



Research report

The effect of poor sleep quality on mood outcome differs between men and women: A longitudinal study of bipolar disorder



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ABSTRACT

Background: Sleep disturbance is bi-directionally related to mood de-stabilization in bipolar disorder (BD), and sleep quality differs in men and women. We aimed to determine whether perception of poor sleep quality would have a different effect on mood outcome in men versus women.

Methods: We assessed association between sleep quality (Pittsburgh Sleep Quality Index (PSQI)) at study intake and mood outcome over 2 years in subjects from the Prechter Longitudinal Study of Bipolar Disorder ($N=216$; 29.6% males). The main outcome measure was the severity, variability, and frequency of mood episodes measured by self-report over 2 years of follow-up. Multivariable linear regression models stratified by sex examined the relationship between PSQI with mood outcomes, while age, stressful life events, mood state and neuroticism at baseline were controlled.

Results: In women, poor sleep quality at baseline predicted increased severity ($B=0.28$, $p < 0.001$) and frequency of episodes ($B=0.32$, $p < 0.001$) of depression, and poor sleep quality was a stronger predictor than baseline depression; poor sleep quality predicted increased severity ($B=0.19$, $p < 0.05$) and variability ($B=0.20$, $p < 0.05$) of mania, and frequency of mixed episodes ($B=0.27$, $p < 0.01$). In men, baseline depression and neuroticism were stronger predictors of mood outcome compared to poor sleep quality.

Limitations: We measured perception of sleep quality, but not objective changes in sleep.

Conclusions: In a longitudinal study of BD, women reported poorer perceived sleep quality than men, and poor sleep quality predicted worse mood outcome in BD. Clinicians should be sensitive to addressing sleep complaints in women with BD early in treatment to improve outcome in BD.

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1. Introduction

Bipolar disorder (BD) is a recurrent, disabling illness. Though BD is an episodic illness, individuals with BD suffer from depressive symptoms up to 32% of the time, and manic symptoms about 9% of the time (Judd et al., 2002). Subsyndromal and mixed symptoms are prevalent, and contribute to restricting the effort of individuals with

BD to achieve life goals in areas such as education, occupation, and personal relationships (Judd et al., 2005).

Poor sleep quality is a state marker and symptom of depressive and manic episodes (Goodwin and Jamison, 2007). Lack of sleep can incite mania, and sleep deprivation has been shown since the 1970s to treat depressions (Wu and Bunney, 1990; Jackson et al., 2003), especially in bipolar disorder (Barbini et al., 1998; Colombo et al., 1999). Insomnia and poor sleep quality has been linked to worse symptom severity and poor outcome in bipolar disorder (Wu and Bunney, 1990; Colombo et al., 1999; Bauer et al., 2006; Perlman et al., 2006; Gruber et al., 2009; Gruber and Miklowitz et al., 2011). Also, sleep-disordered breathing, primary insomnia and sleep phase disorders are often comorbid with bipolar disorder, begging the question of these pathologies being related to the underlying mood pathology (Kripke et al., 1978; Wehr, 1992; Harvey, 2008; Soehner et al., 2013; Naqvi et al., 2014).

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Rates and phenotypes of mood disorders differ between men and women. Women of reproductive age were more prone to depression in the Stanley Foundation bipolar disorder cohort (Altshuler et al., 2010), but not in the STEP-BD study (Baldassano et al., 2005). In addition, the comorbidity of BD with illnesses that present with gender differences (including anxiety disorders (Baldassano et al., 2005; Baldassano, 2006; Altshuler et al., 2010; Saunders et al., 2012), migraine (Fasmer, 2001; Low et al., 2007; Baptista et al., 2012; Saunders et al., 2014), and eating disorders (Baldassano et al., 2005; Baldassano, 2006; Jen et al., 2013)) has been shown to cause more depression and worse course of illness in BD. Women in the general population report more insomnia than men during the reproductive years at a ratio of 1.4:1.0, (Ohayon, 2002; Zhang and Wing, 2006; Phillips et al., 2008; Fernandez-Mendoza et al., 2012; Singareddy et al., 2012; Vgontzas et al., 2012), and persistence of insomnia has been associated with depressive disorders, as well as sleep misperception (Fernandez-Mendoza et al., 2011; Fernandez-Mendoza et al., 2012).

Sleep and gender are both important factors in influencing course of illness in bipolar disorder (Baldassano, 2006; Gruber et al., 2009; Eidelman et al., 2010; Gruber et al., 2011; Saunders et al., 2012; Saunders et al., 2014). Women in the general population have more insomnia than men and women are also more prone to mood disorders and different courses of illness in BD. We investigated the relationship between perceived sleep quality and mood outcome in a cohort of patients with BD that were deeply-phenotyped and followed prospectively for two years. We hypothesized women would be more sensitive to the effect of poor sleep quality on mood outcome, and that sleep would differentially affect mood outcome in men and women with bipolar disorder.

2. Methods

2.1. Participants

The Prechter Longitudinal Study of Bipolar Disorder at the University of Michigan (UM) is an IRB approved observational study of outcomes in bipolar disorder (IRBMED HUM000606). Participants in the Prechter Longitudinal Study were evaluated initially for a baseline and study intake assessment described below and followed long-term with self-reported questionnaires and yearly visits. Patients with BD (bipolar disorder type I, bipolar disorder type II, schizoaffective disorder, bipolar type or bipolar disorder NOS, Table 1) and healthy controls (HC) with no personal or family history of mood or psychotic disorders were included.

2.2. Analytic cohort

The clinical sample for this investigation included participants recruited at the University of Michigan between 2005 and 2010, and data were extracted in 2/2012. Inclusion criteria include: diagnosis of BD; exclusion criteria include: mental retardation, active substance dependence, head injury or medical illness causing BD. The cohort selected for analysis included patients with DSM-IV TR BD I, II, NOS or Schizoaffective disorder, bipolar type ($n=216$) who completed the Pittsburgh Sleep Quality Index (PSQI) at baseline. Participants were excluded in the current analysis if they did not have complete data on the PSQI ($n=75$).

2.3. Process

At baseline, clinicians administered the Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et al., 1994), Hamilton

Depression Rating Scale – 21 with Atypical (HDRS) (Hamilton, 1960) and Young Mania Rating Scale (YMRS) (Young et al., 1978), and recorded height and weight. The DIGS is a clinician-administered diagnostic interview that collects self-reported demographic data including race and ethnicity, and includes the ability to assess the lifetime course of mood disorder as well as associated features of mood illness of the individual, and a comprehensive assessment of psychiatric and medical illnesses. Physicians, psychologists, and masters-level mental health professionals completed standardized training in the study instruments, and a best-estimate procedure was used to verify diagnoses (Leckman et al., 1982). A baseline set of self-rating questionnaires was completed. Follow-up questionnaires including the Patient Health Questionnaire (PHQ-9) and the Altman Self-Rating Mania Scale (ASRM) were sent to participants every two months. Median number of follow-up questionnaires completed in the 24-month period was 9.0 for both PHQ-9 and ASRM (minimum=2, maximum=13).

2.4. Main outcomes

Our dependent variable of interest was mood outcome over time, characterized by severity, variability, and frequency of clinically significant symptoms of depression or mania through the duration of a two-year follow-up period. Severity of depression was defined for each individual by the maximum PHQ-9 score over the follow up period (maximum=27.00, minimum=0); severity of mania was defined for each individual by the maximum ASRM score during follow up (maximum=20.00, minimum=0). Variability of depression was defined for each individual by the standard deviation in PHQ-9 scores over the duration of follow up (maximum=12.73, minimum=0); variability of mania was defined by the standard deviation in ASRM scores over the duration of follow-up (maximum=10.31, minimum=0). The proportion of the follow-up period that the individual had a PHQ-9 or ASRM score over 5 defined the frequency of clinically significant depressive, manic or mixed symptoms (maximum=1.00, minimum=0).

We assessed sleep quality with the Pittsburgh Sleep Quality Inventory (PSQI; Buysse et al., 1989). The PSQI obtains a general measure of sleep quality and the total score is derived from seven subscales: sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, sleep medication, and daytime dysfunction. The Life Events Occurrence Survey (LEOS) assesses for stressful life events in the past 6-month period (McKee et al., 2005). The NEO PI is a dimensional measure of personality, which includes Neuroticism, defined as the tendency to experience negative valence emotions including depression and anxiety (Costa and McCrae, 1992; McCrae and Costa, 2003).

2.5. Data and statistical analysis

Values of continuous variables were compared between males and females using two-sample *t*-tests, and categorical variables were compared using the Pearson chi-square test. All independent variables were standardized, and standardized regression coefficients are reported. Initial models were created to include only PSQI score, gender and the interaction term, which was not significant for any model. Linear multivariate regression models stratified by sex were created to determine the influence of PSQI on mood outcome, accounting for covariates of interest including age, baseline mood symptoms, and recent stressful events and neuroticism. Stress and neuroticism were included because they have been found at baseline to correlate with poor sleep quality independent of mood (Saunders et al., 2013). Models were run on all women, and repeated for all women reported to not be in menopause.

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