore, it is possible that the ideal approach to treating APPS in CHR individuals, or PLEs in the general population, is to take a holistic approach to treatment. Providers can target poor sleep, affective symptoms, coping strategies, and substance use in an effort to reduce overall symptom distress, and provide patients with the skills to cope with, or even maybe prevent, worsened psychosis-spectrum symptoms later in life.

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