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# Interventions for Sleep Disturbance in Bipolar Disorder

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# **Synopsis**

Bipolar disorder is a severe and chronic disorder, ranked in the top 10 leading causes of disability worldwide. Sleep disturbances are strongly coupled with inter-episode dysfunction and symptom worsening in bipolar disorder. Experimental studies suggest that sleep deprivation can trigger manic relapse. There is evidence that sleep deprivation can have an adverse impact on emotion regulation the following day. The clinical management of the sleep disturbances experienced by bipolar patients, including insomnia, hypersomnia delayed sleep phase and irregular sleep-wake schedule, may include medication approaches, psychological interventions, light therapies and sleep deprivation. Psychological interventions, as described here, are advantageous in that they are low in side effects, may be preferred by patients, are durable and have no abuse potential.

# Interventions for Sleep Disturbance in Bipolar Disorder

Bipolar disorder is a common, severe, and chronic disorder. It is often life-threatening with approximately 1 in 5 individuals completing suicide<sup>1</sup>. The lifetime prevalence of Bipolar I and II is 1% and 0.5%, respectively<sup>2</sup>, although more liberal definitions of hypomania identify many more patients with bipolar spectrum disorder. Bipolar disorder type I is defined by the presence of at least one manic or mixed episode. Bipolar II requires at least one hypomanic episode and at least one major depressive episode<sup>2</sup>. The impact that episodes of mania or depression have on the person's life is enormous. After the onset of the disorder, individuals with bipolar disorder who have been hospitalized spend approximately 20% of their life in episodes<sup>3</sup> and approximately 50% of their time unwell<sup>4</sup>. Not surprisingly, bipolar disorder is ranked as one of the top 10 leading causes of disability worldwide.

There have been important advances in pharmacological and nonpharmacological treatments for bipolar disorder. However, even with continued adherence a high proportion of patients are seriously symptomatic in the inter-episode period<sup>5</sup> and the risk of relapse over five years is as high as 73%<sup>6</sup>. In response to these high relapse rates, research continues to try to improve pharmacotherapy and also to develop adjunctive psychosocial treatments<sup>7</sup>. The latter include interpersonal and social rhythm therapy (IPSRT), family therapy,

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psychoeducation and cognitive behavior therapy (CBT) administered individually or in groups, as well as combination approaches. Even with the combination of pharmacological and adjunctive interventions the rates of relapse remain of concern and many individuals remain highly symptomatic between episodes<sup>7</sup>.

## Why is Sleep Important in Bipolar Disorder?

### Bipolar disorder and sleep disturbance often coexist

Reduced need for sleep is a classic symptom of mania. During episodes of depression, insomnia or hypersomnia are common. Even in the inter-episode period, sleep is disturbed; up to 70% of bipolar disorder patients report insomnia<sup>8</sup>, which is associated with risk for relapse and suicide attempts<sup>9</sup>. Hypersomnia is experienced by roughly 25% of bipolar 1 patients during the inter-episode period<sup>10</sup> and by 40–80% during episodes of depression<sup>11</sup>. Sleep disturbance is characteristic across the bipolar spectrum. In fact, total sleep time is shortest in bipolar disorder-not otherwise specified, relative to bipolar 1 disorder and bipolar 2 disorder, but the three subtypes are equally impaired in night-to-night variability<sup>12</sup>. Mean variability in total sleep time across a week in bipolar patients is approximately 2.78 h (SD = 3.02)12, almost equivalent to flying from the east to west coast of continents like America and Australia. The human circadian rhythm cannot easily adapt to these fast shifts. Indeed, in inter-episode bipolar disorder, lower and more variable sleep efficiency and variability in falling asleep time are related to worse illness course and outcome<sup>13</sup>. Relative to the interepisode phase, sleep disturbance escalates just before an episode, worsens during an episode<sup>14–16</sup> and does not always resolve with medication. Among individuals treated with 'best practice' mood stabilizers in STEP-BD<sup>17</sup> 66% still experienced significant sleep disturbance<sup>1218</sup>.

#### Sleep disturbance contributes to affective dysregulation

Multiple studies suggest that sleep disturbance contributes to affective dysregulation in bipolar disorder: a) sleep disturbance is a common prodrome of relapse<sup>16</sup>; b) short sleepers exhibited more symptoms of mania, depression, anxiety and irritability, lower scores on functioning and life satisfaction compared to bipolar disorder patients with longer sleep times<sup>12</sup>. Moreover, shorter total sleep time was associated with increased mania and depression severity over 12 months<sup>18</sup>; c) in a 7-day diary study, total wake time was associated with next-day morning negative mood in bipolar disorder while evening negative mood was associated with subsequent total wake time in both bipolar disorder and insomnia<sup>19</sup>; d) experimentally-induced sleep deprivation is associated with the onset of hypomania or mania<sup>15</sup>; e) sleep has a critical mood regulatory function, and sleep deprivation involves the loss of top-down inhibitory control usually exerted by medial prefrontal cortex on amygdala<sup>20</sup>; f) circuits involved in emotion regulation and sleep regulation interact in bi-directional ways<sup>21</sup>. In sum, sleep disturbance is a pathway leading to affective instability and relapse via well-recognized neural circuits.

#### Sleep disturbance contributes to inter-episode functional impairment

Even with good adherence to medication, a high proportion of patients with bipolar disorder remain seriously symptomatic in the inter-episode period. Clinically significant insomnia is

one of the most common residual symptoms<sup>8</sup>. Insomnia in itself has a significant negative psychosocial, occupational, health, and economic impact<sup>22</sup>. Our analysis of STEP-BD data indicates that sleeping less than 6.5 hours per night is associated with greater symptom severity and greater impairment relative to sleeping 6.5–8.5 hours<sup>18</sup>.

Taken together these data highlight 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 improve sleep as a pathway for improvement mood and reducing impairment.

## Managing Sleep Disturbance in Bipolar Disorder

Pharmacological treatment of bipolar disorder is inseparable from the treatment of sleep disturbance. Here we focus on describing a non-pharmacologic approach because: 1) there are fewer side effects or interactions with other treatments for the bipolar disorder and other conditions; 2) while hypnotics are efficacious and clinically indicated in some situations (e.g., acute insomnia), concerns remain about the durability, daytime residual effects, tolerance, dependence, and rebound insomnia; 3) given the comorbidity between bipolar disorder and substance use disorders<sup>23</sup>, certain classes of insomnia medications—most important, the FDA-approved benzodiazepine receptor agonists—pose a risk of abuse.

As already mentioned, several psychological adjunctive interventions have been developed for patients with bipolar disorder including IPSRT, family therapy, CBT and psychoeducation. Each of these include one or more components designed to target sleep. However, specific sleep outcomes have not been reported, and these treatments have yet to draw from advances in knowledge of the effectiveness of cognitive behavior therapy for insomnia (CBT-I). Evidence documenting the efficacy of CBT-I for patients with chronic insomnia (i.e., non-bipolar insomnia patients) has been summarized in several quantitative and systematic reviews of the literature including three meta analyses and two review/ practice parameter papers commissioned by the American Academy of Sleep Medicine<sup>24</sup>. These sleep improvements are well sustained up to two years after cessation of treatment<sup>25</sup>. Evidence is accruing to suggest that insomnia that co-occurs with a range of psychiatric disorders can be improved with CBT-I. Hence, the treatment approach described below draws on CBT-I. The unique features of sleep disturbance in bipolar disorder led to modifications of typical CBT-I procedures and the addition of elements from both IPSRT<sup>26</sup> and motivational interviewing (MI)<sup>27</sup>. However, it should be noted that this approach is currently being evaluated for bipolar disorder and there has been a need to adapt some components for use with bipolar patients as detailed below.

#### Functional analysis/case formulation and goal setting

The frequency, intensity and duration of insomnia and its antecedents are discussed (with the patient?). Sleep-related behaviors and consequences are assessed: before bed (e.g., bedtime routine), during the night (e.g., cell phone left on), on waking (e.g., sleepiness, lethargy) and during the day (e.g., caffeine use). The relationship between sleep-specific thoughts, emotions, and behaviors are charted across the night and day. Specific goals are identified (e.g., increase total sleep time, earlier 'lights out' time).

## Motivational interviewing (MI)

A straightforward review of perceived pros and cons of the change (what change?) is conducted, recognizing that many sleep-incompatible/interfering behaviors are rewarding. For example, patients often struggle with waking up at around the same time weekdays and weekends. Allowing the patient to generate advantages and disadvantages with therapist guidance facilitates behavior change (ref.). MI is revisited in future sessions as additional strategies are introduced.

## Sleep and circadian education

Education relevant to the circadian system includes definitions, explanation of environmental influences (particularly light), the importance of circadian and social rhythms (following IPSRT) and the tendency to drift toward a delayed sleep phase. Sleep inertia, or the subjective feeling of grogginess after awakening, is defined and normalized. Sleep disturbance is identified as a common prodrome of relapse. A link is drawn between sleep disturbance and daytime mood dysfunction, including the mood regulatory function of sleep. Finally, we highlight the different behavioral strategies needed for treatment of the current sleep problem and for sleep problems in the future (e.g., hypersomnia, reduced sleep need, delayed phase). In later sessions, we return to this topic and adapt each sleep principle so patients have a well-developed decision tree and menu of options for managing the range of sleep problems they may experience.

#### **Behavioral components**

a) Stimulus control<sup>28</sup>, one of the most effective treatment components of CBT-I<sup>24</sup>, focuses on regularizing the sleep-wake cycle and strengthening associations between the bed and sleep<sup>28</sup>. For certain patients we adapt the instruction to get out of bed if it risks the patient engaging in rewarding and arousing activities that prevent sleep. b) Restricting time in bed<sup>29</sup> is derived from the observation that excessive time in bed perpetuates insomnia. We limit time in bed to the actual time slept, and gradually increase it back to an optimal sleep time. In order to avoid changes in mood related to short-term sleep deprivation, minimum time in bed is never lower than 6.5 hours and we carefully monitor mood for changes in manic/ hypomanic symptoms. The goal is to maximize sleep efficiency to > 85–90%. More consolidated sleep is experienced as more satisfying. c) Regularizing sleep and wake times. IPSRT is utilized to regularize sleep and wake times across the week. Building motivation for the patient to wake at the same time (including on weekends<sup>30</sup>) is a key focus. This promotes consistent sleepiness in the evening; particularly when naps are avoided, and enable patients with a tendency toward eveningness to progressively move their bedtime forward by 20–30 minutes per week (small enough that the circadian system can adapt). d) Wind-down. Patients need assistance to devise a 'wind-down' of 30-60 minutes in which relaxing, sleep-enhancing activities are introduced, in dim light conditions. This helps the circadian phase advance in patients who are evening-types, and maintains entrainment<sup>31</sup>. A central issue is the use of interactive electronic media (internet, cell phones, MP3 players). MI and behavioral experiments are used to facilitate voluntarily *choosing* an electronic curfew, recognizing that many patients are socially isolated and rely on pre-bedtime internet-based social interaction. Many patients prefer to set an alarm on a cell phone to

remind themselves of this curfew. e) <u>Wake-up</u>. This individualized intervention draws on principles from IPSRT and includes: not hitting snooze, opening the curtains to let sunlight in, spending the first 30–60 minutes after waking outside or in a room with bright lights, encouraging morning activity and social contact to counteract sleep inertia, and making the bed so the incentive to get back in is reduced.

#### Cognitive components

a) <u>Challenging unhelpful beliefs</u> about sleep is important<sup>32</sup>. Unhelpful beliefs about sleep are common in bipolar disorder<sup>8</sup> and include: 'there is no point going to bed earlier because I won't be able to fall asleep', 'the TV helps me fall asleep', and 'medication is the only thing that contributes to my feeling drowsy'. Guided discovery and individualized experiments test the validity and utility of the beliefs<sup>33</sup>. b) Patients with bipolar disorder are anxious about their sleep, in part because they know that sleep loss can herald a relapse<sup>8</sup>. As anxiety is antithetical to sleep onset, we use individualized strategies to <u>reduce bedtime</u> worry, <u>rumination and vigilance</u> including cognitive therapy, diary writing or scheduling a 'worry period'. c) <u>Monitoring</u>. Bipolar patients with disturbed sleep often monitor for signs of fatigue upon waking or throughout the day. Helping the patient understand that feelings groggy upon waking is normal (sleep intertia), and introducing behavioral experiments and attention strategies for monitoring in the daytime, can reduce anxiety and preoccupation with sleep.

#### **Daytime coping**

Patients with bipolar disorder typically believe the only way they can feel less tired in the daytime is to sleep more. Hence, a behavioral experiment is devised to allow the patient to *experience* the energy generating effects of activity<sup>33</sup>. This is also an opportunity to develop a list of 'energy generating' and 'energy sapping' activities that can be used to manage daytime tiredness, the 'post-lunch' circadian dip in alertness and build resilience to inevitable bouts of occasional sleep deprivation.

## Relapse prevention

The goal is to consolidate skills and prepare for setbacks. Patients and therapists together discuss potential obstacles to maintaining gains and problem-solve around areas of future sleep disturbance. An individualized summary of learning and achievements guides relapse prevention work. Areas needing further intervention are addressed by setting specific goals and creating plans for achieving each goal.

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## **Key Points**

1. Sleep disturbance is associated with decreased quality of life and mood relapse in bipolar disorder.

- 2. Sleep disturbance persists at high rates in bipolar disorder despite adequate pharmacological treatment for mood disturbance.
- **3.** Cognitive behavioral therapy for insomnia leads to clinically significant and sustained improvement in sleep for chronic insomniacs.
- **4.** Adjunctive non-pharmacological sleep intervention drawing upon principles from cognitive behavioral therapy for insomnia, interpersonal and social rhythm therapy, and motivational interviewing is a viable treatment for sleep disturbance in bipolar disorder.
- **5.** Psychological interventions for sleep disturbance are advantageous in that they are low in side effects, may be preferred by patients, are durable and have no abuse potential.