Title
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Journal
Sleep Medicine Clinics, 8(3)

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Publication Date
2013-09-01

DOI
10.1016/j.jsmc.2013.04.007

Peer reviewed

Published in final edited form as:
Sleep Med Clin. 2013 September ; 8(3): 361–371. doi:10.1016/j.jsmc.2013.04.007.

Insomnia comorbid to severe psychiatric illness

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Abstract

In psychiatric illness, there is a growing body of evidence indicating that sleep disturbances exert a detrimental influence on the course of these disorders and contribute to impaired function. Even when psychiatric disorders are successfully treated or stabilized, insomnia and other sleep disturbances often fail to remit. The present review focuses on sleep in two severe mental illnesses, namely bipolar disorder and schizophrenia. This article discusses the role of sleep disturbances and altered sleep architecture in relation to symptom status, functional impairment, quality of life, and the course of these disorders. Current evidence regarding pharmacological and psychological treatment approaches for insomnia in these populations is presented. This review also notes considerations for adapting Cognitive Behavioral Therapy for insomnia (CBT-I) procedures for severe mental illness and proposes directions for future research.

Keywords

Insomnia; Bipolar Disorder; Schizophrenia; CBT-I

Introduction: Nature of the Problem

There is robust evidence that insomnia frequently co-occurs with a wide range of psychiatric disorders. Indeed, it is estimated that 20–40% of individuals with mental illness experience insomnia (1–3). Because insomnia can be associated with a variety of psychiatric disorders and/or medical illnesses, diagnostic classification systems such as the DSM-IV-TR (4) and ICSD-2 (5) distinguish between “primary” and “secondary” insomnia. Primary insomnia is considered a freestanding condition, while secondary insomnia is diagnosed when the insomnia is considered subordinate to a primary condition, such as a psychiatric disorder. Yet, the relationship between insomnia and a co-occurring psychiatric disorder can vary considerably across patients. Indeed, the distinction between primary and secondary insomnia has been blurred by epidemiological research suggesting that insomnia may predate, and predict, psychiatric illness (2, 6). As a result, a recent National Institute of Health (NIH) state-of-the-science conference (7) concluded that the term “secondary” should be replaced with “comorbid” on the basis of evidence that insomnia that is comorbid with another disorder likely contributes to the maintenance of the disorder (8, 9).

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In cases of comorbid insomnia, additional empirical and clinical attention is especially important, as there appears to be a cyclical relationship between sleep disturbance and medical or psychiatric illness. For example, worsening sleep problems can lead to exacerbated psychiatric symptoms and daytime distress, with psychiatric symptoms and daytime distress then worsening the sleep problems (9–11). Fortunately, there is a growing body of evidence suggesting that insomnia responds to Cognitive Behavioral Therapy for Insomnia (CBT-I) even if the psychiatric or medical disorder is not under control (12). Smith et al. (9) concluded that treatment effects are generally moderate to large for CBT-I administered in medical and psychiatric illnesses, and are comparable to treatment effects in primary insomnia.

The goal of the present review is to summarize the role of insomnia and disturbed sleep architecture in two severe mental illnesses (bipolar disorder, schizophrenia). Although the research we review largely examines the importance of insomnia as a mechanism in severe psychiatric illness, it is noteworthy that there is increasing interest in the possibility that hypersomnia, delayed sleep phase and reduced sleep need may also be mechanisms (13, 14). Current knowledge regarding pharmacological and psychological treatment approaches for insomnia in these populations are briefly reviewed, as well as challenges clinicians may encounter adapting CBT-I procedures in severe mental illness.

Bipolar Disorder (BD)

Overview of sleep disturbance across the phases of BD

Sleep disturbance is a core feature of mood episodes in BD. During periods of mania, the majority of patients (69–99%) experience reduced need for sleep, which has been corroborated by both self-report and polysomnographic investigations (see 15 for review). Additionally, several small studies have shown that, relative to healthy non-patients, individuals with mania tend to exhibit shortened Rapid Eye-Movement (REM) sleep latency and increased REM density (16, 17).

The rates of insomnia in bipolar depression vary considerably across studies, with one study reporting that 100% of depressed bipolar patients experienced insomnia (see 15 for review). The rates of hypersomnia during the depressive phase of bipolar illness vary between 23–78% (13). Similar to unipolar depression, patients with bipolar depression tend to experience shortened REM latency relative to healthy adults (18, 19), although there have been non-replications (20). REM density in a bipolar depressed sample was elevated compared to healthy adults and not significantly different from a unipolar depressed group(19). Reduced Non-REM (NREM) stage 3 (N3), or slow wave sleep (SWS), has been observed in small samples of bipolar depressed patients relative to healthy adults (21) and at a level equivalent to unipolar depressed patients (22). However, one study found no differences in N3 relative to healthy adults (20). Finally, in bipolar depressed patients, one investigation reported reduced stage N1 sleep (20), but most reports have not (19, 21).

During the inter-episode period, clinically significant sleep disturbance persists in up to 70% of BD patients (23, 24). Estimates of insomnia prevalence between episodes vary. A recent study in a sample of 14 bipolar participants reported that only 2 (14%) met criteria for

insomnia (25), while an earlier investigation in a larger sample found that 50% of inter-episode BD patients experienced insomnia (23). Another study reported that 25% of inter-episode BD patients experienced hypersomnia (26). With regard to specific sleep characteristics, studies have shown that inter-episode BD patients had longer sleep onset latency (9, 27, 28), longer and more variable periods of wakefulness during the night (29), more nighttime awakenings (28, 30), increased sleep duration (27), poorer sleep efficiency (23, 28), and more night-to-night variability of sleep patterns (27) relative to healthy adults. During the inter-episode period, two studies have found evidence for increased REM density in both unmedicated (31) and medicated bipolar samples (32). However, one study found no differences between sleep architecture in healthy adults and inter-episode bipolar participants (30). In all three studies there were no observed differences in NREM sleep in the bipolar samples relative to healthy adults (30–32).

Even among BD patients treated with ‘best practice’ mood stabilizers in STEP-BD (33), 66% experienced significant sleep disturbance (34, 35). Furthermore, sleep disturbance is characteristic across the bipolar spectrum. In a recent investigation, out of a sample of 116 euthymic bipolar outpatients, 27.1% of those with BD type 1 reported ongoing sleep disturbance, as well as 21.7% of those with BD type II, and 16.6% of those with BD NOS (24). Although, the authors note that these percentages may underestimate patients with underlying sleep disturbance that were receiving treatment with hypnotics and/or sedating antipsychotics (24). Another study found that total sleep time is shortest in BD NOS, relative to BD type 1 and BD type II, but the three subtypes are equally impaired in night-to-night variability in sleep duration (34).

Significance of insomnia in BD

Sleep disturbance is an early marker for BD. In a study of early-onset BD, sleep disturbance was retrospectively reported to be one of the earliest symptoms observed by parents (36). In another study, sleep disturbances were identified as an antecedent to the first onset of BD in a subset of high-risk youth (37). A thorough review of early symptoms of mania and depression by Jackson and colleagues (38) identified sleep disturbance as the most common prodrome of manic relapse and sixth most common prodrome of depressive relapse in BD. In response to experimental sleep deprivation, a substantial proportion of individuals with BD depression show a rapid alleviation of depressed mood, but a subset of participants experienced an onset of hypomania or mania (39–41). Furthermore, a recent cross-sectional study found that BD patients who habitually slept less than six hours a night exhibited both greater manic and depressive symptoms relative to BD patients with normal sleep duration (34). In the same study, BD participants sleeping greater than nine hours also endorsed more depressive symptomatology than did the BD group that slept between 6.5 and 8.5 hours.

Prospective investigations have reported similar findings. Shortened sleep duration has been found to predict increased daily manic symptoms (42, 43) and depressive symptoms at a 6-month follow-up (44). Lengthened sleep duration also predicted heightened daily depressive symptoms (43) and depressive symptoms at a 6-month follow-up (26). Lower and more variable sleep efficiency and variability of sleep onset latency in inter-episode BD were related to more lifetime depressive episodes and more current depressive symptoms (45).

There is also evidence to suggest that disturbed sleep in inter-episode BD has considerable functional consequences. Disturbed sleep and short habitual sleep duration (<6 hours) were associated with impaired psychosocial functioning and poorer quality of life in inter-episode BD patients (34, 46).

Few investigations have examined the relationship between sleep architecture, mood, and outcome in bipolar disorder. In one study of inter-episode BD, sleep architecture was not correlated with concurrent mood symptoms (32). However, greater REM density was correlated with more severe depressive symptoms and greater functional impairment at 3 months, while prolonged duration of the first REM period and a greater amount of slow wave sleep were positively correlated with manic symptoms and impairment at 3 months. Additionally, the amount of N2 sleep was negatively correlated with manic symptoms and impairment at 3 months. Hudson et al. (47) found that time spent asleep and REM percentage inversely correlated with mania severity in currently manic patients.

Treating insomnia in BD

Taken together, these data have highlighted the complexity and multiple sleep disturbances that are characteristic of bipolar disorder (insomnia, hypersomnia, delayed sleep phase, irregular sleep wake schedule, reduced sleep need) and the importance of an intervention to treat sleep problems as a pathway for improving mood and reducing impairment. However, few studies have explored treatment options for sleep disturbance in bipolar disorder. A chart review in a private clinic showed that non-benzodiazapine hypnotics appear safe, and 46% of BD patients prescribed hypnotics were using these medications chronically (48). In a case report, gabapentin found to be helpful for treatment-resistant insomnia in BD (49, 50). However, case reports on benzodiazepines for insomnia in BD have not been encouraging (50).

Open trials of medications targeting the circadian system, such as melatonin (51) and agomelatine (52) are promising, but preliminary. Two small clinical trials have recently evaluated ramelteon for sleep disturbance in bipolar disorder. One study evaluated the efficacy and tolerability of ramelteon in BD type I with manic symptoms and insomnia (53). Twenty-one outpatients were randomized to receive either 8mg/day of ramelteon (N=10) or placebo (N=11) in an 8-week double-blind treatment design. While ramelteon did not significantly differ from placebo in reducing symptoms of insomnia, mania, and global severity of illness, it was tolerable and associated with improvement in a global rating of depressive symptoms. Another recent study of ramelteon focused on treating sleep disturbance in euthymic BD patients (54). Participants were randomized to receive ramelteon (n=42) or placebo (n=41) for up to 24 weeks. Relative to the placebo group, participants receiving ramelteon had marginally better subjective sleep quality, and overall risk for depression and mania relapse was cut nearly in half during the 24-week treatment period.

While these preliminary results using pharmacologic interventions for sleep in BD are encouraging, it is important to develop and test non-pharmacologic approaches to treating sleep in bipolar disorder because: 1) there are fewer side effects or interactions with other treatments for the bipolar disorder and other conditions; 2) concerns remain about treatment

durability, daytime residual effects, tolerance, dependence, and rebound insomnia with pharmacotherapy; 3) certain classes of insomnia medications—most important, the FDA-approved benzodiazepine receptor agonists—pose a risk of abuse given the comorbidity between bipolar disorder and substance use disorders (55).

CBT-I may be a particularly useful intervention to stabilize sleep and circadian rhythms in BD. As described above, individuals with bipolar disorder display night-to-night variability in total sleep time (34) along with reduced sleep efficiency and increased nighttime wakefulness (23, 32) that may respond well to sleep restriction and stimulus control. However, in adapting CBT-I for bipolar disorder it may be important to modify certain components that could lead to sleep deprivation due to the strong link between sleep loss and relapse (56). For example, the stimulus control instruction to get out of bed may lead some patients to engage in rewarding and arousing activities that prevent sleep. Also, in order to avoid changes in mood related to short-term sleep deprivation, minimum time in bed during sleep restriction should likely be no lower than 6.5 hours. Throughout treatment, it is particularly important to monitor depression and/or mania symptoms at the start of each session and negotiate a safety plan with the patient prior to the start of therapy, should mood grow unstable during treatment. If symptoms of depression or mania emerge, changes in total sleep time that may be contributing to these symptoms should be evaluated, and consideration should be given to modifying or temporarily suspending sleep restriction or stimulus control if necessary. Notwithstanding such concerns, we recently reported preliminary findings suggesting the safety of regularizing bed and wake times using stimulus control and sleep restriction strategies with BD patients (57).

Summary and future directions

Thus far, research evidence consistently supports a link between sleep, mood, impairment and quality of life in BD. However, several important gaps in knowledge remain. At a foundational level, more research is needed to understand the prevalence of sleep disturbances (insomnia, hypersomnia, delayed sleep phase, reduced sleep need) across the bipolar disorder subtypes and during mixed mood episodes (i.e., when diagnostic criteria are met for *both* a manic episode and an episode of depression). Additionally, the nature and role of sleep architecture in the course of BD remains understudied, with the majority of polysomnographic investigations in BD having been conducted approximately 2–3 decades ago.

It will also be crucial to identify causal, and potentially bi-directional, pathways between sleep disturbance and mood in BD. There is robust behavioral and neuroimaging evidence among healthy non-patient samples that sleep deprivation undermines emotion regulation the following day (58). Additionally, an interesting study of medical residents by Zohar et al. (59) suggests that the context in which the emotion is experienced is important for determining the direction of the effect of sleep disturbance on affective functioning. Specifically, sleep loss increased negative affect following a goal-thwarting event and diminished positive emotions following a goal-enhancing event. Individuals with mood disorders, who already have a vulnerable emotion regulation system, would likely

experience even more adverse effects from sleep disturbances. However this assumption has yet to be tested in a BD sample.

Given the high rates of sleep disturbance in BD, it is surprising that few controlled trials of medication or psychological interventions for sleep have been conducted in this population. There is exciting preliminary evidence that treating sleep or circadian disturbance with ramelteon can reduce the risk of manic and depressive relapse, supporting the idea that treating sleep can improve the course of illness (54). A recent report has provided exciting preliminary evidence of the efficacy and safety of CBT-I in BD (60). However, certain treatment complexities in bipolar disorder need to be better understood, such as: Should a clinician approach treating sleep disturbance differently at distinctive phases of the BD illness? During manic or mixed episodes, a pharmacological approach for sleep may be most appropriate to aid in fully stabilizing a patient. Yet, during bipolar depression or the inter-episode period, psychological approaches may be preferable due to the reduced risk of negative side effects. In unipolar depression, CBT-I improves sleep and depressive symptoms when administered in combination with antidepressants (61) or as a standalone treatment (62). Larger controlled trials testing psychological and pharmacological therapies in BD hold promise for not only improving sleep, but also for stabilizing mood stability and enhancing quality of life.

Schizophrenia and psychotic disorders

Overview of sleep in Schizophrenia

Sleep disturbance is prevalent in schizophrenia, during both psychosis and remission. An early investigation conducted in psychiatric inpatients found that 83% of 12 acutely ill schizophrenia patients and 47% of 17 patients with chronic psychosis had at least one type of sleep complaint, such as difficulty falling asleep, early morning awakening, awakening during the night, not sleeping soundly, and having increased time in bed (63). A later report found that, out of 93 stable outpatients with schizophrenia, early insomnia was endorsed by 26% of the patients, middle insomnia by 23%, and early morning awakening by 16% of the patients (64). Within the Clinical Antipsychotic Trials of Intervention Effectiveness study, 16–30% of patients across treatment arms reported insomnia and 24–31% reported hypersomnia despite management of symptoms with antipsychotic medication (65). In a sample of 44 adults with schizophrenia, another study reported poor sleep quality at a rate of 52% using the Pittsburgh Sleep Quality Index (66). More recently, a study conducted with 175 clinically stable outpatients suffering from schizophrenia or schizoaffective disorder found that 44% of met criteria for clinical insomnia using the Insomnia Severity Index (67).

Consistent with the sleep complaints described above, self-report and polysomnographic investigations of medicated patients with schizophrenia report prolonged sleep latency, low sleep efficiency, poor sleep quality, and shortened sleep duration (68–72) These patterns are also observed in drug-free or medication naïve patients with schizophrenia. A meta-analysis of PSG studies in 321 patients and 331 controls reported that the schizophrenia group experienced increased sleep latency, decreased total sleep time, increased wake after sleep onset and reduced sleep efficiency compared to healthy controls (73).

Prospective studies involving actigraphy have also provided interesting insights. In a study of 28 older patients with schizophrenia and age-matched controls, monitoring of sleep–wake function with actigraphy showed greater wake time at night, longer time in bed, more sleep during the day and less robust circadian rhythmicity in the schizophrenia group (74). Similarly, a sample of 20 middle-aged schizophrenia outpatients took longer to fall asleep and slept longer than those in the control group regardless of sleep onset time. Furthermore, 50% of the individuals in the schizophrenia group showed markedly delayed and/or free-running sleep-wake cycles (75). Thus, in addition to sleep continuity problems, disrupted circadian rhythmicity is also evident in individuals with treated schizophrenia.

There is also a growing body of evidence demonstrating altered sleep architecture in schizophrenia (14, 76, 77). The majority of studies indicate that slow wave sleep, NREM delta activity, and REM latency are reduced in schizophrenia, whether the patients are drug-naïve, acutely psychotic, or medicated and clinically stable (i.e., (55, 72, 78–85)). Some studies have found elevated REM density (16, 86), but previously treated and drug-naïve patients with schizophrenia typically exhibit normal REM density (79, 81, 84, 85, 87, 88). More recently, reduced spindle activity has been observed in schizophrenia relative to healthy adults (89).

Significance of insomnia in schizophrenia

Sleep disturbances have also been associated with exacerbated symptoms in schizophrenia, particularly positive symptoms. Positive symptoms include delusions, hallucinations, disorganized thinking and behavior. For example, a recent actigraphic investigation found that, relative to schizophrenia patients experiencing predominantly negative symptoms on the Positive and Negative Syndrome Scale (PANSS), those with predominantly positive symptoms experienced more sleep-wake disturbances (90). Similarly, prolonged sleep latency in inpatients with schizophrenia was associated with greater ‘Thinking Disturbance’ on the Brief Psychiatric Rating Scale (91). In another study, moderate or severe insomnia symptoms were present in more than 50% of a medicated sample experiencing persecutory delusions (92). Schizophrenia patients with insomnia symptoms, low total sleep time and poor sleep efficiency were also at a greater risk for worsening of positive symptoms after antipsychotic discontinuation (93, 94). Interestingly, studies have generally found that negative symptoms (i.e., anhedonia, social withdrawal, loss of motivation, poor self-care) were unrelated to insomnia symptoms. Finally, a substantial number of studies have reported that sleep continuity disturbances and poor sleep quality detrimentally affect quality of life in patients with schizophrenia, even while on stable medication regimens (1, 64, 67, 68, 71, 73, 95, 96).

Polysomnographic investigations have demonstrated relationships between sleep architecture and symptom severity in schizophrenia (for review see (14, 77, 97)). Overall illness severity, as assessed by the BPRS or PANSS, has generally been associated with altered REM sleep, such as increased REM percentage, shorter REM latency, and decreased REM density (i.e.,(79, 84, 98, 99)). Greater positive symptom severity is typically associated with lower REM density or shortened REM latency in medicated, unmedicated and drug-naïve patients (79, 84, 88, 98–100). REM density was also found to correlate specifically

with hallucinatory behavior, as assessed by the BPRS (87). A more recent study reported that spindle activity and spindle number were inversely related to both positive and negative symptoms on the PANSS, namely the stereotyped thinking, conceptual disorganization and hallucination subscales (89). With regard to negative symptoms, studies have largely reported an association between increased negative symptoms and reduced SWS duration, SWS percentage or delta activity (81, 101–105), although there have been some non-replications (79, 84, 89). Some investigations have also found REM latency (79, 98, 101) and REM density (106) to be inversely correlated with negative symptoms.

In addition to the relationship between acute symptomatology and sleep parameters, SWS and REM latency have been found to predict clinical outcome. Keshavan et al. (107) reported that lower percentage of delta sleep at baseline predicted poorer functional outcomes at 1 and 2 year follow-up. Another investigation found that shorter REM latency in medication-free schizophrenia inpatients predicted poorer global functioning 1 year after hospital discharge (108). Similarly, relative to 6 schizophrenia inpatients with sleep onset REM episodes, 30 schizophrenia inpatients without this sleep abnormality had better global functioning 1 year after assessment (109).

Treating insomnia in schizophrenia

As is the case for bipolar disorder, minimal work has been done to explore treatment options for sleep disturbance associated with schizophrenia despite the high prevalence, persistence and clinical consequences of sleep disturbance in this mental disorder. In the case of insomnia linked with schizophrenia, treatment most frequently involves antipsychotics and sedative hypnotics (97). Most first and second-generation antipsychotics, except for risperidone, appear to facilitate an increase in total sleep time and/or sleep efficiency in schizophrenia patients (for review see (10, 77)). However, as previously noted, a large proportion of patients continue to experience insomnia and hypersomnia despite treatment with atypical antipsychotics (65).

Much less is known about the safety and efficacy of hypnotic medications in the context of schizophrenia. Generally, these medications do not have long-term efficacy and are associated with residual sedation during the daytime (97). In a survey of 93 clinically stable medicated schizophrenia outpatients, 33 reported using hypnotic medication, but 14 (35.5%) of those patients still considered their sleep to be disturbed (64). Another study of 6 male schizophrenia outpatients treated with benzodiazepine hypnotics in combination with antipsychotics found that substituting zopiclone for the benzodiazepine hypnotic improved subjective soundness of sleep and delta activity (110). However, a recent review of the literature highlighted that no controlled trials of non-benzodiazepine hypnotics or benzodiazepine hypnotics have been conducted in schizophrenia (111).

Preliminary findings from treatment trials testing melatonin in schizophrenia have been promising. In outpatients with chronic schizophrenia, Shamir et al. (112) used a randomized, blinded, crossover study design to examine the effects of melatonin replacement (2 mg, controlled release) on their sleep. Melatonin improved sleep efficiency measured via actigraphy, particularly for low-efficiency sleepers. A second study reported that melatonin improved the subjective quality of sleep in a randomized, double-blinded, placebo-

controlled trial in 40 stable schizophrenia outpatients with sleep onset insomnia (113). Patients were randomly assigned to augment their current medication regimen with either flexibly dosed melatonin (3–12 mg/night; N = 20) or placebo (N = 20). Relative to placebo, melatonin significantly improved sleep quality, reduced the number of nighttime awakenings, increased the duration of sleep, and improved mood. Importantly, melatonin was not associated with self-reported 'hangover' symptoms, such as headache, early morning dullness or head heaviness that can be associated with conventional hypnotic medications. No concurrent changes in positive and negative symptoms were noted in these melatonin treatment trials.

With regard to psychological approaches, a recent open trial tested CBT-I in patients with persecutory delusions (114). Participants included outpatients with persecutory delusions that had persisted for at least 6 months (N=15), including individuals with a diagnosis of schizophrenia (N=10), psychotic disorder (N=2), delusional disorder (N=1) and psychosis (N=1). A 4-session CBT-I intervention resulted in clinically significant reductions in insomnia severity and improved sleep quality. Furthermore, there was a significant reduction in paranoid thinking, depressive symptoms, and anxiety symptoms following CBT-I. These improvements were maintained at though a one-month follow-up assessment, indicating short-term durability of this intervention. In this case, the adapted CBT-I intervention included sleep psycho-education, sleep hygiene recommendations, and a stimulus control intervention. Cognitive approaches for insomnia and sleep restriction were not employed in the 4-session protocol. While these preliminary results are promising and support the notion that improving sleep is beneficial in a variety psychological domains, the small sample size and lack of a control condition prevent definitive conclusions from being drawn about the efficacy of CBT-I in psychotic disorders. Additionally, as demonstrated by Myers et al. (114), in adapting CBT-I for schizophrenia it may be important to eliminate certain traditional CBT-I components, such as sleep restriction which could lead to reduced sleep time and exacerbation of psychotic symptoms (94). It may also be particularly important to monitor positive symptoms at the start of each session throughout treatment and negotiate a safety plan with the patient prior to the start of therapy, should psychotic symptoms emerge during treatment.

Summary and future directions

Overall, the literature suggests that sleep problems, namely insomnia and circadian disturbances, are frequent in schizophrenia. Moreover, these sleep disturbances are generally associated with greater symptom severity, impaired quality of life and the course of schizophrenia. While there is a growing body of work investigating sleep architecture in schizophrenia, more research examining the rates of sleep disorders using gold-standard diagnostic methods (115) are needed. Facets of both REM and NREM sleep architecture appear altered in schizophrenia, although findings regarding these components of sleephave not been consistent. This is perhaps due to small sample sizes and heterogeneities in the patient populations (i.e., not subdividing into paranoid, catatonic and undifferentiated patient groups), issues that should be addressed in future studies. Additionally, though there is considerable evidence supporting an association between sleep (primarily poor sleep continuity and altered sleep architecture) with symptoms and outcome, much work is still

needed to disentangle causal relationships. Future research involving prospective and experimental designs could shed light on the important causal links between sleep disturbance and disease severity.

Two sleep treatment studies in outpatient schizophrenia populations, one testing melatonin (113) and the other testing adapted CBT-I (114), have provided the best preliminary evidence that normalization of sleep is related to improved clinical outcome. These interventions demonstrated that treating sleep led to improvements in residual positive symptoms and/or mood, and lay the groundwork for future sleep interventions in schizophrenia. Further investigations testing sleep interventions in larger scale controlled trials would help more rigorously clarify the clinical utility of treating sleep disturbances in schizophrenia. Finally, the timing and selection of sleep treatments requires examination. For instance, certain insomnia interventions may be more effective at different phases of illness (acute vs. stable) or based on schizophrenia subtype. While many gaps remain in the literature, the findings available highlight the importance of developing and testing sleep interventions for schizophrenia, with the aim of reducing symptom burden and improving functional outcomes.

Conclusion

In both bipolar disorder and schizophrenia, sleep disturbance is a prominent feature regardless of medication status and phase of the disorder. Insomnia is the most frequent sleep problem in each of these patient populations, yet hypersomnia and circadian rhythm disturbances are also common. These sleep problems, as well as altered sleep architecture, are associated with exacerbated disease-specific symptoms, reduced quality of life, impaired daily functioning, and poor clinical outcome. While gaps in knowledge remain, these observations suggest a need for more research focusing on treatment of insomnia in severe psychiatric illness. A few small sleep-focused treatment studies in bipolar disorder and schizophrenia have provided preliminary evidence that treatment of sleep disturbance may have clinical utility, reducing residual symptoms and risk of acute relapse. Future intervention trials would benefit from use of polysomnography and sample sizes large enough to assess whether improvements in these psychiatric conditions are driven by the improvement in sleep.

CBT-I appears to be a particularly promising avenue for reducing sleep disturbance, given its effectiveness in other psychiatric disorders and its low side effect profile. That said, at least one study has documented that greater symptom severity in major depression is associated with poorer adherence to CBT-I (116), and symptom severity or fluctuation in bipolar disorder or schizophrenia may present similar challenges to treatment adherence. Some have raised concerns over residual positive, negative and cognitive symptoms in schizophrenia that may also hinder adherence to CBT-I (117). It is clear that both pharmacological and psychological treatments for insomnia, as separate or interwoven interventions, require further testing in bipolar disorder and schizophrenia. However, the evidence reviewed here suggests an encouraging possibility - that treatment of sleep disturbance, in conjunction with the management of severe psychiatric illness, could lead to a more successful outcome and improved quality of life.

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Key Points

- Insomnia, as well as hypersomnia and circadian rhythm disturbances, are common in schizophrenia and bipolar disorder
- Poor sleep continuity and abnormal sleep architecture are associated with disease-specific symptoms, poor quality of life, and greater impairment in schizophrenia and bipolar disorder
- CBT-I and melatonin agonists may be useful sleep treatments in severe mental illness
- Preliminary evidence indicates that treatment of sleep can improve psychiatric symptoms in severe mental illness