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You'll feel better in the morning: Slow wave activity and overnight mood regulation in interepisode bipolar disorder

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Abstract

Background—Sleep disturbances are prominent correlates of acute mood episodes and inadequate recovery in bipolar disorder (BD), yet the mechanistic relationship between sleep physiology and mood remains poorly understood. Using a series of pre-sleep mood inductions and overnight sleep recording, this study examined the relationship between overnight mood regulation and a marker of sleep intensity (non-rapid eye movement sleep slow wave activity; NREM SWA) during the interepisode phase of BD.

Methods—Adults with interepisode BD type 1 (BD; n=20) and healthy adult controls (CTL; n=23) slept in the laboratory for a screening night, a neutral mood induction night (baseline), a happy mood induction night, and a sad mood induction night. NREM SWA (0.75–4.75Hz) was derived from overnight sleep EEG recordings. Overnight mood regulation was evaluated using an affect grid pleasantness rating post-mood induction (pre-sleep) and the next morning.

Results—Overnight mood regulation did not differ between groups following the sad or happy inductions. SWA did not significantly change for either group on the sad induction night compared to baseline. In BD only, SWA on the sad night was related to impaired overnight negative mood regulation. On the happy induction night, SWA increased relative to baseline in both groups, though SWA was not related to overnight mood regulation for either group.

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Conclusions—These findings indicate that SWA disruption may play a role in sustaining negative mood state from the previous night in interepisode BD. However, positive mood state could enhance SWA in bipolar patients and healthy adults.

Introduction

Bipolar disorder (BD) is characterized by mood regulation impairment, oscillating between persistently elevated or irritable mood and sustained periods of depressed mood (APA, 2013). Even between episodes, individuals with BD remain seriously symptomatic (Joffe *et al.*, 2004) and exhibit significant mood lability (Aas *et al.*, 2014). Though sleep disturbances are among the most prominent correlates of mood episodes and inadequate recovery in BD (Harvey, 2008), it remains unclear how specific aspects of sleep physiology may relate to negative and positive mood dysregulation.

Disrupted sleep homeostasis is a hypothesized contributor to sleep and mood impairments in affective disorders (Borbely and Wirz-Justice, 1982). Sleep homeostasis is a physiological sleep regulatory process defined by increasing pressure to sleep during extended wakefulness, followed by dissipating sleep intensity across the sleep period (Borbely *et al.*, 2016). The amount of slow wave activity (SWA; EEG power density 0.75–4.75 Hz) during non-rapid eye movement (NREM) sleep is the best-characterized marker of sleep intensity (Borbely *et al.*, 2016). The S-deficiency hypothesis of depression proposes that deficient build-up of sleep pressure and reduced sleep intensity (SWA) may produce or sustain depressed mood (Borbely and Wirz-Justice, 1982). In accord with this hypothesis, SWA deficits and reduced visually-staged slow wave sleep (SWS; NREM stage 3 and 4) are generally observed in unipolar depression relative to controls (See Armitage, 2007 for review). Moreover, selective slow-wave sleep deprivation can have an antidepressant effect among unipolar depressed patients (Cheng *et al.*, 2015, Landsness *et al.*, 2011), which may be due to a "resetting" of waking sleep pressure and greater SWA rebound the next night (Landsness *et al.*, 2011). While the precise mechanisms linking SWA and depressed mood remain to be delineated, research suggests that increased sleep intensity may facilitate cortical plasticity in brain regions supporting a host of cognitive-affective processes implicated in affective disorders (Huber *et al.*, 2008, Tononi, 2009).

SWA has been less extensively studied in BD. Only one study in bipolar depression (n = 8 per group) has measured SWA, reporting no differences relative to matched controls (Mendelson *et al.*, 1987). However, studies assessing visually-staged sleep indicate lower SWS in bipolar depression relative to healthy adults, at levels akin to unipolar depression (Asaad *et al.*, 2016, Fossion *et al.*, 1998, Gillin *et al.*, 1979, Linkowski *et al.*, 1986). While no studies to date have selectively deprived slow-wave sleep in bipolar depression, sleep deprivation also has antidepressant effects in bipolar depression and can induce (hypo)mania in a subset of cases (Benedetti and Colombo, 2011). SWS deficits in (hypo)mania may be comparable to depression (Asaad *et al.*, 2016, Linkowski *et al.*, 1986), though findings are inconsistent (Hudson *et al.*, 1988). While altered SWS has not been observed in interepisode BD (Eidelman *et al.*, 2010, Knowles *et al.*, 1986, Sitaram *et al.*, 1982), one study reported that higher baseline SWS predicted greater mania symptom severity at 3-month follow-up (Eidelman *et al.*, 2010).

Overall, there is some support for SWS deficits in bipolar depression and (hypo)mania. This raises the possibility that BD patients, like their unipolar depressed counterparts, may be vulnerable to mood-related changes in sleep intensity. Initial prospective findings in interepisode BD, along with the well-documented antidepressant response to sleep deprivation, suggest that altered sleep intensity could play a role in generating or sustaining mood disturbance in BD. However, whether waking mood affects sleep intensity remains unclear. Initial experimental work in healthy adults suggests that pre-sleep affect may alter slow wave sleep (Talamini *et al.*, 2013). Among those with affective disorders, who are more vulnerable to mood regulation impairments, it is important to disambiguate whether acute change in waking mood produces SWA deficits and/or whether deficient SWA maintains mood disturbances overnight. The interepisode phase of BD provides unique opportunity to experimentally probe such relationships.

The aim of the present study was to examine whether adults with interepisode BD experience experimentally-induced mood disruptions in SWA, and whether deficient SWA is related to impaired overnight mood regulation. This study involved further analysis of an existing dataset (Eidelman *et al.*, 2010, Talbot *et al.*, 2009). Adults with interepisode BD and healthy adult controls spent 4 nights in the sleep laboratory: 1 screening night, 1 neutral (baseline) mood induction night, 1 negative (sad) mood induction night, and 1 positive (happy) mood induction night. The first aim was to assess whether interepisode bipolar patients and healthy adults exhibited an overnight reduction in negative and positive mood following the sad and happy mood inductions, respectively. Due to documented mood regulation deficits in interepisode BD (e.g., Aas *et al.*, 2014), it was hypothesized that the bipolar group would exhibit a smaller overnight change in mood. The second aim was to evaluate the effects of the sad and happy mood inductions on SWA relative to baseline. Based on evidence of reduced SWA in depression and (hypo)mania, we predicted that SWA would be lower after both mood inductions relative to baseline in the bipolar group, but not in the control group. The final aim was to assess associations between SWA and overnight changes in mood on the sad and happy induction nights. We predicted that lower SWA would be associated with impaired overnight mood regulation in bipolar patients.

Methods

Participants

Participants included: 20 adults with interepisode *DSM-IV-TR* bipolar disorder type I (BD) and 23 healthy adult controls (CTL) with no history of psychiatric or sleep disorders. Participants were drawn from a larger protocol, results from which have been described in previous reports (e.g., Eidelman *et al.*, 2010, Talbot *et al.*, 2009). All procedures contributing to this work comply with the ethical standards of relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Inclusion criteria for all participants were: (a) negative for narcolepsy, sleep apnea (AHI>5), restless leg syndrome or periodic limb movement disorder (PLMA>15) on the basis of polysomnography; (b) met criteria for interepisode symptom cutoffs based on prior research (Chengappa *et al.*, 2003; Thompson *et al.*, 2005): a score of 7 on the Young Mania Rating Scale (YMRS; Young *et al.*, 1978) and a score of 11 on the Inventory of Depressive

Symptomatology–Clinician Rated (ISD-C; Rush *et al.*, 1996); (c) had no history of severe head trauma, stroke, neurological disease, or severe medical illness. BD were included if they: (a) met *DSM–IV–TR* bipolar I disorder (American Psychiatric Association, 2000); (b) did not meet criteria for substance or alcohol abuse or dependence in the past 3 months; (c) were under the care of a psychiatrist. CTL could not meet *DSM–IV–TR* criteria for any lifetime Axis I disorder.

In order to be included in the present analysis, participants had to meet criteria for BD type I, and complete the baseline (neutral mood induction) and at least one mood induction (sad or happy) sleep recording. From the original sample (BD n=28; CTL n=28), 4 BD participants had BD type II. Additional participants were excluded on the basis of poor quality sleep recording/excessive EEG artifact on the baseline night (BD=2; CTL=4) or both mood induction nights (BD=2, CTL=1). For the sad induction night, additional participants were lost to dropout (BD=1) or poor quality recordings (BD=2; CTL=2), leading to a total of 17 BD and 21 CTL participants for sad night analyses. Similarly, for the happy induction night additional participants were lost to dropout (BD=1; CTL=1) or poor quality recordings (BD=3; CTL=1), leading to a total of 16 BD and 21 CTL participants for happy night analyses.

Clinical Functioning Measures

Structured Clinical Interview for DSM-IV (SCID; First *et al.*, 1997)—*DSM-IV-TR* Axis I diagnoses were confirmed using the SCID.

Manic and Depressive Symptoms—Current symptoms of mania were measured using the 11-item, clinician rated Young Mania Rating Scale (YMRS; Young *et al.*, 1978). Current symptoms of depression were assessed using the 30-item, clinician-rated Inventory of Depressive Symptomatology (IDS-C; Rush *et al.*, 1996). YMRS (7) and IDS-C (11) scores were used to confirm current interepisode status (i.e., neither currently manic nor depressed) for both groups.

Illness Course—BD course characteristics were assessed using a validated charting procedure (National Institute of Mental Health retrospective Life-Charting Methodology; Denicoff *et al.*, 1997, Leverich and Post, 1997). Age of BD onset, illness duration, and the number of lifetime manic and depressive episodes were derived.

Medication Tracking and Dosage—Medication name and dosage were recorded at each visit. Medication effects were examined using an approach developed for neuroimaging research (Phillips *et al.*, 2008a). Each medication was re-categorized by medication class, and dose was categorized as 0(no medication), 1(low), or 2(high) based on published parameters and chlorpromazine-equivalent mean effective daily doses (Davis and Chen, 2004, Sackeim, 2001). A composite measure of medication load was created for each participant by summing across dosage strength codes and classes (Almeida *et al.*, 2009).

Sleep Measures

***Duke Structured Interview for Sleep Disorders* (DSISD; Edinger *et al.*, 2004)—** The DSISD is a semi-structured interview that assesses research diagnostic criteria for sleep disorders; it has good reliability and validity (Edinger, 2009).

***Polysomnography* (PSG)—**Sleep was recorded using overnight PSG with a Compumedics 802 Siesta system (Compumedics, Charlotte, NC). PSG involves the continuous and simultaneous recording of EEG, electrooculogram (EOG), and electromyogram (EMG) to score sleep. Recording channels included four EEG derivations (C3/A2, C4/A1, O1/A2, O2/A1), two EOG leads, and two submental EMG sensors. On the first overnight visit, heart rate, blood oxygen, nasal and oral air flow, thoracic and abdominal effort, and leg motion were monitored. PSG data were staged in 30-second epochs using standard Rechtscaffen & Kales criteria (Rechtschaffen, 1968).

Power Spectral Analysis—Sleep EEG analyses were performed offline in MATLAB R2011b (Mathworks, Natick, MA) and EEGLAB11 (http://sccn.ucsd.edu/eeglab/). Power spectral analysis was carried out in accordance with published methods (van der Helm *et al.*, 2011). EEG channels were re-referenced to the average of the left and right mastoid (A1, A2), run through high-pass (0.5Hz) and low-pass (55Hz) Finite Impulse Response (FIR) filtering, and split into 5-second epochs. EEG recordings were visually inspected for 5-second epochs containing muscle, cardiac and eye-movement artifacts; artifact-laden epochs were manually rejected. Power spectral density ($\mu V^2/Hz$) was calculated using a Fast Fourier Transform (FFT) on each hamming-windowed 5-second epoch at 128Hz, yielding a frequency resolution of 0.2Hz. FFT results were sorted according to sleep stage and averaged across NREM (stages 2–4). NREM SWA was defined as integrated power in the 0.75–4.75 Hz range. Relative SWA (expressed as a percentage) was derived by dividing SWA by the integrated power of the entire spectrum. For each night, values ±3.0 standard deviations were Winsorized (<1% of all data). Relative SWA derived from the central EEG derivation C4 was used for hypothesis testing.

Mood Ratings

Affect Grid—The affect grid (Russell *et al.*, 1989) is a self-report rating of pleasure on the horizontal axis (–4=*extremely unpleasant*, 0=*neutral*, 4=*extremely pleasant)* and arousal on the vertical axis (–4=*extremely low arousal*, 0=*neutral*, 4=*extremely high arousal*); it has adequate reliability and validity (Russell *et al.*, 1989).

Mood Induction

Mood Induction—The mood induction technique was adapted from well-validated procedures (Albersnagel, 1988, Eich *et al.*, 1994, Stein *et al.*, 2000, Williams *et al.*, 2002) that combine continuous music with autobiographical recall. For the happy and sad mood inductions, participants were told that they would listen to a selection of music to assist them in developing a happy (or sad) mood, and then were then instructed to try hard to develop an intense mood state by concentrating on ideas and images that make them feel happy (or sad). For the neutral induction, participants were asked to focus on neutral topics (e.g., directions

to a familiar place or the layout of furniture at home) while listening to the classical music. See Supplemental Methods regarding music selection.

Procedure

At the first laboratory visit, participants completed written informed consent. Participants were then administered the SCID, DSISD, YMRS, IDS-C, and life chart to assess diagnostic status, symptom severity, and clinical course. Eligible participants were provided with an instruction sheet for the day prior to subsequent overnight lab visits; these included: (1) restrict caffeine intake to <2 cups coffee (or equivalent) before noon and (2) refrain from taking over-the-counter medications.

For all overnight visits, participants arrived at the laboratory 2 hours prior to their habitual bedtime. Overnight visit eligibility was then assessed by a clinician, including compliance with overnight instructions, medication use, and interepisode status using the YMRS and IDS-C. If YMRS or IDS-C scores exceeded interepisode cut-offs, a safety assessment was completed before the participant was sent home (without completing the overnight). Overnight visits were each approximately 2 weeks apart; some participants did not complete all visits (see Supplemental Procedures for details).

At the first overnight, participants underwent full clinical polysomnography to assess for sleep disorders (e.g., sleep apnea, PLMD). At the three subsequent overnight visits, mood inductions were administered. A neutral mood induction was administered at the second overnight visit, and then the order of the happy and sad inductions was counterbalanced between the third and fourth overnight visits. In order to reduce demand effects, participants were told that they were engaging in two different experiments at these visits, a music study and a sleep study.

At each mood induction overnight visit (neutral, sad, happy), PSG equipment was first attached, followed by the mood induction administration in a private room. During mood inductions, participants rated their current affect, pleasure, and arousal at baseline, and every 5 minutes thereafter, using a computerized version of the Affect Grid. The neutral mood induction was 15 minutes for all participants and there was no mood cut-off at the end. Affect Grid mood thresholds of at least −3 (pleasure) for the sad induction and +3 (pleasure) for the happy induction were set based on previous methods (Eich *et al.*, 1994). Mood inductions ended at these thresholds, or at 40 minutes after the start of the induction. The final Affect Grid of the mood induction was used as the pre-sleep (post-induction) measure. Immediately after the mood induction, participants were escorted to the laboratory bedroom and allowed to sleep. Participants were awakened at the time they requested (approx. 9:00am at the latest). To mitigate the effects of sleep inertia upon morning mood reports, participants completed the Affect Grid roughly 20 minutes after awakening. Participants were debriefed at the end of their last visit.

Analytic Approach

Analyses were conducted in SPSS 20.0 (IBM Corporation, Somers, NY, 2012). Affect Grid pleasantness ratings were used to evaluate mood just prior to each mood induction (pre-induction), at the end of each mood induction (post-induction) and the morning following

the mood induction (morning). A 2 (Group; BD vs. CTL) × 3 (Time; pre-induction, post-induction, morning) repeated-measures analysis of variance (ANOVA) was conducted for each the sad and happy mood inductions. Overnight mood change was evaluated using a difference score (morning – post-induction affect grid pleasantness rating).

The effect of pre-sleep sad and happy mood inductions on SWA was examined using a series of 2 (Night; neutral vs. sad or happy mood induction) × 2 (Group; BD vs. CTL) repeated-measures ANOVA models. The neutral mood induction was used as a baseline night. As a few individuals did not complete both the happy and sad mood induction overnights, separate ANOVAs compared each mood induction (sad, happy) to baseline, to maximize statistical power.

In each group, spearman's rho correlation analyses evaluated whether SWA on the sad or happy mood induction nights was associated with overnight mood change (morning – post-induction affect grid pleasantness ratings) that same night.

On an exploratory basis, we conducted an analysis with sleep architecture variables paralleling the main sleep aims. Exploratory spearman rho correlations were also conducted to examine effects of illness course characteristics (see Supplemental Results), pre-sleep arousal, and medication load on SWA. The significance level was set at $p<0.05$ (two-sided) for all analyses.

Results

Baseline Demographic and Clinical Characteristics

The two groups did not significantly differ on any sociodemographic characteristics (Table 1). While BD exhibited significantly higher baseline manic and depressive symptoms (ps<0.05), scores were well below established interepisode cut-offs. Baseline (neutral induction night) bedtime and sleep duration sleep did not significantly differ between groups, though waketime was later in BD than CTL ($p<0.05$). Spearman correlation analyses assessed whether age, sex, depressive or manic symptoms scores were meaningfully associated with any mood or sleep EEG outcomes. No significant correlations emerged; therefore, these variables were not included as covariates in subsequent analyses.

Sad Mood Induction

Overnight Mood Regulation—There was neither a significant main effect of Group, $F(1,36)=2.61$, $p=0.115$, nor a significant Group X Time interaction effect, $F(1,36)=0.44$, $p=0.513$, on affect grid mood ratings across the sad mood induction overnight (Figure 1a). However, there was a significant main effect of Time, $F(1, 36)=92.70$, $p<0.001$. Posthoc paired samples t-tests confirmed a significant increase in negative mood from pre- to post-mood induction, $t(36)=9.68$, $p<0.001$, and a significant overnight decrease in negative mood from post-induction to morning, $t(36)=-8.15$, $p<0.001$.

Mood Induction Effects on SWA—Figure 2a illustrates SWA means on the baseline and sad mood induction overnights. There were no significant effects SWA across Group,

$F(1,36)=2.27$, $p=0.140$, Night, $F(1,36)=1.13$ $p=0.295$, or Group X Night, $F(1,36)=0.42$, $p=0.520$.

SWA-Overnight Mood Regulation Associations—Sad mood induction night SWA positively correlated with overnight mood change on the affect grid ($r=0.56$, $p=0.018$; Figure 3a) in BD such that higher SWA was related to greater improvement in negative mood; this association was not observed in CTL ($r=0.34$, $p=0.143$; Figure 3b).

Happy Mood Induction

Overnight Mood Regulation—There was neither a significant main effect of Group, $F(1, 41)=0.32$, $p=0.575$, nor a significant Group X Time interaction effect, $F(1,35)=0.92$, $p=0.343$, on mood ratings across the happy mood induction overnight (Figure 1b). There was a significant main effect of Time, $F(1, 35)=27.61$, $p<0.001$. Posthoc paired samples t-tests confirmed a significant increase in positive mood from pre- to post-mood induction, $t(36)=-4.79$, $p<0.001$, and a significant overnight reduction in positive mood from post-induction to morning, $t(36)=4.80$, $p<0.001$.

Mood Induction Effects on SWA—Figure 2b shows SWA on the baseline and happy mood induction overnights. There was a significant main effect of Night, $F(1,35)=5.64$, $p=0.023$, whereby SWA increased on the happy mood induction night relative to baseline in both groups. Effects of Group, $F(1,35)=0.00$, $p=0.996$, and Group X Night, $F(1,35)=1.25$, $p=0.271$, were non-significant.

SWA-Overnight Mood Regulation Associations—On the happy mood induction night, overnight mood change on the affect grid was not significantly correlated with SWA for both BD ($r=0.02$, $p=0.430$; Figure 3c) and CTL ($r=-0.14$, $p=0.543$; Figure 3d).

Sleep Architecture

Table 2 reports results from repeated measures ANOVAs evaluating sleep architecture variables (TST, TWT, N1, N2, SWS, REM) on the neutral vs. happy or sad induction nights. Baseline night means differ slightly between the sad and happy mood induction nights since a few individuals did not participate in both mood nights and a repeated measures analysis of variance excludes a participant if there is missing data on any of the observation points. Baseline sleep architecture has been described in previous reports from the full sample (Eidelman *et al.*, 2010, Talbot *et al.*, 2009). There were no significant effects of Group, Night or Group X Night for TST, N1, N2, or SWS (all $p>0.05$). There was a Group effect for TWT, such that BD had greater TWT than CTL at baseline relative to both the sad night and happy nights (both $p<0.05$). There was a main effect of Night for sad night REM sleep relative to baseline, such that both groups had greater REM relative to baseline ($p<.05$). Sleep architecture variables did not correlate with overnight mood change on the sad or happy nights (all $p>0.05$) with the exception of SWS. Paralleling SWA findings, sad night SWS was positively correlated with overnight negative mood change in BD ($r=0.61$, $p=0.009$), but not CTL ($r=-0.27$, $p=0.259$).

Pre-Sleep Arousal Ratings

No significant differences were observed between BD and CTL on post-induction affect grid arousal ratings for the sad (−1.41 vs. −1.55; $t(35)=-0.23$, $p=0.822$) and happy mood induction nights (−0.81 vs. −0.33; $t(35)=-0.61$, $p=0.543$). Post-induction arousal ratings did not correlate with SWA on the mood induction nights for either group ($ps>0.05$).

Medication Effects

In BD, medication load did not significantly differ between baseline versus the sad (4.29 vs. 4.12; $F(1,16)=1.31$, $p=0.269$) and happy mood induction nights (4.44 vs. 4.38; $F(1,15)=0.14$, $p=0.718$). Medication load and SWA were not significantly correlated on the baseline and sad mood induction nights ($ps>0.05$). Higher medication load correlated with lower happy night SWA at a trend level ($r=-0.45$, $p=0.083$).

Discussion

This study tested relationships between overnight mood regulation impairment, sleep intensity (indexed by SWA), and interepisode BD diagnosis. Findings included that: (1) overnight mood regulation in interepisode BD did not significantly differ from healthy adults, (2) inducing a positive mood state prior to sleep increased SWA relative to baseline across all participants, and (3) lower SWA was associated with attenuated overnight regulation of negative mood, but not positive mood, in bipolar patients.

Taking findings from the sad mood induction first, the prediction that the bipolar group would exhibit impaired overnight mood regulation was not supported. Both the bipolar and control groups exhibited intact overnight mood regulation, with negative mood prior to sleep generally regularizing to a neutral rating by the morning. This is consistent with previous research indicating that negative mood typically improves overnight in healthy adults (Cartwright *et al.*, 2003, Cartwright *et al.*, 1998). Impaired mood regulation in interepisode BD might only be evident after shorter spans of time during waking hours, though to our knowledge this question has not yet been systematically investigated. The present findings indicate that *overnight* mood regulation capabilities in interepisode BD may generally be comparable to healthy adults.

The sad mood induction did not have differential effects on SWA across the two groups. However, lower SWA on the sad mood induction night was related to attenuated overnight improvement in negative mood for bipolar patients only. This coheres with predictions of the S-deficiency hypothesis (Borbély, 1982), which proposes that deficient SWA may sustain depressed mood. Exploratory sleep architecture analyses further support this notion; lower sad night SWS also correlated with impaired overnight negative mood regulation in BD. A lack of correlation with REM sleep and other NREM stages suggest a *specific* role for sleep intensity (SWA/SWS) in overnight regulation of negative mood, consistent with prior reports (Cheng *et al.*, 2015). These results raise the possibility that slow-wave deficits in BD might sustain negative mood overnight.

Predictions for the happy mood induction night were generally not supported. On average, positive mood state prior to sleep decreased to a neutral rating by morning for both groups,

thus the bipolar group did not exhibit impaired overnight mood regulation relative to controls. Also contrary to our hypothesis, both groups exhibited *increased* SWA following the happy mood induction. Positive affect has previously been observed to be beneficial for sleep quality and efficiency in some studies (Ong *et al.*, 2013, Steptoe *et al.*, 2008), though this is the first study to our knowledge that has explored the effects of positive mood on SWA. Finally, there was not a significant association between SWA and overnight change in positive mood. The absence of a statistically significant relationship between SWA and overnight change in positive mood, in the presence of both positive mood-induced SWA changes and a reduction in positive mood from night to morning, raises the possibility that SWA may not be driving *overnight* change in positive mood. Perhaps overnight changes in positive versus negative mood are driven by different sleep-wake regulatory mechanisms. Tightly controlled forced desynchrony and constant routine protocols have determined that there is a circadian pattern in positive affect (Boivin *et al.*, 1997, Murray *et al.*, 2002), while there is less evidence for a clear 24-hr rhythm in negative affect (Boivin *et al.*, 1997). Thus, overnight change in positive mood may primarily be modulated by circadian, rather than homeostatic, factors.

Overall, these results may indicate differing associations between mood state and SWA. Though sad mood did not induce changes in SWA, lower SWA correlated with attenuated overnight improvement in negative mood in BD, adding to existing literature supporting the relevance of sleep homeostatic mechanisms for negative mood regulation. There was greater inter-individual variation in sad night SWA among BD (Figure 3a–b). Inter-individual differences in vulnerability to SWA disruption, and its impact on negative mood, may be linked to genetic susceptibility to affective disorders. For example, PER3 polymorphisms more prevalent in affective disorders are also related to inter-individual differences in homeostatic sleep pressure (Artioli *et al.*, 2007, Dallaspezia *et al.*, 2016). Conversely, the happy mood induction led to increased SWA relative to baseline in both groups, but SWA was uncorrelated with overnight change in positive mood. Effects of positive mood on central and peripheral physiology (Admon and Pizzagalli, 2015, Shiota *et al.*, 2011) may acutely bolster SWA, separate from circadian mechanisms proposed to govern 24-hr fluctuation in positive mood. Relevant to depression, and other psychiatric conditions with SWA deficiencies (e.g., schizophrenia; Hoffmann *et al.*, 2000), increasing pre-sleep positive mood may be means of enhancing SWA, as an alternative to sleep deprivation. However, further work is necessary to delineate the potentially distinct physiological mechanisms underpinning links between negative and positive mood with SWA.

While a key strength of this study is its unique combination of experimental mood manipulation with repeated within-subject PSG sleep assessments in BD, several limitations merit consideration. Only central sleep EEG derivations were analyzed. SWA deficits can be more pronounced in prefrontal and frontal areas (Plante *et al.*, 2012, Werth *et al.*, 1997), thus future studies of sleep in BD would benefit from utilizing hdEEG to explore topographic hypotheses. Sex differences in SWA are sometimes observed in unipolar depression, with some reports observing greater SWA in females (e.g., Plante *et al.*, 2012). While sex differences in SWA were not observed here, this may be due to the predominantly female sample and resulting lack of power to detect sex effects. Prior sleep and wakefulness also impact SWA (Borbély and Achermann, 2000). As this study was not initially designed to

assess SWA, participants were not instructed to keep a regular sleep-wake schedule before sleep monitoring; future studies should address this design limitation. This was a medicated sample of bipolar participants. Though medication load was not significantly associated with overnight mood change, medication could be affecting sleep physiology. Because this study was conducted across a span of several months, an unmedicated sample would be unfeasible and unsafe. More broadly, research on severe mental illness would be seriously hindered and lack generalizability if done in only medication-free samples (Phillips *et al.*, 2008b). The present findings remain clinically important given that the vast majority of BD patients are medicated.

In summary, the present findings provide preliminary support for a relationship between mood and sleep intensity(indexed by SWA) in interepisode BD. Lower SWA was associated with impaired overnight regulation of pre-sleep negative mood in BD, but not in controls. Pre-sleep positive mood increased SWA in both groups relative to baseline, though SWA was not related to overnight change in positive mood. The present findings suggest a potential interplay between mood and sleep intensity that may carry relevance for the management of mood dysregulation and sleep-wake disturbances in interepisode BD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

References

Aas M, Pedersen G, Henry C, Bjella T, Bellivier F, Leboyer M, Kahn JP, Cohen RF, Gard S, Aminoff SR, Lagerberg TV, Andreassen OA, Melle I, Etain B. Psychometric properties of the Affective Lability Scale (54 and 18-item version) in patients with bipolar disorder, first-degree relatives, and healthy controls. J Affect Disord. 2014; 172C:375–380.

Admon R, Pizzagalli DA. Corticostriatal pathways contribute to the natural time course of positive mood. Nat Commun. 2015; 6:10065. [PubMed: 26638823]

Albersnagel FA. Velten and musical mood induction procedures: a comparison with accessibility of thought associations. Behav Res Ther. 1988; 26:79–96. [PubMed: 3341999]

Almeida JR, Akkal D, Hassel S, Travis MJ, Banihashemi L, Kerr N, Kupfer DJ, Phillips ML. Reduced gray matter volume in ventral prefrontal cortex but not amygdala in bipolar disorder: significant effects of gender and trait anxiety. Psychiatry Res. 2009; 171:54–68. [PubMed: 19101126]

American Psychiatric Association. Diagnostic and statistical manual of mental disorders (4th Edition, Text revision). American Psychiatric Association; Washington, D.C.: 2000.

APA. Diagnostic and statistical manual of mental disorders: DSM-5. American Psychiatric Association; Washington, D.C.: 2013.

Armitage R. Sleep and circadian rhythms in mood disorders. Acta Psychiatr Scand Suppl. 2007:104–15. [PubMed: 17280576]

Artioli P, Lorenzi C, Pirovano A, Serretti A, Benedetti F, Catalano M, Smeraldi E. How do genes exert their role? Period 3 gene variants and possible influences on mood disorder phenotypes. Eur Neuropsychopharmacol. 2007; 17:587–94. [PubMed: 17512705]

Asaad T, Sabry W, Rabie M, El-Rassas H. Polysomnographic characteristics of bipolar hypomanic patients: Comparison with unipolar depressed patients. J Affect Disord. 2016; 191:274–9. [PubMed: 26688496]

Benedetti F, Colombo C. Sleep deprivation in mood disorders. Neuropsychobiology. 2011; 64:141–51. [PubMed: 21811084]

Boivin DB, Czeisler CA, Dijk DJ, Duffy JF, Folkard S, Minors DS, Totterdell P, Waterhouse JM. Complex interaction of the sleep-wake cycle and circadian phase modulates mood in healthy subjects. Archives of General Psychiatry. 1997; 54:145–52. [PubMed: 9040282]

Borbely A, Wirz-Justice A. Sleep, sleep deprivation and depression. Human Neurobiology. 1982; 1:205–210. [PubMed: 7185793]

Borbély AA. A two process model of sleep regulation. Hum Neurobiol. 1982; 1:195–204. [PubMed: 7185792]

Borbély, AA., Achermann, P. Homeostasis of human sleep and models of sleep regulation. In: Kryger, MH.T, R., Dement, WC., editors. Principles and Practice of Sleep Medicine. W. B. Saunders; Philadelphia: 2000. p. 377-390.

Borbely AA, Daan S, Wirz-Justice A, Deboer T. The two-process model of sleep regulation: a reappraisal. J Sleep Res. 2016; 25:131–43. [PubMed: 26762182]

Cartwright R, Baehr E, Kirkby J, Pandi-Perumal SR, Kabat J. REM sleep reduction, mood regulation and remission in untreated depression. Psychiatry Res. 2003; 121:159–67. [PubMed: 14656450]

Cartwright R, Luten A, Young M, Mercer P, Bears M. Role of REM sleep and dream affect in overnight mood regulation: a study of normal volunteers. Psychiatry Res. 1998; 81:1–8. [PubMed: 9829645]

Cheng P, Goldschmied J, Casement M, Kim HS, Hoffmann R, Armitage R, Deldin P. Reduction in delta activity predicted improved negative affect in Major Depressive Disorder. Psychiatry Res. 2015; 228:715–8. [PubMed: 26123231]

Dallaspezia S, Locatelli C, Lorenzi C, Pirovano A, Colombo C, Benedetti F. Sleep homeostatic pressure and PER3 VNTR gene polymorphism influence antidepressant response to sleep deprivation in bipolar depression. J Affect Disord. 2016; 192:64–9. [PubMed: 26707349]

Davis JM, Chen N. Dose response and dose equivalence of antipsychotics. J Clin Psychopharmacol. 2004; 24:192–208. [PubMed: 15206667]

Denicoff KD, Smith-Jackson EE, Disney ER, Suddath RL, Leverich GS, Post RM. Preliminary evidence of the reliability and validity of the prospective life-chart methodology (LCM-p). J Psychiatr Res. 1997; 31:593–603. [PubMed: 9368200]

Edinger JD, Bonnet MH, Bootzin RR, Doghramji K, Dorsey CM, Espie CA, Jamieson AO, McCall WV, Morin CM, Stepanski EJ. Derivation of research diagnostic criteria for insomnia: report of an American Academy of Sleep Medicine Work Group. Sleep. 2004; 27:1567–96. [PubMed: 15683149]

Edinger JD, Wyatt JK, Olsen MK, Stechuchak KM, Carney CE, Chiang A, et al. Reliability and validity of the Duke Structured Interview for Sleep Disorders for insomnia screening. 23rd Annual Meeting of the Associated Professional Sleep Societies, LLC. 2009

Eich E, Macaulay D, Ryan L. Mood dependent memory for events of the personal past. Journal of Experimental Psychology: General. 1994; 123:201–215. [PubMed: 8014613]

Eidelman P, Talbot LS, Gruber J, Hairston I, Harvey AG. Sleep architecture as correlate and predictor of symptoms and impairment in inter-episode bipolar disorder: taking on the challenge of medication effects. J Sleep Res. 2010; 19:516–24. [PubMed: 20408930]

First, M., Spitzer, R., Gibbons, M., Williams, J. Structured Clinical Interview for DSM IV Axis 1 Disorders: clinician version. American Psychiatric Press; Washington, DC: 1997.

Fossion P, Staner L, Dramaix M, Kempenaers C, Kerkhofs M, Hubain P, Verbanck P, Mendlewicz J, Linkowski P. Does sleep EEG data distinguish between UP, BPI or BPII major depressions? An age and gender controlled study. J Affect Disord. 1998; 49:181–7. [PubMed: 9629947]

Gillin JC, Duncan W, Pettigrew KD, Frankel BL, Snyder F. Successful separation of depressed, normal and insomniac subjects by EEG sleep data. Archives of General Psychiatry. 1979; 36:85–90. [PubMed: 216331]

Harvey AG. Sleep and circadian rhythms in bipolar disorder: seeking synchrony, harmony, and regulation. Am J Psychiatry. 2008; 165:820–9. [PubMed: 18519522]

Hoffmann R, Hendrickse W, Rush AJ, Armitage R. Slow-wave activity during non-REM sleep in men with schizophrenia and major depressive disorders. Psychiatry Res. 2000; 95:215–25. [PubMed: 10974360]

Huber R, Maatta S, Esser SK, Sarasso S, Ferrarelli F, Watson A, Ferreri F, Peterson MJ, Tononi G. Measures of cortical plasticity after transcranial paired associative stimulation predict changes in electroencephalogram slow-wave activity during subsequent sleep. J Neurosci. 2008; 28:7911–8. [PubMed: 18667623]

Hudson JI, Lipinski JF, Frankenburg FR, Grochocinski VJ, Kupfer DJ. Electroencephalographic sleep in mania. Arch Gen Psychiatry. 1988; 45:267–73. [PubMed: 3341881]

Joffe RT, MacQueen GM, Marriott M, Trevor Young L. A prospective, longitudinal study of percentage of time spent ill in patients with bipolar I or bipolar II disorders. Bipolar Disorders. 2004; 6:62–6. [PubMed: 14996142]

Knowles JB, Cairns J, MacLean AW, Delva N, Prowse A, Waldron J, Letemendia FJ. The sleep of remitted bipolar depressives: comparison with sex and age-matched controls. Can J Psychiatry. 1986; 31:295–8. [PubMed: 3708522]

Landsness EC, Goldstein MR, Peterson MJ, Tononi G, Benca RM. Antidepressant effects of selective slow wave sleep deprivation in major depression: a high-density EEG investigation. J Psychiatr Res. 2011; 45:1019–26. [PubMed: 21397252]

Leverich GS, Post RM. The NIMH Life Chart Manual for Recurrent Affective Illness: The LCM-S (Self Version). NIMH Monograph, Biological Psychiatry Branch. 1997

Linkowski P, Kerkhofs M, Rielaert C, Mendlewicz J. Sleep during mania in manic-depressive males. Eur Arch Psychiatry Neurol Sci. 1986; 235:339–41. [PubMed: 3743573]

Mendelson WB, Sack DA, James SP, Martin JV, Wagner R, Garnett D, Milton J, Wehr TA. Frequency analysis of the sleep EEG in depression. Psychiatry Res. 1987; 21:89–94. [PubMed: 3615694]

Murray G, Allen NB, Trinder J. Mood and the circadian system: investigation of a circadian component in positive affect. Chronobiol Int. 2002; 19:1151–69. [PubMed: 12511032]

Ong AD, Exner-Cortens D, Riffin C, Steptoe A, Zautra A, Almeida DM. Linking stable and dynamic features of positive affect to sleep. Ann Behav Med. 2013; 46:52–61. [PubMed: 23483378]

Phillips ML, Travis MJ, Fagiolini A, Kupfer DJ. Medication effects in neuroimaging studies of bipolar disorder. American Journal of Psychiatry. 2008a; 165:313–20. [PubMed: 18245175]

Phillips ML, Travis MJ, Fagiolini A, Kupfer DJ. Medication effects in neuroimaging studies of bipolar disorder. Am J Psychiatry. 2008b; 165:313–20. [PubMed: 18245175]

Plante DT, Landsness EC, Peterson MJ, Goldstein MR, Riedner BA, Wanger T, Guokas JJ, Tononi G, Benca RM. Sex-related differences in sleep slow wave activity in major depressive disorder: a high-density EEG investigation. BMC Psychiatry. 2012; 12:146. [PubMed: 22989072]

Rechtschaffen, A. A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. Brain Information Service/Brain Research Institute; Los Angeles: University of California; 1968.

Rush AJ, Gullion CM, Basco MR, Jarrett RB, Trivedi MH. The Inventory of Depressive Symptomatology (IDS): Psychometric properties. Psychological Medicine. 1996; 26:477–486. [PubMed: 8733206]

Russell JA, Weiss A, Mendelsohn GA. Affect Grid: A single-item scale of pleasure and arousal. Journal of Personality and Social Psychology. 1989; 57:493–502.

Sackeim HA. The definition and meaning of treatment-resistant depression. J Clin Psychiatry. 2001; 62(Suppl 16):10–7.

Shiota MN, Neufeld SL, Yeung WH, Moser SE, Perea EF. Feeling good: autonomic nervous system responding in five positive emotions. Emotion. 2011; 11:1368–78. [PubMed: 22142210]

Sitaram N, Nurnberger JI Jr, Gershon ES, Gillin JC. Cholinergic regulation of mood and REM sleep: potential model and marker of vulnerability to affective disorder. Am J Psychiatry. 1982; 139:571–6. [PubMed: 7072840]

Stein KD, Goldman MS, Del Boca FK. The influence of alcohol expectancy priming and mood manipulation on subsequent alcohol consumption. Journal of Abnormal Psychology. 2000; 109:106–115. [PubMed: 10740941]

Steptoe A, O'Donnell K, Marmot M, Wardle J. Positive affect, psychological well-being, and good sleep. J Psychosom Res. 2008; 64:409–15. [PubMed: 18374740]

Talamini LM, Bringmann LF, de Boer M, Hofman WF. Sleeping worries away or worrying away sleep? Physiological evidence on sleep-emotion interactions. PLoS One. 2013; 8:e62480. [PubMed: 23671601]

Talbot LS, Hairston IS, Eidelman P, Gruber J, Harvey AG. The effect of mood on sleep onset latency and REM sleep in interepisode bipolar disorder. J Abnorm Psychol. 2009; 118:448–58. [PubMed: 19685943]

Tononi G. Slow wave homeostasis and synaptic plasticity. J Clin Sleep Med. 2009; 5:S16–9. [PubMed: 19998870]

van der Helm E, Yao J, Dutt S, Rao V, Saletin JM, Walker MP. REM sleep depotentiates amygdala activity to previous emotional experiences. Curr Biol. 2011; 21:2029–32. [PubMed: 22119526]

Werth E, Achermann P, Borbely AA. Fronto-occipital EEG power gradients in human sleep. J Sleep Res. 1997; 6:102–12. [PubMed: 9377529]

Williams JMG, Healy H, Eade J, Windle G, Cowen PJ, Green MW, Durlach P. Mood, eating behaviour and attention. Psychological Medicine. 2002; 32:469–481. [PubMed: 11989992]

Young R, Biggs J, Ziegler V, Meyer D. A rating scale for mania: reliability, validity and sensitivity. British Journal of Psychiatry. 1978; 133:429–425. [PubMed: 728692]
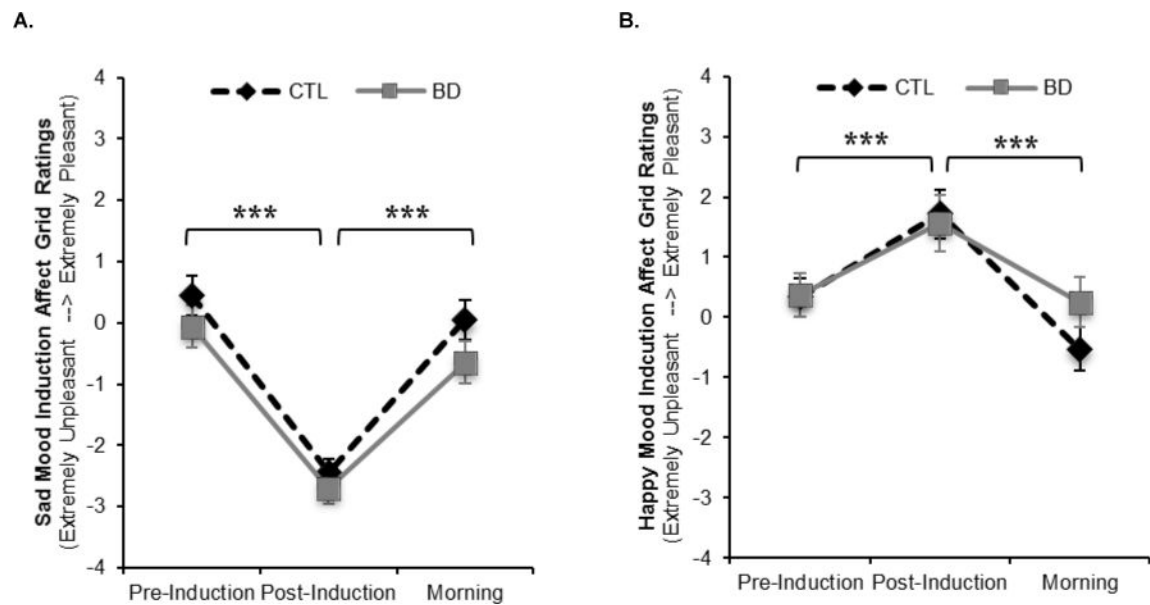
Figure 1.
Affect grid pleasantness ratings for BD and CTL groups on the **(A)** sad mood induction and **(B)** happy mood induction nights, assessed at the beginning of the mood induction (Pre-Induction), at the end of the mood induction (Post-Induction) and upon awakening the following morning (Morning). BD=bipolar disorder group (Sad night N=17; Happy night N=16); CTL=healthy control group (Sad night N=21; Happy night N=21); $^*p$<.05, $^{**}p$<.01, $^{***}p$<.001.
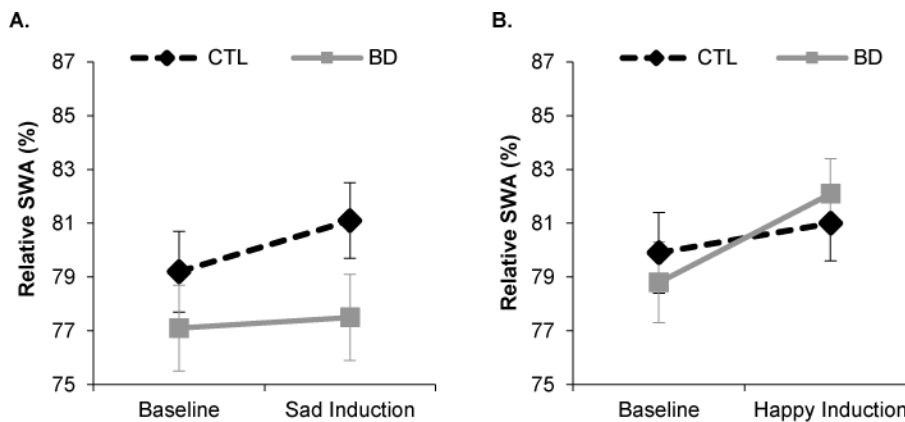
Figure 2.
Mean relative slow wave activity (SWA) on the baseline night relative to the **(A)** sad mood induction and **(B)** happy mood induction nights. Baseline night was the neutral mood induction night. Baseline night means differ slightly between the sad and happy mood induction analysis since a few individuals did not participate in both mood induction nights. BD=bipolar disorder group (Sad night N=17; Happy night N=16); CTL=healthy control group (Sad night N=21; Happy night N=21); $^*p<.05$, $^{**}p<.01$, $^{***}p<.001$.
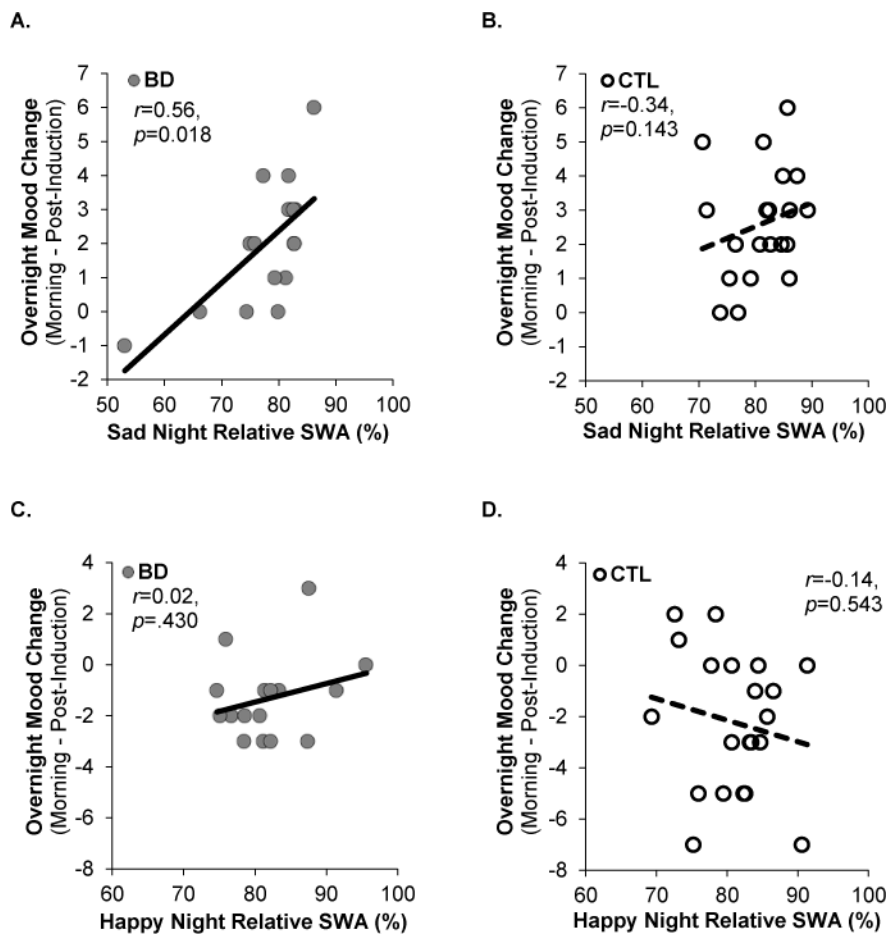
Figure 3.
Overnight mood change on the affect grid pleasantness ratings plotted as a function of SWA for BD and CTL groups on the sad mood induction night **(A, B)** and happy mood induction night **(C, D)**. BD=bipolar disorder group (Sad night N=17; Happy night N=16); CTL=healthy control group (Sad night N=21; Happy night N=21).

Table 1

Sociodemographic and clinical characteristics by diagnostic group.

Demographic	Bipolar n = 20	Control n = 23	Statistic	p
Age (Years)	32.85(10.55)	38.65(12.83)	$t(41) = 1.60$	0.116
Gender (%)			$\chi^2(1) = 1.08$	0.298
Male	2(10.0%)	5(21.7%)		
Female	18(90.0%)	18(78.3%)		
Ethnicity (%)			$\chi^2(5) = 3.02$	0.697
African American	1(5.3%)	1(4.8%)		
Asian/Pacific Islander	5(26.3%)	4(19.0%)		
Hispanic	2(10.5%)	3(14.3%)		
Native American	0(0.0%)	0(0.0%)		
White	9(47.4%)	9(42.9%)		
Other	1(5.3%)	4(19.0%)		
Education (%)			$\chi^2(5) = 4.75$	0.448
High school	1(5.0%)	1(4.3%)		
Some college	7(35.0%)	5(21.7%)		
2yr college	1(5.0%)	4(17.4%)		
4yr college	9(45.0%)	9(39.1%)		
Master's	1(5.0%)	4(17.4%)		
Doctorate	1(5.0%)	0(0.0%)		
Employed (%)			$\chi^2(2) = 5.17$	0.076
Full-time	7(35.0%)	16(69.6%)		
Part-time	7(35.0%)	4(17.4%)		
Unemployed	6(20.0%)	3(13.0%)		
Clinical				
YMRS	5.59 (6.23)	1.65 (1.60)	$t(35) = -2.54$	0.021
IDS-C	2.80 (2.60)	0.56 (0.92)	$t(44) = -3.19$	0.005
BD Age of Onset (years)	18.65 (9.70)	–	–	–
BD Illness Duration (years)	14.60 (8.61)	–	–	–
# (Hypo)manic Episodes	7.20 (6.39)	–	–	–
# Depressive Episodes	9.45 (10.16)	–	–	–
Psychotropic Medications		–	–	–
Polytherapy (%)	16(80.0%)	–	–	–
Mood Stabilizer (%)	15(75.0%)	–	–	–
Antipsychotic (%)	10(50.0%)	–	–	–
Antidepressant (%)	15(75.0%)	–	–	–
Anxiolytic (%)	4(20.0%)	–	–	–
Sedative Hypnotic (%)	2(10.0%)	–	–	–
Stimulant (%)	1(5.0%)	–	–	–
Medication Composite	1.81 (2.47)	–	–	–

Demographic	Bipolar n = 20	Control n = 23	Statistic	p
Baseline Sleep Recording				
Total Sleep Time (minutes) *Range (min-max)*	445.25 (81.97) *293.50–592.00*	402.13 (81.42) *203.50–548.00*	$t(41) = -1.73$	0.092
Bedtime (minutes) *Range (min-max)*	22:52 (01:14) *20:23–00:50*	23:14 (00:57) *21:46–01:16*	$t(41) = 1.08$	0.285
Waketime (minutes) *Range (min-max)*	7:23 (00:57) *5:36–9:08*	6:33 (00:59) *4:51–8:36*	$t(41) = -2.82$	0.007

Note. Mean values are displayed with standard deviations in parentheses where applicable; BD = Bipolar Disorder; YMRS = Young Mania Rating Scale; IDS-C = Inventory of Depressive Symptoms-Clinician Rated.

Table 2

Sleep architecture on the mood induction nights.

Sad Mood Induction Analysis[a]

Sleep Variable	Baseline Bipolar	Baseline Control	Sad Night Bipolar	Sad Night Control	Group F	Group p	Night F	Night p	Group X Night F	Group X Night P
TST	442.74(85.66)	412.69(71.29)	438.93(93.61)	414.67(149.16)	2.37	0.133	0.28	0.597	0.23	0.63
TWT	62.71(61.33)	26.76(36.06)	55.62(71.08)	25.43(24.47)	7.49	0.010	0.15	0.701	0.07	0.793
N1	9.66(6.59)	8.77(7.47)	10.95(5.51)	5.52(4.10)	1.89	0.178	0.93	0.341	0.69	0.413
N2	80.44(45.66)	73.57(33.18)	98.00(39.09)	94.36(32.27)	1.12	0.296	0.63	0.432	0.16	0.696
SWS	97.56(40.14)	95.40(34.80)	82.26(60.52)	82.83(30.63)	0.01	0.932	1.90	0.177	0.02	0.894
REM	80.44(45.67)	73.57(33.1)	98.00(39.09)	94.36(32.37)	0.31	0.584	6.32	0.017	0.05	0.834

Happy Mood Induction Analysis[b]

Sleep Variable	Baseline Bipolar	Baseline Control	Happy Night Bipolar	Happy Night Control	Group F	Group p	Night F	Night p	Group X Night F	Group X Night P
TST	453.03 (85.5)	399.78(84.96)	418.72(102.46)	377.21(84.96)	3.75	0.061	3.47	0.071	0.15	0.703
TWT	60.34(58.84)	25.97(36.30)	41.47(30.97)	26.14(31.25)	5.68	0.023	1.29	0.264	1.33	0.256
N1	41.09(36.49)	35.60(34.68)	36.09(28.74)	25.60(13.82)	0.92	0.344	2.24	0.143	0.25	0.621
N2	206.09(70.72)	195.69(65.64)	198.91(71.56)	179.00(63.57)	0.60	0.446	1.28	0.266	0.20	0.656
SWS	106.72(43.23)	90.21(35.36)	94.87(37.55)	83.02(34.39)	2.28	0.139	1.37	0.250	0.08	0.776
REM	99.13(50.60)	78.29(35.81)	86.22(50.55)	84.67(52.46)	0.64	0.428	0.20	0.657	1.76	0.194

Note. Mean (standard deviation) are presented. Units are minutes for all variables. TST = total sleep time; TWT = total wake time; N1 = NREM Stage 1; N2 = NREM Stage 2; SWS = Slow wave sleep or NREM Stages 3 and 4;

[a] Bipolar *n* = 17, Control *n* = 21;

[b] Bipolar *n* = 16, Control *n* = 21.