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Sleep Disturbance in Bipolar Disorder Across the Lifespan

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Abstract

The aim of this article is to highlight the importance of the sleep–wake cycle in children, adolescents, and adults with bipolar disorder. After reviewing the evidence that has accrued to date on the nature and severity of the sleep disturbance experienced, we document the importance of sleep for quality of life, risk for relapse, affective functioning, cognitive functioning, health (sleep disturbance is implicated in obesity, poor diet, and inadequate exercise), impulsivity, and risk taking. We argue that sleep may be critically important in the complex multifactorial cause of interepisode dysfunction, adverse health outcomes, and relapse. An agenda for future research is presented that includes improving the quality of sleep measures and controlling for the impact of bipolar medications.

Keywords

adolescents; adults; bipolar disorder; children; hypersomnia; insomnia; sleep

SLEEP IN BIPOLAR DISORDER

Sleep disturbance is a core symptom of bipolar disorder. The diagnostic criteria indicate that during manic episodes there may be a reduced need for sleep and during episodes of depression, insomnia or hypersomnia can be experienced nearly every day (American Psychiatric Association, 2000). The aim of this article is to highlight the importance of the sleep–wake cycle in bipolar disorder.

Table 1 presents an overview of the studies reporting the nature and extent of sleep disturbance in adults with bipolar disorder. As evident, during a manic episode there is a reduced need for sleep in 69–99% of patients and longer sleep onset latency. The majority of sleep architecture findings during mania focus on rapid eye movement (REM) sleep, including shortened REM latency and increased REM density. During an episode of depression, bipolar patients experience insomnia and/or hypersomnia; one study found that 100% experienced insomnia while another reported that 78% experienced hypersomnia. Again, during depression, longer sleep latency is present and REM appears to be the aspect of sleep architecture most affected. In particular, although there are some discrepancies across the studies, there appears to be shortened REM latency and a tendency toward longer REM periods and increased REM density. In the only study of patients in a mixed episode, sleep disturbance was pervasive. Table 1 also includes three studies indicating the presence of considerable sleep disturbance even during the interepisode period.

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Table 2 presents an overview of the studies reporting the nature and extent of sleep disturbance in children and teenagers with bipolar disorder. Overall, the data suggest that sleep disturbance is a prominent feature of bipolar disorder in youth. The studies in which sleep was estimated via self- or parent-report indicate that reduced need for sleep was commonly observed. A few of these studies also document high rates of insomnia and parasomnias. A parasomnia is defined as a sleep disorder that is characterized by arousals during sleep. Only three studies were located in which sleep was estimated using objective measures (i.e., polysomnography, actigraphy). These indicate that compared to healthy controls, youth with bipolar disorder exhibit lower sleep efficiency, longer slow wave sleep, and reduced REM sleep (Faedda & Teicher, 2005; Jones, Tai, Evershed, Knowles, & Bentall, 2006; Mehl et al., 2006).

Interestingly, there is preliminary evidence suggesting that sleep disturbance may be an early marker for the disorder in youth. For example, in a study examining the phenomenology of early-onset bipolar disorder in 82 children, researchers found that sleep disturbance was reported by about half of the parents as one of the earliest symptoms they observed (Faedda, Baldessarini, Glovinsky, & Austin, 2004). Consistently, sleep disturbances (and anxiety disorders) were identified as antecedents to the onset of bipolar disorder in a subset of high-risk youth (Duffy, Alda, Crawford, Milin, & Grof, 2007).

Sleep may help to distinguish manifestations of bipolar illness from the early development of other psychopathology. Specifically, compared to children with ADHD and healthy controls, children diagnosed with bipolar disorder have significantly higher rates of sleep difficulties (Geller et al., 2002). Another study indicates that a decreased need for sleep is significantly more common among children with bipolar profile symptoms than in children with comparable levels of psychopathology excluding bipolar disorder symptoms (Holtmann et al., 2007). Finally, Dahl et al. (1990) prospectively followed adolescents with unipolar depression for seven years (when they were in their early 20s). A clinical interview was administered to determine their disease course (Rao et al., 2002). Five of the 26 patients who were diagnosed with unipolar depression at the first assessment had switched to bipolar disorder by the time of the follow-up. Based on these new categorizations, the original polysomnography data were reanalyzed. The results indicated that depressed participants who followed a unipolar course showed reduced REM latency, higher REM density, and increased overall REM sleep, whereas those who moved to a bipolar course demonstrated increased Stage 1 sleep and decreased Stage 4 sleep. These findings raise the possibility that adolescent sleep abnormalities may distinguish bipolar from unipolar trajectories.

In summary, the evidence suggests that pervasive sleep disturbance is characteristic of bipolar disorder. Sleep disturbance is a feature of bipolar disorder in adults as well as children and teenagers. In adults, it has also been shown to be a feature across phases of the illness, although the particular aspect of sleep affected and the severity of the disturbance appear to vary across phases. Parallel information is not yet available in youth diagnosed with bipolar disorder, possibly because compared to adults, youth tend to display less clear episode distinction and instead a more chronic pattern of disturbance (or very rapid cycling; Biederman et al., 2004). Two themes emerge from an overview of the studies reviewed. First, the evidence of longer sleep onset latency is consistent with bipolar disorder being characterized by difficulties regulating mood. As strong mood states are cognitively and physiologically arousing, they are likely to be antithetical to sleep onset (Espie, 2002). Second, the associations between bipolar disorder and REM sleep are particularly intriguing as they are consistent with the evidence of a relationship between REM sleep and affective functioning (Cartwright, Baehr, Kirkby, Pandi-Perumal, & Kabat, 2003).

WHY DOES SLEEP DISTURBANCE IN BIPOLAR DISORDER MATTER?

We will now move on to consider seven reasons this pervasive sleep disturbance is of considerable concern.

Sleep Disturbance Impairs Quality of Life

In the absence of bipolar disorder, poor sleep is known to have a significant negative psychosocial, occupational, health, and economic impact (Ancoli-Israel & Roth, 1999). For example, relative to good sleepers, individuals with chronic sleep disturbances report more psychological distress and impairments of daytime functioning, they take more frequent sick leave, and they utilize more healthcare resources. The adverse consequences of poor sleep on mood, motivation, and cognitive functioning are particularly relevant to bipolar disorder (Ancoli-Israel & Roth). These negative sequelae of poor sleep seem highly likely to exert significant functional consequences on individuals with bipolar disorder.

Sleep Disturbance Contributes to Relapse

There are multiple lines of evidence suggesting that sleep contributes to relapse in bipolar disorder. While any one line of evidence is not strong, the convergence of results provides a compelling case.

Prodromes of Episodes—A prodrome is an early symptom, or warning signal, that appears before an episode of depression or mania. In a systematic review of 73 reports of prodromal symptoms in bipolar disorder and unipolar depression, Jackson et al. (2003) reported that the majority of patients (over 80%) were able to identify early symptoms. Among patients with bipolar disorder, sleep disturbance was the most common prodrome of mania and the sixth most common prodrome of depression.

Sleep Deprivation in Bipolar Patients—A handful of experimental studies and case studies have reported that induced sleep deprivation is associated with the onset of hypomania or mania in a proportion of patients. Wehr, Goodwin, Wirz-Justice, Breitmaier, and Craig (1982) sleep deprived nine rapidly cycling patients who were in a depressed phase stay for 40 hours (i.e., one night's sleep deprivation). This triggered mania or hypomania in seven of the nine individuals. Later Wehr, Sack, and Rosenthal (1987) reported four cases in which mania immediately followed induced sleep deprivation (through "real-world" circumstances such as a transatlantic flight). In a more recent study, focusing on the potential therapeutic effects of total sleep deprivation, Colombo and colleagues (1999) recruited 206 depressed bipolar patients. The participants received one night of total sleep deprivation followed by either a recovery night or a recovery night in combination with several medications (lithium salts, fluoxetine, amineptine, pindolol). The results indicated that 4.85% of patients switched into mania and 5.83% switched into hypomania. Given these results, most based on just one night of sleep deprivation, it seems possible that with chronic sleep deprivation (either full or partial), the proportion of patients to relapse would be much greater.

Therapeutic Sleep Extension—Wehr et al. (1998) reported a case study of a patient with rapid cycling bipolar disorder who was treated with extended bed rest and darkness. The patient was instructed to remain in his bed and in the dark for 14 hours each night (gradually reducing to 10 hours per night). Long-term monitoring indicated that this patient's sleep and mood stabilized when he adhered to the bed rest prescriptions. This study raised the possibility that increasing and stabilizing sleep may have therapeutic benefits for reducing rapid cycling. In 2005, a preliminary trial of "dark therapy" was published by Barbini et al. The 16 bipolar patients in a manic episode were given 14 hours of enforced

darkness for three consecutive days. Those who received dark therapy exhibited a decrease in manic symptoms relative to the 16 patients given treatment as usual. Taken together, the evidence that extending sleep seems to stabilize mood symptoms indirectly supports the possibility that insufficient sleep may contribute to destabilization of mood.

Prospective Monitoring of Sleep and Mood in Bipolar Disorder—Four studies have prospectively monitored sleep and episode status. First, Leibenluft et al. (1996) asked 11 patients with rapid cycling bipolar disorder to monitor their mood and sleep for 18 months. The impact of three sleep variables (sleep duration, time of sleep onset, time of wake onset) on episodes (depressed, manic, hypomanic) was analyzed. The results indicated that shorter sleep duration predicted mania or hypomania the next day. This association was less consistent for depression.

Second, Barbini et al. (1996) monitored 34 manic patients over three days for sleep duration and manic symptoms (using the Young Mania Rating Scale). Significant correlations were observed such that shorter sleep duration was associated with higher manic symptoms (particularly poor cooperation and irritability) the next day.

Third, Perlman et al. (2006) prospectively studied a group of 54 patients with bipolar I disorder. At baseline 43% of these patients were in an episode of depression, 30% were in an episode of mania, 20% were in a mixed or rapid cycling phase, and 7% had just recently recovered from an episode. Symptoms of bipolar disorder were assessed for the subsequent six months. Shorter sleep duration (indexed by the sleep duration scale of the Pittsburgh Sleep Quality Index) predicted greater depressive symptoms but not manic symptoms.

Fourth, 59 bipolar patients (37 with bipolar I; 22 with bipolar II) were asked to record their mood, sleep, and bed rest over a minimum of 100 days (Bauer et al., 2006). Cross-correlation function was used to analyze the results. The pattern to emerge was that a *decrease* in sleep or bed rest was followed by a shift toward hypomania/mania the next day and an *increase* in sleep or bed rest was followed by a shift toward depression the next day. The latency between the shifts tended to be about one day.

Taken together, the consistent result to emerge from these prospective studies is an association between sleep disturbance and mood, although the nature of the association—particularly whether it is stronger for manic or depressive symptoms—is less clear. The inconsistencies may relate to important differences across studies in the sleep measure employed. For example, Perlman et al. (2006) based their sleep measure on one question asking for an evaluation of sleep globally over a one-month period whereas Bauer et al. (2006) asked patients to record sleep each hour across the 24-hour period for a minimum of 100 days.

Sleep Is Critical for Affect Regulation

In 1996, Pilcher and Huffcutt reviewed 19 studies conducted from 1984 to 1992 of short-term total sleep deprivation (less than or equal to 45 hours), long-term total sleep deprivation (greater than 48 hours), or partial sleep deprivation (sleep period of less than five hours in a 24-hour period). The results indicated that among healthy nonpatient samples, mood was adversely affected by sleep deprivation with large effect sizes ranging from 2.75 to 4.10.

This finding has been replicated in several more recent studies. For example, Dinges et al. (1997) restricted the sleep of healthy nonpatient participants to five hours per night for one week. Mood progressively declined as sleep deprivation accumulated throughout the week. Drake et al. (2001) allocated healthy participants to three schedules of sleep loss: slow (six hours' time in bed for four nights), intermediate (four hours' time in bed for two nights), and

rapid (zero hours' time in bed for one night). A control group who obtained eight hours' time in bed over the same time period was also included. A dose–response relationship between mood and sleep was observed such that greater mood impairment was evident in the rapid sleep loss group as opposed to the slow, cumulative sleep loss group, who experienced more impairment relative to the control group. Finally, a study by Zohar et al. (2005) raised the possibility that context is important for determining the direction of the effect of sleep disturbance on affective functioning. These researchers examined the relationship between sleep loss and emotion reactivity in 78 medical residents who were monitored for five to seven days every six months over a two-year period. The results indicated that sleep loss not only intensified negative emotions following a goal-thwarting event but also, following a goal-enhancing event, diminished positive emotions.

The above findings are consistent with emerging findings at the neural systems level. Circuits involved in affect regulation and circuits involved in sleep regulation interact in bidirectional ways (e.g., Saper, Cano, & Scammell, 2005). For example, in a recent study healthy participants who were sleep deprived for 35 hours or who had slept normally completed an emotional stimulus viewing task (100 images varying in emotional intensity) in an event-related fMRI design (Yoo, Gujar, Hu, Jolesz, & Walker, 2007). As expected, both groups exhibited amygdala activation to negative picture stimuli. However, relative to those who sleep normally, those who were sleep deprived exhibited more than 60% greater amygdala activity and this large increase was associated with a loss of activity in the medial-prefrontal cortex (MPFC). The MPFC exerts top-down control on the limbic area (including the amygdala) and functions to modulate emotional responses so they are appropriate for the context. This finding suggests that sleep contributes to maintaining the connectivity between the MPFC and the amygdala, which is critical for responding appropriately to next-day emotional challenges. Although based on healthy participants, it is certainly tempting to speculate that this finding is particularly relevant to patients with bipolar disorder whose affect regulation system is likely to be even more vulnerable to the adverse consequences of sleep deprivation.

Sleep Is Important for Cognitive Functioning

Adverse effects of sleep deprivation on cognitive functioning have been clearly demonstrated. For example, a study of young adults whose sleep was restricted for four, six, or eight hours a night over 14 nights showed a dose–response decrement in performance on a psychomotor vigilance task, a working memory task, and a cognitive processing task (Van Dongen, Maislin, Mullington, & Dinges, 2003). A recent report by Walker and Stickgold (2006) demonstrated a critical role for sleep during the encoding and consolidation of memories. Participants were either allocated to 36 hours of sleep deprivation or were allowed to sleep normally. Participants then performed an incidental memory encoding task comprised of emotionally neutral, negative, and positive words. Relative to the normal sleepers, those who were sleep deprived exhibited a 40% decrement in memory retention across all word types. The most profound decrement was evident for positive words. The potential implications for patients with psychiatric disorders are provocative; one pathway by which sleep disturbance may contribute to maintenance of symptoms and impairment may be poorer memory for the positive domains or events in their lives.

We emphasize that adverse effects in this domain are likely to be particularly critical for youth, whose education achievements (relying on cognitive function) will have far-reaching and long-term consequences.

Sleep Impacts Health

It has been surprising for the field to realize that the suffering associated with bipolar disorder is not limited to the psychiatric symptoms. Bipolar disorder is associated with a wide range of medical problems, with the most common being cardiovascular disease, diabetes mellitus, and thyroid disease (Krishnan, 2005). The etiology of these concerning conditions will likely be complex and multifactorial. Side effects of medications are one possible cause of the observed health effects. But there are likely to be many other contributors. Here we speculate about the possibility that sleep disturbance may be one additional, but currently unrecognized, contributor. We present our reasoning below by focusing on three possible mediators of the poor health outcomes observed in bipolar samples; namely, obesity, poor diet, and insufficient exercise.

Obesity—There is evidence that bipolar patients have elevated rates of obesity relative to the rate in the general population (McElroy et al., 2004). Fagiolini et al. (2003) reported that 68% of patients with bipolar disorder were overweight, with 32% meeting criteria for obesity (less than 20% of controls met criteria for obesity). These individuals suffered a range of poorer outcomes including shorter time to recurrence of an episode, particularly of depression, and had a greater number of previous episodes of depression and mania (Fagiolini et al., 2003). Similarly, McElroy et al. (2002) reported that 58% of bipolar patients were overweight and 21% were obese. The associated adverse outcomes included arthritis, hypertension, and diabetes mellitus. The higher rate of obesity is also of concern given the adverse impact of obesity on quality of life (Fontaine & Bartlett, 1998), social life (Wolf & Colditz, 1996), and self-esteem (Kawachi, 1999).

There is no doubt that medications used to treat bipolar disorder are associated with weight gain (Elmslie, Silverstone, Mann, Williams, & Romans, 2000; Zimmermann, Kraus, Himmerich, Schuld, & Pollmacher, 2003). Also, depressive symptoms may be associated with physical inactivity, which contributes to obesity. An additional explanation, given that sleep deprivation increases appetite, weight gain, and insulin tolerance (Spiegel, Tasali, Penev, & Van Cauter, 2004), is that sleep disturbance may be an additional contributor. Indeed, the results of a recent meta-analysis involving 30 studies (12 in children, 18 in adults) and 634,511 participants are compelling. There was a 60–80% increase in the odds of being a short sleeper among both adults and children who were obese. Moreover, adults sleeping five hours or fewer versus more than five hours had significantly greater odds of being obese, and an increase of one hour per night of sleep was associated with a decrease of 0.35 body mass index (Cappuccio et al., 2008).

Diet—In a comparison of 2,032 patients with bipolar disorder and a random sample of non-mentally-ill individuals, Kilbourne et al. (2007) reported that patients with bipolar disorder were more likely to report poorer eating behaviors relative to individuals without a serious mental illness, including having fewer than two daily meals (odds ratio [OR] = 1.32) and difficulty obtaining or cooking food (OR = 1.48). Again, there are going to be multiple contributors, one of which may be sleep disturbance. The latter seems plausible given that sleep deprivation can be associated with hormonal responses that increase appetite and caloric intake (Spiegel et al., 2004; Taheri, Lin, Austin, Young, & Mignot, 2004; Vgontzas, Bixler, & Chrousos, 2003).

Exercise—Kilbourne et al. (2007) reported that patients with bipolar disorder were more likely to report poor exercise habits relative to individuals without a serious mental illness, including infrequent walking (OR = 1.33) and infrequent strength exercises (OR = 1.28). Another study reported predominately sedentary routine daily activities in a sample of bipolar patients (Chuang, Mansell, & Patten, 2008). Given the evidence that healthy

participants have less tolerance for exercise after sleep deprivation (Martin, 1981) and fitter individuals sleep longer than less fit individuals (Montgomery, Trinder, & Paxton, 1982), we hypothesize that the sleep disturbance that is characteristic of bipolar disorder may result in lower daytime energy levels which, in turn, may adversely affect motivation and likelihood of engaging in exercise. It is reasoned that bipolar individuals are less likely to exercise following sleep disturbance, and their resulting lack of fitness may result in more sleep disturbance, thus maintaining a vicious cycle.

In summary, evidence has been presented to suggest that future research should consider if sleep disturbance is a factor in the adverse health outcomes associated with bipolar disorder; namely, obesity, poor diet, and inadequate exercise. Both psychological (e.g., motivation) and biological (e.g., hormonal responses to sleep deprivation) pathways are hypothesized to mediate this link.

Sleep Deprivation Is Associated With Substance Use

The National Institute of Mental Health's Epidemiologic Catchment Area Study compared all Axis 1 disorders and found that individuals with bipolar I disorder have the highest lifetime rates of alcohol use disorder (46%) and drug use disorder (41%; Regier et al., 1990). Alcohol use and drug use disorders have been associated with more severe subtypes (e.g., rapid cycling), manic symptoms, mood lability, impulsivity, and violence, as well as increased rates of hospitalization, slower remission, and increased rates of suicide attempts (Levin & Hennessy, 2004).

In terms of nicotine use, a population-based study of 4,411 individuals with psychiatric disorders reported the current prevalence of smoking among bipolar patients to be the highest at 60.6% (81.8% lifetime prevalence; Lasser et al., 2000). The rate of smoking in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) sample was lower (31.2%), a finding that may be attributable to demographic characteristics (the STEP-BD sample was less racially diverse and more educated relative to other bipolar samples; Waxmonsky & Wilens, 2005).

We wish to offer the possibility that the sleep disturbance that is characteristic of bipolar disorder may be one contributor to the high rate of comorbidity with substance use problems. In regard to alcohol, our reasoning is based on evidence that at low to moderate doses alcohol has stimulatory effects whereas at higher doses alcohol is sedating (Papineau, Roehrs, Petrucelli, Rosenthal, & Roth, 1998; Roehrs & Roth, 2001). The sedating effects at higher doses may be sought to promote sleep when moods are difficult to regulate. The stimulant properties of nicotine at lower doses (Newhouse, Potter, & Singh, 2004) may render it another strategy adopted by patients to cope with the effects of sleep deprivation. Several findings, in combination, are consistent with this hypothesis. Zhang et al. (2006) reported on the largest study of polysomnography-scored sleep involving 6,420 participants from the Sleep Heart Study (2,916 were "never smokers," 2,705 were "former smokers," and 799 were "current smokers"). Relative to "never smokers," "current smokers" took longer to fall asleep, slept less overall, and experienced more Stage 1 sleep and less slow wave sleep. This study does not address the direction of the effect; the results may reflect participants coping with sleep deprivation by smoking or participants' smoking contributing to sleep deprivation (or both). However, it is interesting to note that Poston et al. (2008) reported that air force and army personnel cited sleep deprivation as among the most important reasons for smoking. Also, among a Finnish sample of adolescents, irregular sleep schedules and daytime sleepiness accounted for 26% of the variance in substance use in 15-year-old boys and 12% in 15-year-old girls (Tynjala, Kannas, & Levalahti, 1997). Another large study of 4,500 12- to 17-year-olds found that adolescents who had trouble sleeping

reported greater use of alcohol (OR = 2.6), marijuana (OR = 2.4), and cigarettes (OR = 2.2; Johnson, Breslau, Roehrs, & Roth, 1999).

Taken together, the possibility that the sleep disturbance experienced by individuals with bipolar disorder may be an additional but underrecognized factor contributing to high rates of comorbid substance use should be explored in future research. This seems plausible based on accruing evidence linking sleep disturbance, alcohol use, and nicotine use.

Sleep Deprivation Contributes to Impulsivity and Risk Taking

Impulsivity has been defined by Moeller et al. (2001) as the predisposition to rapid unplanned action without regard for consequences. Impulsivity has been linked to serious adverse outcomes such as suicidal behavior (Simon et al., 2001). Swann et al. (2008) compared patients with bipolar disorder who were interepisode or who met criteria for depression, mania, or a mixed state on the Barratt Impulsiveness Scale (Moeller et al., 2001). This scale distinguishes between (a) attentional impulsivity, which is a lack of cognitive persistence coupled with difficulty tolerating cognitive complexity; (b) motor impulsivity, which is taking action on the spur of the moment; and (c) nonplanning impulsivity, which is difficulty retaining a sense of the future (Patton, Stanford, & Barratt, 1995). Swann et al. (2008) reported that these aspects of impulsivity were associated with different phases of the bipolar illness; attentional impulsivity was associated with depression and mania, motor impulsivity was associated with mania, and nonplanning impulsivity was associated with depression.

Several studies suggest that sleep deprivation may contribute to impulsivity. For example, a study by Haynes et al. (2006) found that improvements in sleep time were associated with significant decreases in reporting aggressive thoughts and actions among adolescents with substance dependence difficulties. In adults, greater risk taking on the Iowa Gambling Task was observed among healthy adults who were sleep deprived for 49.5 hours, relative to when they were rested (Killgore, Balkin, & Wesensten, 2006). In another study, using the Lottery Choice Task, adults who were sleep deprived took more risks when considering gain but fewer risks when considering loss, relative to a non-sleep-deprived control group (McKenna, Dickinson, Orff, & Drummond, 2007).

The neural basis of risky decision making under conditions of sleep deprivation is starting to emerge. For example, Venkatraman et al. (2007) reported that following sleep deprivation, risky choices elicited greater activation in the right nucleus accumbens. Given that activation of this region is associated with anticipated gains, the latter was interpreted as indicating elevated expectation of reward under conditions of sleep deprivation.

In summary, the possibility that sleep disturbance may contribute to impulsivity and risk-taking behavior, including suicidality, is a critical domain to consider in future research. Specific neural pathways for the association have begun to be investigated in healthy participants. The replication of these in bipolar patients is likely to be a fruitful domain for future research.

METHODOLOGICAL LIMITATIONS INCLUDING MEDICATIONS

Given the likely importance of sleep disturbance as a contributor to a wide range of adverse outcomes in bipolar disorder, grappling with the methodological complexities in studying sleep in bipolar disorder is an important next step.

Tables 1 and 2 raise a number of methodological issues. Across studies a wide variation in reported rates of insomnia and hypersomnia in bipolar disorder are noted. It is too early in

the growth of knowledge to make sense of these differences, although future research should seek to standardize methods and examine the possibility that subtypes, illness severity, and the age/sex of the sample contribute. The selection of sleep measures in future studies should be guided by current standards for assessing sleep as summarized in Buysse et al. (2007). To achieve more representative findings, a mix of larger samples, both inpatient and outpatient, is an important future direction. Other limitations include absence of a control group and limited assessments of psychiatric comorbidity. Finally, the strategy for dealing with the effect of medication varied across the studies, with several studies not reporting the details. The impact of medications on sleep is an important methodological issue to which we will now turn.

Psychotropic medications for bipolar disorder are likely to impact sleep and, thus, may present as a confounding variable in research on sleep in bipolar disorder. However, medication-free samples of bipolar disorder patients would be both unfeasible and unrepresentative. For example, Clark and Goodwin (2004) point out that cognitive testing cannot typically be done with patients in acute mania until antipsychotic treatment has begun. An option could be medication-free periods, but these create significant safety concerns. Furthermore, while previous research on depression has suggested that one week may be a sufficient washout period to eliminate effects of medication on polysomnography outcome (Lauer, Wiegand, & Krieg, 1992), more recent research suggests that due to the long half-lives of many medications for bipolar disorder, the washout period for bipolar participants may need to last up to several months (Philips, Travis, Fagiolini, & Kupfer, 2008). This length of time may not be viable for most studies and may also constitute a selection bias in that individuals who can tolerate such washout periods are likely to be less symptomatic and unrepresentative of bipolar patients (Philips et al.).

Hence, given the fact that it is typically not feasible or representational to study only bipolar individuals who are medication-free, a number of strategies can be used to address the potential confound of medications. We will discuss four of these approaches below. Importantly, for any of these approaches it is necessary to maintain detailed and careful records of all participant medications and dosages throughout the study, as well as information about the start date of each medication.

Approach 1: Study Design

The first strategy is to carefully consider study design in order to reduce the effect of medication on outcome. For example, the use of a within-subject design can be advantageous, particularly if participants are able to remain on the same medication regimen throughout the study, if approved by their prescribing physician. This strategy can often be used in conjunction with other approaches.

Approach 2: Subgroup Analyses

The second strategy is to split bipolar individuals into subgroups according to either type or class of medication (e.g., mood stabilizers, antipsychotics; e.g., Wessa et al., 2007), or according to the medication's effect on sleep (e.g., somnolence or insomnia side effects) or sleep architecture (e.g., REM-sleep enhancing or REM-sleep suppressing). However, there are limitations to this approach. One issue is that the subgroups formed by such samples may be quite small, limiting statistical power. A second issue is that these approaches do not account for the interactions among different psychotropic medications. For example, the same medication may promote somnolence in one individual but the opposite side effect (insomnia) in another (e.g., Effexor; PDR Staff, 2007), making classification of such medications into sedating versus nonsedating groups difficult. In another example, if a patient is being treated with a medication that is REM-sleep enhancing and another

medication that is REM-sleep suppressing, an additive approach resulting in a "canceling out" of REM effects may be used, but studies documenting the interaction between two or more drugs are needed to examine the validity of such an approach. A third limitation is that it may not be possible to use this approach in longitudinal studies ((i.e., studies lasting several weeks or more) in which many participants change their medications. A fourth limitation is that it is not uncommon for individuals to experience side effects only early in the treatment; hence, in some cases, the presumed impact of side effects on the dependent variable long after the participant began the medication may be irrelevant (Ketter & Wang, 2002). A final difficulty is that, of course, side effects are idiosyncratic and even medications with the strongest effects on sleep may only impact a proportion of individuals taking the medication, so that some individuals in a medication side effect subgroup may not actually be experiencing the predicted side effects.

Approach 3: Conversion to Prototypical Medication Dose Equivalents

A third strategy, somewhat overlapping with the second, is to convert doses of medications within classes to prototypical medications for the class, such as converting antipsychotics into chlorpromazine dose equivalents (e.g., Gruber, Rogowska, & Yurgelun-Todd, 2004). These dose equivalents are then correlated with dependent variables to determine how medication doses may be associated with outcomes in subgroups. This strategy faces many of the limitations discussed for the second strategy, particularly the problem of drug–drug interactions due to polypharmacy.

Approach 4: Not Controlling for Medication Effects

A final strategy is to elect to not control for medication effects, due to the many discussed limitations. This approach may be most relevant for small samples of longer duration in which most participants take numerous psychotropic medications and change their medications throughout the course of the study.

We note that problems relating to the impact of medications are not unique to sleep research. Research using functional imaging (Philips et al., 2008) and neuropsychological assessment (Clark & Goodwin, 2004), among many other areas, face the same challenge. The strategies used by Clark and Goodwin included the second and third approaches discussed above. They demonstrated that repeating their study analyses for subgroups of patients on lithium and off lithium did not change the results, nor did the study outcome variable correlate with antipsychotic dosage expressed as chlorpromazine equivalent. They also used another related strategy, which involved conducting post-hoc analyses to show that there were not correlations between the outcome variable and lithium dosage or length of time on lithium. Clark and Goodwin reasoned that these post hoc analyses indicated that the study outcomes could not "be attributed wholly to medication effects" (p. 64). Indeed, despite the potential confound of the impact of medication, substantial progress can still be made. Certainly, researchers must use caution and outline limitations when drawing conclusions from medicated samples, but the challenges in studying this disorder should not deter future research on representative, medicated samples. At the same time, it is clear that studies more directly addressing the impact of bipolar medication on sleep are needed.

SUMMARY AND IMPLICATIONS

Sleep disturbance is pervasive across the phases of bipolar disorder and across affected youth and adults. Given the adverse impact of sleep disturbance on quality of life, emotional and cognitive functioning, and health, we suggest that further studies are needed correcting for the methodological problems raised. Even more importantly, future work is needed to develop a mechanistic understanding of the role of sleep in bipolar disorder. In particular,

several novel hypotheses have been posited as to the importance of sleep in aspects of functioning that are currently underrecognized and untested, such as cognitive deficits, health, and impulsivity/risk taking. Importantly, sleep deprivation may be one modifiable contributor to a range of the adverse outcomes associated with bipolar disorder. Several of the current psychosocial treatment approaches include a component that targets sleep disturbance, including interpersonal and social rhythm therapy (Frank, Swartz, & Kupfer, 2000; Frank et al., 1999), family therapy (e.g., Miklowitz & Goldstein, 1997; Simoneau, Miklowitz, Richards, Saleem, & George, 1999), and cognitive behavior therapy administered individually (Lam et al., 2003) or in groups (Patelis-Siotis et al., 2001). However, there are not yet data on sleepspecific outcomes and these approaches have yet to fully draw from advances in knowledge on the effectiveness of psychological treatments for sleep difficulty among individuals with insomnia (Morin et al., 2006). The seeds of sleep interventions for adults with bipolar disorder have started to be developed for insomnia (Harvey, 2008; Harvey & Li, in press) and hypersomnia (Kaplan & Harvey, in press), although much work remains to be done. Importantly, specific sleep interventions are starting to be developed for youth with bipolar disorder (Harvey, in press). For the latter, we note that there are a range of unique developmental issues that will need to be considered (e.g., Dahl & Harvey, 2007). We feel hopeful that the contribution of research across these areas has the potential to substantially impact the course and outcome of this serious and minimally understood disorder.

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Table 1

Summary of Studies Documenting Sleep in Adults With Bipolar Disorder

Authors	Sleep disturbance	Measure of sleep disturbance	*N* in bipolar group	Comparison group	Comorbid psychiatric and medical conditions	Medication excluded?	No. of polysomnography nights	Inpatient or outpatient
Mania								
Clayton and Pitts (1965)	94% reduced need for sleep	Structured interview	31	Manic-depressive depressed	Excluded severe alcoholism and severe drug intake	Not reported	N/A	Inpatient
Winokur et al. (1969)	90% reduced need for sleep 34% initial insomnia 24% terminal insomnia	Hospital staff observations and sleep charting	61	None	Not reported	No	N/A	Inpatient
Loudon et al. (1977)	69% reduced need for sleep	Present State Examination; Modified Manic State	16	None	Comorbid diagnoses included two with paranoid schizophrenia, one with schizoaffective disorder, two with hysteroid personality disorder, one with acute schizophrenic episode; excluded preexisting psychiatric conditions including schizophrenia, anxiety neurosis, obsessive–compulsive neurosis, hysteria, alcoholism, drug dependency, antisocial personality, homosexuality and other sexual deviations, mental retardation, and organic brain syndrome	No	N/A	Inpatient
Cassidy et al. (1998)	90% decreased sleep present but of minimal severity 78% indisputably present	Scale for Manic States (developed and validated in this study)	273	Bipolar mixed	Not reported	Not reported	N/A	Inpatient
Serretti and Olgiati (2005)	Bipolar 1 = 99% reduced need for sleep Bipolar II = 97% reduced need for sleep	OPCRIT, using information from patients, relatives, and medical records	158 bipolar I, 122 bipolar II	Bipolar II; major depressive disorder	Excluded mental retardation, dementia, substance abuse/dependence, neurological disorder, and clinical/laboratory indications of severe organic disease	Not reported	N/A	Inpatient
Hudson et al. (1988)	Relative to healthy nonpatients, bipolar patients exhibited: • decreased time spent asleep • increased time awake in the last two hours of recording • shortened rapid eye movement sleep latency • increased REM activity	PSG	9	Healthy control	Excluded primary sleep disorders	Yes: no use of alcohol or drugs for two weeks	Two to three nights	Inpatient

Authors	Sleep disturbance	Measure of sleep disturbance	*N* in bipolar group	Comparison group	Comorbid psychiatric and medical conditions	Medication excluded?	No. of polysomnography nights	Inpatient or outpatient
	• increased REM density							
Hudson et al. (1992)	Relative to healthy nonpatients, bipolar and unipolar patients exhibited: • disturbed sleep continuity • increased percentage of stage 1 sleep • shorter REM latency • increased REM density	PSG	19	Major depression; healthy control	Excluded history of major medical illness or primary sleep disorders (sleep apnea syndrome, periodic limb movements of sleep, or narcolepsy)	Yes: no use of alcohol or drugs	Two to four nights	Inpatient
Linkowski et al. (1986)	Relative to healthy nonpatients, bipolar patients exhibited: • poorer sleep efficiency • longer sleep onset latency • reduced sleep period time	PSG	6	Bipolar depressed; unipolar depressed; healthy control	Excluded if not in good physical health	Yes: no use of drugs for at least eight days; no regular lithium treatment in three months prior to study	One acclimation + three nights	Inpatient
Bipolar Depression								
Winokur et al. (1969)	100% insomnia 58% difficulty falling asleep 27% EMA 23% hypersomnia	Hospital staff observations and sleep charting	61	None	Not reported	No	N/A	Inpatient
Detre et al. (1972)	78% hypersomnia 17% hypsomnia 29% restless sleep	Questionnaire; some patients' relatives also completed a similar questionnaire to assess reliability	65	Unipolar depressed	Excluded nonpsychiatric illnesses that complicated the mood disorder	Not reported	N/A	Inpatient
Casper et al. (1985)	85% global sleep dist. 77% EMA 60% difficulty falling asleep 23% hypersmnia	Sleep disturbance items from the HDS, SADS, VIBES, ADRS, and HSCL-90	47	Unipolar depressed; healthy control	Not reported	Yes: washout period from day of hospital admission to day 14; study data are from day 10	N/A	Inpatient
Duncan et al. (1979)	Relative to unipolar patients and healthy nonpatients, bipolar patients exhibited: • greater fragmentation of REM periods	PSG	22	Unipolar depressed; healthy control	Not reported	Yes: free of all psychoactive medication for a minimum of two weeks prior to study	At least two nights	Inpatient

Authors	Sleep disturbance	Measure of sleep disturbance	*N* in bipolar group	Comparison group	Comorbid psychiatric and medical conditions	Medication excluded?	No. of polysomnography nights	Inpatient or outpatient
Gillin et al. (1979)	Relative to healthy nonpatients, bipolar patients exhibited: • lower REM latency • less total sleep • longer sleep latency • more early morning awakening • more intermittent awake time • less delta sleep • less sleep efficiency	PSG	56	Primary insomnia; healthy control	Excluded patients with significant physical or medical illness	Yes: free of all psychoactive and sleep medications for two weeks (depressed patients and normal volunteers) and four weeks (insomniacs)	One acclimation + three to six nights	Inpatient
Giles et al. (1986)	No differences between bipolar I and II. Compared to unipolar depression, bipolar II exhibited: • longer REM latency • greater total sleep time	PSG	10 bipolar I, 12 bipolar II	Unipolar endogenous depressed	Not reported	Yes: free of medication for two weeks prior to study	Two nights	Not reported
Jernajczyk (1986)	Relative to healthy nonpatients, bipolar patients exhibited: • reduced REM latency • greater standard deviation in activity and density of eye movements	PSG	10	Healthy control	Excluded history of alcohol or drug abuse, prior history of head injury; all had to be physically sound with normal routine EEG	Yes: free of all psychotropic medication for two weeks prior to study	One acclimation + one night	Not reported
De Maertelaer et al. (1987)	Compared to unipolar depression, bipolar patients exhibited: • longer sleep onset latency • trend toward greater number of spindles	PSG	11	Unipolar depressed; healthy control	Not reported	Yes: free of monoamine oxidase inhibitors, neuroepileptic drugs, and lithium for one month prior to study; free of tricyclic antidepressants for two weeks prior to study	One acclimation + three nights	Not reported
Thase et al. (1989)	Relative to healthy nonpatients, bipolar patients exhibited: • fewer minutes in Stage 1. Did NOT observe:	PSG	7 bipolar I, 19 bipolar II	Healthy control	Excluded concurrent alcoholism or drug abuse, borderline or antisocial personality disorder, mental retardation, schizophrenia, schizoaffective disorder, seizure disorder, and psychotic episode of major depression; also excluded if	Yes: free of drugs and alcohol for two weeks prior to study	Two nights	Outpatient

Authors	Sleep disturbance	Measure of sleep disturbance	*N* in bipolar group	Comparison group	Comorbid psychiatric and medical conditions	Medication excluded?	No. of polysomnography nights	Inpatient or outpatient
	• shorter mean REM latency • poor sleep continuity • low Stages 3 and 4				rapid cycling bipolar disorder, medical conditions associated with depression, or history of nonresponse or intolerance to tranylcypromine and imipramine (as these medications were used in the study protocol)			
Lauer et al. (1992)	Relative to healthy nonpatients, both unipolar and bipolar patients exhibited: • prolonged slow wave sleep latency • reduced REM latency • increased REM density	PSG	10	Unipolar depressed; healthy control	Excluded physical illness, narcolepsy, sleep apnea, restless leg syndrome; excluded subjects who experienced sleep deprivation, excessive alcohol/ caffeine intake, shift work, or time shifts (> three hours) in three months prior to study; current/lifetime substance abuse	Yes: free of medication for at least one week prior to study	One acclimation + one night	Inpatients
Fossion et al. (1998)	Relative to unipolar depression: • there was a trend for higher percentage of awakenings in bipolar I Relative to bipolar II: • there was a trend for greater fragmentation of REM sleep relative to bipolar I	PSG	14 bipolar I, 14 bipolar II	Unipolar depressed	Excluded somatic pathology	Yes: free of drugs and alcohol two weeks prior to study	One to two acclimation + one night	Not reported
Mixed								
Cassidy et al. (1998)	Decreased sleep “present but of minimal severity” = 100% “indisputably present” = 91 %	Scale for Manic States (developed and validated in this study)	43	Bipolar manic	Not reported	Not reported	N/A	Inpatient
Interepisode								
Sitaram et al. (1982)	Relative to healthy nonpatients, bipolar patients exhibited: • higher REM density in first REM period • higher percentage of REM sleep	PSG	14	Healthy control; individuals with personal or family history of affective disorders	Not reported	Yes: free of psychotropic medications for at least two weeks prior to study	One to two acclimation + two nights	Outpatient
Millar et al. (2004)	Relative to healthy nonpatients, bipolar patients exhibited:	Actigraphy; self-report sleep diary	19	Healthy control	Excluded if met criteria for a major psychiatric disorder other than bipolar I and/or if being treated for drug or	No	Five days and nights	Outpatient

Authors	Sleep disturbance	Measure of sleep disturbance	*N* in bipolar group	Comparison group	Comorbid psychiatric and medical conditions	Medication excluded?	No. of polysomnography nights	Inpatient or outpatient
	• more variability of sleep duration and night wake time (actigraphic) • longer sleep onset latency (subjective) • longer sleep duration (subjective)				alcohol problems; excluded shift workers			
Jones et al. (2005)	Relative to healthy nonpatients, bipolar patients exhibited: • no differences in mean values or variability in any of the sleep indices • less stable and more variable activity patterns	Actigraphy	19	Healthy control	Excluded if diagnosis of schizoaffective illness and/or current primary alcohol or drug addiction problem	No	Seven days and nights	Outpatient
Harvey et al. (2005)	70% exhibited clinically significant sleep disturbance. Relative to healthy nonpatients, bipolar patients exhibited: • longer total sleep time (actigraphic) • longer sleep onset latency (subjective)	Actigraphy; self-report sleep diary	20	Healthy control; insomnia	Included and reported psychiatric comorbidities	No	Eight days and nights	Outpatient

Note: EMA = Early Morning Awakening; OPCRIT = Operational Criteria for Psychotic Illness Checklist; PSG = Polysomnography; HDS = Hamilton Depression Scale; SADS = Schedule for Affective Disorders and Schizophrenia; VIBES = Video Interview Behavior Evaluation Scale; ADRS = Affective Disorder Rating Scale; HSCL-90 = Hopkins Symptom Checklist; REM = Rapid Eye Movement.

Table 2

Summary of Studies Documenting Sleep in Youth With Bipolar Disorder

Authors	Sleep disturbance	Measure of sleep disturbance	*N* in bipolar group	Comparison group	Comorbid psychiatric and medical conditions	Medication excluded?	No. of polysomnography/ actigraphy nights	Inpatient or outpatient or community
Ballenger et al. (1982)	67% reduced need for sleep in child group vs. 100% in adult group	Medical records, observations by patients' families and referring physicians, and patient and family interviews	21	Adult manic patients	Schizophrenic symptoms (significantly higher rate found in child group than in adult group)	No	N/A	Inpatient
Duffy et al. (2007)	Compared to offspring of controls, offspring of lithium responders and offspring of lithium nonresponders exhibited: significantly higher rates of sleep disorders No differences between the two high-risk groups were found in rates of sleep disorders	K-SADS parent and child report	67 offspring of lithium responders	Offspring of lithium nonresponders; offspring of healthy controls	Comorbid diagnoses included schizoaffective disorder, major depressive disorder, anxiety, eating, adjustment, substance use, sleep, conduct, and somatoform disorder, and ADHD and/or learning disability	Not reported	N/A	Outpatient
Faedda et al. (2004)	45.1% reported that sleep disturbance was an initial symptom of the disorder and 95.1 % exhibited some form of sleep disturbance (including insomnia and parasomnias)	Medical records, semistructured interviews with parents	82	None	Lifetime diagnoses included: ADHD (60%), anxiety disorders (39%), major depression (37%), ODD or CD (21%). Current conditions: psychotic features (32%), OCD (27%) and other anxiety disorders in (23%)	No	N/A	Outpatient

Authors	Sleep disturbance	Measure of sleep disturbance	*N* in bipolar group	Comparison group	Comorbid psychiatric and medical conditions	Medication excluded?	No. of polysomnography/ actigraphy nights	Inpatient or outpatient or community
Faedda & Teicher (2005)	Compared to normative data, children with bipolar disorder exhibited: • decreased sleep efficiency and sleep duration • increased sleep onset latency • increased nocturnal activity	Actigraphy and M-MAT	2	Age- and gender-matched ADHD and normative data	Not reported	No	Five to seven	Outpatient
Ferreira et al. (2007)	87.5% decreased need for sleep and parasomnias	Medical records, CBCL, DICA-IV interviews (child and parent reports)	8 bipolar I	None	ADHD (50%)	No	N/A	Outpatient
Findling et al. (2001)	72.2% decreased need for sleep	K-SADS	90 bipolar I	None	Overall 81.1% of sample met criteria for comorbid diagnoses, including disruptive behavior disorders (74.4%), ADHD (70.0%), ODD (46.7%), CD (16.7%), and substance abuse (17.6%).	No	N/A	Outpatient
Geller et al. (2002)	39.8% decreased need for sleep (vs. 6.2% reduced need in ADHD vs. 1.1 % in controls)	K-SADS	93 bipolar I and II, cyclothymia	ADHD; healthy controls	Excluded for pervasive developmental disorders, schizophrenia, epilepsy, major medical or neurological disorder, substance	Not reported	N/A	Outpatient

Authors	Sleep disturbance	Measure of sleep disturbance	*N* in bipolar group	Comparison group	Comorbid psychiatric and medical conditions	Medication excluded?	No. of polysomnography/ actigraphy nights	Inpatient or outpatient or community
					dependency, pregnancy.			
Holtmann et al. (2007)	The bipolar disorder profile group reported 66.7% reduced need for sleep compared to both clinical control (39.3%) and healthy control (10.2%) groups.	CBCL (parent report)	21 bipolar disorder profile	Clinical controls (children with levels of psychopathology comparable to bipolar disorder group); healthy controls	Comorbid conditions included social withdrawal (61.9%), somatic complaints (28.6%), anxiety/ depression (100%), thought problems (47.6%), attention problems (100%), delinquent behavior (57.1 %), and aggressive behavior (100%).	Not reported	N/A	Community
Jerrell & Shugart (2004)	21% reported reduced need for sleep	Medical records	83 bipolar I	None	ADHD (42%), schizophrenia (30%), CD (25%), PTSD (18%)	No	N/A	Inpatient and outpatient
Jones et al. (2006)	Compared to children of control parents, children of bipolar disorder parents exhibited: • shorter sleep latency (actigraphic) • trend toward less variable sleep (actigraphic) • trend toward greater sleep duration (actigraphic)	Actigraphy, PSQI	25 children of bipolar disorder parents	Children of control parents	Not reported	No	Seven days and nights	Outpatient

Authors	Sleep disturbance	Measure of sleep disturbance	*N* in bipolar group	Comparison group	Comorbid psychiatric and medical conditions	Medication excluded?	No. of polysomnography/ actigraphy nights	Inpatient or outpatient or community
	• lower PSQI score (overall)							
Lofthouse et al. (2007)	96.2% had moderate to severe sleep problems. Initial insomnia was the most pervasive problem.	CSHQ (parent report)	133	None	Overall 64% of sample met criteria for comorbid diagnoses, including separation anxiety, specific phobia, enuresis, and GAD.	No	N/A	Mixed: clinical and community sources (e.g., psychologists' referral, community ads)
Lofthouse et al. (2008)	98.6% reported mood-related sleep problems. Also, 96.9% had psychosocial impairment (home, school, or with peers) and nearly two-thirds (64.0%) had problems across all three spheres. Phase shifts were also associated with sleep difficulties (e.g., three-day weekends, daylight savings)	CSHQ (parent report)	494	None	ADHD (60.7%), anxiety disorders (39.1%), ODD (29.4%), pervasive developmental disorders (12.6%), CD (5.1%), psychotic disorders (2.8%), substance abuse/ dependence (0.2%), another disorder (8.7%). Also reported sleep disorder comorbidities: sleep terror (9.9%), primary insomnia (8.3%), nightmare disorder (4.3%), sleepwalking disorder (2.8%),	No	N/A	Community

Authors	Sleep disturbance	Measure of sleep disturbance	*N* in bipolar group	Comparison group	Comorbid psychiatric and medical conditions	Medication excluded?	No. of polysomnography/ actigraphy nights	Inpatient or outpatient or community
					breathing-related sleep disorder (2.6%), circadian rhythm disorder (2.2%), primary hypersomnia (1.0%), parasomnia-NOS (1.0%), dyssomnia-NOS (0.4%), narcolepsy (0.2%)			
Mehl et al. (2006)	PSG: Compared to control group, bipolar disorder group exhibited sleep continuity disturbance, lower sleep efficiency, less REM sleep, longer slow wave sleep, and a trend toward more awakenings. Subjective measures: Compared to control group, bipolar disorder group reported more difficulty initiating sleep, more restless sleep, nightmares, and morning headaches.	PSG	13	Healthy controls	Comorbid conditions included ADHD symptoms and anxiety symptoms	No: but control group matched for medication usage	One night	Community
Papolos et al. (2007)	Strongest concordance coefficients between probands and siblings and widest contrasts between bipolar disorder sibling pairs and comparison sibling pairs included sleep-wake cycle disturbances	CBQ (parent report)	260 bipolar profile sibling pairs	Age- and gender-matched control sibling pairs	Comorbid diagnoses included ADHD (58.1%), OCD (21.2%), and GAD (20.8%).	Not reported	N/A	Community
Rao et al. (2002): seven-year follow-up study to	Compared to children with unipolar course, children who developed BD by follow-up exhibited:	PSG	59	Unipolar depressed; healthy controls	Excluded for anorexia nervosa, autism, and schizophrenia	Yes: at initial assessment required two-week washout period	Three (consecutive)	Outpatient

Authors	Sleep disturbance	Measure of sleep disturbance	*N* in bipolar group	Comparison group	Comorbid psychiatric and medical conditions	Medication excluded?	No. of polysomnography/ actigraphy nights	Inpatient or outpatient or community
Dahl et al. (1990)	• more Stage 1 sleep • a trend toward reduced Stage 4 sleep No differences found in sleep continuity measures							

Note: K-SADS = Kiddie Schedule for Affective Disorders and Schizophrenia; M-MAT = McLean Motion Analysis Test; CBCL = Child Behavior Checklist; DICA-IV = Diagnostic Interview for Children and Adolescents—*DSM–IV* Version; PSQI = Pittsburgh Sleep Quality Index; CSHQ = Children's Sleep Habits Questionnaire; REM = rapid eye movement; PSG = Polysomnography; CBQ = Child Bipolar Questionnaire; ADHD = attention-deficit/hyperactivity disorder; BD = bipolar disorder; CD = conduct disorder; GAD = generalized anxiety disorder; OCD obsessive-compulsive disorder; ODD = oppositional-defiant disorder; PD = posttraumatic stress disorder.