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Overlapping prefrontal systems involved in cognitive and emotional processing in euthymic bipolar disorder and following sleep deprivation: A review of functional neuroimaging studies

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HIGHLIGHTS

- Sleep and circadian disruption is a core feature of bipolar disorder.
- Prefrontal-mediated cognitive and emotional processing deficits are features of bipolar disorder.
- Sleep interacts with observed prefrontal deficits through overlapping neurobiological systems.

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ABSTRACT

Prefrontal cortex (PFC) mediated cognitive and emotional processing deficits in bipolar disorder lead to functional limitations even during periods of mood stability. Alterations of sleep and circadian functioning are well-documented in bipolar disorder, but there is little research directly examining the mechanistic role of sleep and/or circadian rhythms in the observed cognitive and emotional processing deficits. We systematically review the cognitive and emotional processing deficits reliant upon PFC functioning of euthymic patients with bipolar disorder and in healthy individuals deprived of sleep. The evidence from two parallel lines of investigation suggests that sleep and circadian rhythms may be involved in the cognitive and emotional processing deficits seen in bipolar disorder through overlapping neurobiological systems. We discuss current models of bipolar highlighting the PFC–limbic connections and discuss inclusion of sleep-related mechanisms. Sleep and circadian dysfunction is a core feature of bipolar disorder and models of neurobiological abnormalities should incorporate chronobiological measures. Further research into the role of sleep and circadian rhythms in cognition and emotional processing in bipolar disorder is warranted.

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Contents

Abbreviations: BD, bipolar disorder; PFC, prefrontal cortex; fMRI, functional magnetic resonance imaging; CLOCK, circadian locomotor output cycles kaput; PER, period homologue; REM, rapid eye movement; NREM, non-REM; SWS, slow wave sleep.

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1. Introduction

Bipolar disorder (BD) is a complex mental illness characterized by vacillations of mood between the highs of mania and the lows of depression with periods of relatively normal mood in between. Alterations of brain structure and function combined with environmental factors (e.g., stressors, sleep deprivation) are thought to cause a dysregulation of mood, sleep, cognition, endocrine function, and motor systems forming complex and dynamic interactions (Catapano, Chen, Jing, Zarate, & Manji, 2009). Additionally, there is considerable heterogeneity of clinical characteristics including the frequency of mood cycling, age of first occurrence of symptoms, and the degree to which depressive and manic episodes co-occur (mixed states), which adds to the complexity of the disorder. The multifaceted nature of symptoms experienced by those with BD leads to difficulties with everyday functioning in both social and occupational arenas, with cognitive and emotional processing deficits playing a particularly important role in these difficulties (Bearden et al., 2011; Bora, Yucel, & Pantelis, 2009; Torres, Boudreau, & Yatham, 2007). Cognitive impairments in several domains have been observed in BD (Glahn et al., 2010; Kurtz & Gerraty, 2009; Martinez-Arán et al., 2004) and many of these deficits have been linked to functional outcome (Bearden, Woogen, & Glahn, 2010). Furthermore, in addition to detrimental effects of high and low mood on social and vocational achievement (Simon, Bauer, Ludman, Operskalski, & Unutzer, 2007), deficits in emotional processing at a more basic level may not only result in mood instability, but may directly impact everyday functioning (Gopin, Burdick, DeRosse, Goldberg, & Malhotra, 2011; Nilsson, Jorgensen, Craig, Straarup, & Licht, 2010). While functional disability and cognitive/emotional processing deficits are most severe during a mood episode, many patients continue to have poor functioning and altered cognitive/emotional processing during periods of remission or euthymia (Gopin et al., 2011; Robinson & Ferrier, 2006). Sleep/circadian impairment is also prevalent in BD patients, even when clinical symptoms are in remission (Harvey, 2008). Several lines of research suggest that sleep/circadian disturbance is a core feature of BD related to many aspects of the disease progression and symptoms such as emotional dysregulation (for a review see Murray & Harvey, 2010). This is not unsurprising considering the close link between sleep timing, circadian disruption, and mental health (Wulff, Gatti, Wettstein, & Foster, 2010). Despite this long-recognized association, the causal role of sleep in brain function has been debated. Recently, there have been remarkable breakthroughs in our understanding of the neural and genetic basis for sleep and circadian rhythm functioning in the healthy brain and the relationship of these to normal cognitive and emotional operations. Unfortunately, there is little research directly examining the mechanistic role of sleep and/or circadian rhythms in the cognitive and emotional processing deficits seen in BD. Considering the emerging findings that sleep and circadian rhythms play an important role in cognitive and emotional functioning more generally, the dearth of research on this topic in BD is unfortunate, but provides an exciting opportunity for future studies.

2. Review aims

This paper aims to systematically review the literature examining the cognitive and emotional processing in BD and sleep specifically involving the prefrontal cortex (PFC) neural circuitry in an attempt to postulate possible roles of sleep and circadian dysfunction in the PFC-mediated cognitive and emotional processing sequelae of BD. Several excellent review articles have already examined the broader literatures covering bipolar and cognitive/emotional processes, sleep and cognitive/emotional processes, and bipolar and sleep/circadian rhythms (Bearden, Hoffman, & Cannon, 2001; Chen, Suckling, Lennox, Ooi, & Bullmore, 2011; Murray & Harvey, 2010; Walker, 2009). Our more specific goal is to examine findings from these literatures implicating the PFC as a core neural structure in both BD and sleep. In light of a lack of research directly examining the mechanistic role of sleep and circadian rhythms in the cognitive/emotional processes of BD, we chose to focus this review on the following areas: 1) *Prefrontal Cortex*: although both sleep disruption and BD are likely to influence multiple neural systems in the brain, the PFC plays an important role in higher order cognitive and emotional processing. Further, abnormalities within this region have been highlighted as core features of BD and, independently, sleep. Thus, the PFC is an area where interactions between cognitive and emotional processing, BD, and sleep disturbance are likely to occur. 2) *Euthymic Bipolar Patients*: we chose to focus only on studies of euthymic bipolar patients in order to examine trait-like PFC brain-behavior changes in the disorder that may be impacted by sleep/circadian disruption, independent of mood disruption. 3) *Sleep Deprivation*: the vast majority of studies examining the relationship between sleep and PFC functioning employ sleep deprivation protocols in healthy adults. By depriving an individual of sleep and measuring the change in brain response, researchers are able to isolate brain regions that are thought to play a role in the interaction between sleep and cognition. Therefore, we chose to examine sleep deprivation studies in healthy adults in order to draw parallels between the impact of BD and sleep disruption in PFC-mediated functions. While studies of sleep disordered populations (e.g., insomnia and obstructive sleep apnea) also yield valuable information about the underlying neural correlates of cognitive and emotional processes, they are confounded by clinical characteristics of the studied population.

3. Article inclusion criteria

The relevant articles were searched using Pubmed and Psychinfo with the following search terms: 1) Bipolar and cognit* (or emot*), and prefrontal (or executive function); 2) sleep, cognit* (or emot*), and prefrontal (or executive function); 3) circadian, cognit* (or emot*), and prefrontal (or executive function); and 4) bipolar, sleep, cognit* (or emot*), prefrontal (or executive function). For each search the findings yielded: 1) 355 studies with respect to BD and cognition and 147 with respect to emotion; 2) 238 studies with respect to sleep and cognition and 67 with respect to emotion; 3) 39 studies with respect to circadian rhythms and cognition and 8 with respect to emotion; and