Journal of Affective Disorders 215 (2017) 30–36

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Longitudinal sleep phenotypes among offspring of bipolar parents and community controls

Jessica C. Levenson[a,*], Adriane Soehner[a], Brian Rooks[a], Tina R. Goldstein[a], Rasim Diler[a], John Merranko[a], David Axelson[b], Ben I. Goldstein[c], David A. Brent[a], Danella Hafeman[a], Mary Beth Hickey[a], Kelly Monk[a], Dara Sakolsky[a], David J. Kupfer[a], Boris Birmaher[a]

[a] Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA
[b] Nationwide Children's Hospital Research Institute and The Ohio State University College of Medicine, Columbus, OH, USA
[c] Department of Psychiatry, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

ARTICLE INFO

Keywords:
Mood
Latent transition analysis
Longitudinal
At-Risk
Phenotype

ABSTRACT

Background: Sleep disturbances are a prominent feature of bipolar disorder (BP). However, it remains unclear how sleep *phenotypes* may evolve among at-risk youth, and their relevance to BP onset.
Methods: Pittsburgh Bipolar Offspring Study (BIOS) offspring (ages 10–18) and their parents completed assessments approximately every two years pertaining to current psychopathology and offspring sleep habits. A latent transition analysis (LTA) identified latent sleep groups within offspring based on their ratings of six sleep domains using the School Sleep Habits Survey. Demographic and clinical characteristics were compared between sleep groups. Logistic regression tested links between sleep group and BP onset at the subsequent assessment.
Results: The LTA model identified latent groups of good, poor, and variable sleepers. We observed an overall trend of good sleep becoming variable, and then poor, as youth age. Offspring in the poor sleep group were more likely to have psychopathology. Adjusting for age and depression, poor sleepers had nearly twice the odds of developing BP relative to good (OR=1.99, CI=0.45–8.91) or variable (OR=2.03, CI=0.72–5.72) sleepers.
Limitations: Limitations include the use of *proximal* sleep phenotypes to predict BP onset, and a self-report measure of sleep
Conclusions: We found three non-overlapping sleep phenotype groups in a large sample of offspring of bipolar probands and offspring of demographically-matched community control parents. Clinicians should consider that youth will likely experience variable and/or poor sleep as they age, and that at-risk youth with *poor* sleep may be at increased risk of developing MDD and BP at their next assessment.

1. Introduction

Incidence rates of bipolar disorder (BP) rise during the mid-teens and early twenties (Kessler et al., 2005), making adolescence a particularly vulnerable time for youth at clinical and familial risk for BP. As compared to adult onset BP (> 18 yr), the development of BP during youth is associated with a more adverse course of illness, including greater symptom severity, fewer days euthymic, comorbid psychopathology, and greater functional impairment (Perlis et al., 2009; Post et al., 2010; Suominen et al., 2007). Thus, there is a need to identify and characterize modifiable factors that contribute to BP risk in adolescents at high risk for developing the disorder. Recent work indicates that sleep disturbances play a central role in mood dysregulation and BP illness onset in those with a genetic vulnerability to the disorder (e.g.,Meyer and Maier, 2006; Levenson et al., 2015). Thus, the present study examines the role of sleep behavior as a factor that increases risk of BP among youth at familial risk for the disorder.

Sleep disturbances are a prominent and complex feature of BP, which may include features of insomnia (e.g., sleep continuity disturbances), hypersomnolence (e.g., excessive sleepiness), irregular sleep-wake schedules (e.g., variable sleep timing), delayed sleep phase (e.g., late sleep schedule), or reduced sleep need (Kanady et al., 2015). Studies of BP in adult and pediatric populations consistently show that sleep disturbances occur during acute episodes and persist between episodes in the majority of BP patients (Ng et al., 2014; Kanady et al., 2015; for review see Harvey, 2008; Harvey et al., 2005, 2006).

* Correspondence to: 3811 O'Hara Street, Pittsburgh, PA 15213, USA.
E-mail address: levensonjc@upmc.edu (J.C. Levenson).

http://dx.doi.org/10.1016/j.jad.2017.03.011
Received 19 December 2016; Received in revised form 27 January 2017; Accepted 5 March 2017
Available online 06 March 2017
0165-0327/

Moreover, sleep is significantly disturbed in individuals *at risk* for BP; for example, baseline sleep variables, such as frequent waking during the night, significantly predict the onset of BP among offspring of bipolar parents (Levenson et al., 2015). Still, findings have been inconsistent with regard to which sleep disturbances are most relevant to the onset of BP (Ritter et al., 2011). Work in offspring of bipolar parents (OBP) has predominantly focused on sleep symptoms embedded within diagnostic criteria for depression and (hypo)mania (Correll et al., 2014). Since sleep disturbances in BP may include a complex combination of features, these clusters or patterns of sleep disturbances may not fit neatly into traditional diagnostic categories for sleep disorders. It remains unclear how sleep phenotypes may evolve among high-risk youth, and their relevance to the onset of BP.

Understanding the evolution of sleep phenotypes across the school age years may be particularly vital for youth at-risk for BP, as sleep patterns undergo great change from childhood into adolescence even in typically developing youth (Carskadon et al., 2004). Sleep patterns are biologically regulated by two processes: a circadian rhythm that determines our daily sleep and wake rhythms based on structures in the hypothalamus of the brain, and a homeostatic process that determines sleep drive based on prior sleep and wakefulness of the individual (Harvey et al., 2006; Borbely, 1982). Shifts in these interrelated, but *distinct,* sleep regulatory processes during adolescence result in delayed sleep-wake patterns. These biological changes, in conjunction with psychosocial factors – such as earlier school start times, extracurricular activities, and peer socializing – contribute to developmental increases in insufficient sleep (Carskadon, 2011). Importantly, developmental shifts in sleep patterns overlap with those disrupted in BP, and thus may be particularly problematic for high-risk youth.

The aim of the present study was to characterize sleep phenotypes, rather than individual sleep parameters, among OBP and offspring of community controls (OC) from ages 10 through 18. The phenotypic approach allows for the identification of latent clusters of co-occurring sleep disturbances, rather than individual sleep parameters, facilitating the assessment of BP risk. To do so we used a data-driven approach that considers six core aspects of sleep. Five sleep domains included here (quality, alertness, timing, efficiency, and duration), identified in Buysse's (Buysse, 2014) recent work defining *sleep health,* were selected because they are associated with health outcomes, are continuous measures, have face validity, and can be measured across several levels of analysis (e.g., self-report, behavioral; (Buysse, 2014)). Importantly, many of these sleep dimensions demonstrate change over development and are implicated in BP (Carskadon, 2011; Harvey et al., 2006).

The longitudinal Pittsburgh Bipolar Offspring Study (BIOS) provides a unique opportunity to address these questions. BIOS prospectively assesses sleep behavior in a large sample of OBP and OC, some of whom (in both groups) had non-BP psychopathology. We aimed to extend the results of our cross-sectional study (Levenson et al., 2015), showing that baseline sleep disturbance may be a prognostic indicator of the development of BP in high-risk youth. Using data from baseline and follow-up BIOS assessments, we characterized the *longitudinal* sleep phenotypes of OBP and OC during the middle- and high-school years. Sleep groups were then compared on their clinical and demographic features at each age. Last, we examined the prospective relationship between sleep phenotype group and onset of BP among OBP.

2. Method

The methodology for BIOS has been described in detail in prior reports (Levenson et al., 2015; Birmaher et al., 2009). This study was approved by the University of Pittsburgh Institutional Review Board.

2.1. Participants

2.1.1. Parents (Probands)

Parents with BP were recruited through advertisements (65%), adult BP studies (31%), outpatient clinics (1.3%), and random digit dialing (2.6%). Parents met criteria for BP I or II according to the Diagnostic and Statistical Manual, Version-IV (DSM-IV) (American Psychiatric, 2000). Community control parents were healthy or diagnosed with non-BP psychiatric disorders, grouped-matched by age, sex, and neighborhood. Community controls were recruited using local population-based random dialing telephone surveys based on the demographic location of the parents with BP. For community control offspring, neither biological parent could have BP and or a first-degree relative with BP. In order to recruit a sample of probands who could feasibly participate in the study, all parents were excluded for: current or lifetime diagnoses of schizophrenia; intellectual disability; mood disorders secondary to substance abuse, medical conditions, or medications; and living more than 200 miles outside the Pittsburgh area.

2.1.2. Offspring

Offspring ages 6–18 from each family were included. Children who were unable to feasibly participate in the research procedures (e.g., for intellectual disability or pervasive developmental disorder) were not included.

2.2. Procedures

Clinicians obtained consent from parents and assent from offspring. Parents and offspring were assessed for psychiatric disorders, sleep patterns and disturbances, and other domains of interest. Parents and offspring repeated assessments roughly every two years (mean=2.18 years, S.D.=0.16) and also completed sociodemographic characteristics and pubertal development questionnaires.

Probands' DSM-IV psychiatric disorders were assessed through structured clinical interview; parents were interviewed about their children, and children were directly interviewed for the presence of lifetime psychiatric disorders and mood symptoms. Bachelors- or masters-level interviewers completed assessments after achieving ≥80% agreement with a certified rater for psychiatric disorders. Independent interviewers assessed parental psychopathology and their offspring's psychopathology. All data were presented to a child psychiatrist for diagnostic confirmation, who was blinded to the psychiatric status of the parents. When necessary, offspring medical and psychiatric records were obtained and reviewed by their interviewers.

Offspring ages 8–18 completed a measure of sleep behavior and circadian preference, the School Sleep Habits Survey (SSHS); (Wolfson and Carskadon, 1998) The SSHS was added to the assessment battery in November 2003 – two years after BIOS started recruiting participants. As with our previous study (Levenson et al., 2015), data from the assessment time point when the SSHS was first completed by both parents and offspring was considered the baseline. Every subsequent follow-up assessment until age 18 was included. Because youth were assisted in completing the SSHS at ages 8 and 9, only SSHS data collected when the offspring were between ages 10 and 18 were included to ensure true self report (n=661, 1433 total observations). Participants had an average of 2.11 assessments (S.D.=0.995, range=1–4); among those who had ≥1 SSHS assessment between ages 10–18 (n=409) the assessments spanned an average of 3.63 years (SD=1.63, range=0.94 to 7.35).

2.3. Measures

The Petersen Pubertal Developmental Scale (PDS); (Petersen et al., 1988) and respective Tanner stages (Marshall and Tanner, 1969, 1970) were used to evaluate pubertal development. Pubertal status was