SLEEP DISRUPTION IN COGNITIVE AND OCCUPATIONAL FUNCTIONING IN BIPOLAR DISORDER

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ABSTRACT

Sleep Disruption in Cognitive and Occupational Functioning in Bipolar Disorder

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Bipolar Disorder is frequently associated with a number of poor outcomes including, but not limited to, a significant impairment in the ability to return to premorbid levels of occupational and psychosocial functioning, often despite the remission of mood symptoms. An extensive line of research has pointed toward deficits in cognitive functioning as playing an important role in this persistent disability, with a number of studies demonstrating the presence of numerous cognitive impairments during the inter-episode period. Also present during affective episodes as well as the inter-episode periods are reports of pervasive sleep disturbance. Sleep disturbance has been associated with the onset of manic episodes and is an oft-reported prodrome of illness onset. Despite the presence of deficits in these two domains of functioning during affective episodes as well as the inter-episode phase, there has been no evaluation of the degree to which these systems may interact to maintain such high rates of functional disability. The current study attempted to integrate these three separate lines of research to examine the role sleep disruption plays in both cognitive and occupational functioning in individuals with bipolar disorder. Seventy-two males and females with bipolar disorder in the euthymic phase (n=24), primary insomnia (n=24) or no psychological or medical diagnoses (n=24) completed a week of prospective assessment of sleep disruption via self-report and actigraphy. At the culmination of the sleep assessment period, all participants were administered a battery of neuropsychological tests of executive functioning, working memory, verbal learning, and attention. Additionally,

participants completed self-reports of mood symptoms and current and lifetime occupational functioning. Results were mixed relative to hypotheses. Data supports persistent sleep disturbance among individuals with bipolar disorder when assessed via self-report, but no significant differences were observed compared to controls when assessed via actigraphy. Bipolar participants exhibited significantly poorer performance on measures of verbal learning and working memory, but no other cognitive deficits were observed relative to insomnia and control participants. Bipolar participants had a greater lifetime history of being fired compared to insomnia or control participants, and deficits in executive inhibition and switching were associated with increased lifetime firings across the sample. Sleep disturbance, either subjective or objective, failed to mediate this association. Findings are partially consistent with previous reports of persistent sleep disturbance and cognitive impairment among individuals with BD in the euthymic phase. More research should be conducted to better understand the underpinnings of functional impairment in BD.

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TABLE OF CONTENTS

LIST OF TABLES

CHAPTER 1

INTRODUCTION

Bipolar Disorder (BD) is a chronic and severe condition that affects roughly 5.7 million adults in the United States, resulting in marked functional impairment for the majority of individuals (National Institute of Mental Health, 2011). According to a 2008 Social Security Disability report, roughly one third of all social security disability benefits went to individuals with mental disorders, including BD (Social Security Administration; 2008). Additionally, the World Health Organization ranks BD as the sixth leading cause of disability in the world (World Health Organization; 2006). Research has consistently uncovered large percentages of individuals with BD who either fail to achieve functional recovery or who demonstrate poor work performance (Huxley et al., 2007; Zarate et al., 2000). These findings are consistent with a growing literature that suggests the concept of complete recovery from an episode of bipolar disorder may be outdated, with researchers opting to conceptualize the disorder as a chronic condition that reflects the prevalence of residual symptoms among those affected.

Examinations of residual symptoms, then, may be central to gaining a better understanding of the mechanisms that underlie sustained functional impairment despite remission of affective symptomatology. Recent investigations into the psychopathology of BD have thus paid specific attention to the euthymic phase. Below we discuss two domains that have been shown to remain disrupted periods of euthymic mood: cognitive functioning and sleep.

Neurocognitive Deficits in Bipolar Disorder

Numerous reports point to widespread cognitive deficits in BD, including deficits in verbal memory, verbal learning, attention, and executive functioning. These deficits have been shown to persist despite remission of mood symptoms, leading some to conceptualize cognitive

dysfunction as a core component of a specific endophenotype of BD (Bora et al., 2009). Importantly, some reports have examined relationships between cognitive deficits and functional outcomes, with verbal memory identified as a strong predictor of psychosocial outcomes (Martinez-Àran, 2004). A separate study on the impact of neurocognitive deficits on functional outcomes reported working memory, attention, and processing speed were significantly associated with occupational recovery (Bearden et al., 2011). Thus, there is mounting evidence to suggest cognitive deficits play some role in maintaining functional disability among individuals with BD.

Characteristics of Cognitive Deficits in the Euthymic Phase of BD

Sustained deficits in the domains of executive functioning, verbal learning and memory, and sustained attention have been observed in individuals in the euthymic phase of BD. Executive functioning is a broad term that can refer to a range of processes including planning, motivation, impulsivity, and inhibition. A recent examination of executive functioning in euthymic BD patients suggested individuals with BD display executive functioning profiles similar to individuals with mild cognitive impairments but no history of bipolar disorder (Osher et al., 2011). This finding builds upon previous research pointing toward pronounced deficits in executive functioning during the euthymic period; indeed six exhaustive meta-analyses revealed large effect sizes for tests of executive functioning relative to normal controls (Arts et al., 2008, Bora et al., 2009; Kurtz et al., 2009; Robinson et al., 2006; Torres et al., 2007; Mann-Wrobel et al., 2011).

However, there is some disagreement in the field as to whether executive functions are broadly impaired or if deficits are more selective in nature. A meta-analysis by Robinson et al. (2006) is suggestive of the latter, with results demonstrating large effect sizes for category

fluency and mental manipulation (i.e., reverse digit span), medium effect sizes for response inhibition, abstraction, and set shifting, and small effect sizes for verbal fluency by letter. A separate meta-analysis by Arts et al. (2008) reported similar findings, with large effect sizes for executive control (in the Trail Making task), concept shifting (Wisconsin Card Sort perseverative errors), and category fluency, and medium effect sizes for executive control (via the Stroop task).

Perhaps clouding the search for specificity, heterogeneity among some of these specific domains of executive functioning, namely executive control, concept shifting, and fluency, was noted in these analyses. Arts et al. refer to three studies that included patients with a large number of previous psychotic episodes and suggest that the inclusion of those patients may have driven differential findings. Accordingly, research has suggested that clinical variables such as greater illness duration, number of episodes, and number of hospitalizations are associated with greater levels of cognitive dysfunction among individuals with BD (Robinson & Ferrier, 2006). Further muddying the waters, inclusion criteria varied in the Robinson and Arts meta-analyses, and it was evident from both reports that individual examinations of cognitive functioning suffered from a lack of a consensus definition of euthymia. Nevertheless, there is overwhelming evidence to suggest executive functions remain disrupted during the euthymic phase.

Neuropsychological accounts of executive functioning deficits are supported by neuroanatomical examinations of individuals with BD that demonstrate abnormalities in the prefrontal cortex (PFC). Reduced neuronal and glial density in the PFC has been reported (Rajkowska et al., 2001, Öngür et al., 1998, Cotter et al., 2002), whereas a functional magnetic resonance imaging (fMRI) study suggests a trait abnormality in the left ventral PFC among individuals with BD (Blumberg et al., 2003). Additional structural abnormalities may be

observed during episodes of depression or (hypo)mania that may partially explain why some cognitive deficits appear to be more pronounced during affective episodes.

In addition to executive functioning deficits, the domains of verbal learning and memory are frequently found to be impaired in individuals in the inter-episode phase of BD. In a 2002 study of euthymic BD patients and controls, Cavanagh et al. found that the only significant differences were observed in tests of verbal learning/memory, namely the California Verbal Learning Test (CVLT). These results are supported by several meta-analyses of previous studies of cognitive functioning (2008 and earlier), which consistently reported medium to large effect sizes compared to healthy controls (Robinson et al., 2006; Arts et al., 2008). Importantly, the authors discussed the potential overlap between executive functioning and verbal learning, wherein executive deficits may affect memory performance. For example, the CVLT requires a fair amount of organization and set-shifting, which taps into the executive system while also being oriented toward verbal memory. More focused studies need to be conducted to establish whether one or two domains of functioning are reliably impaired in BD.

There is also mounting evidence to support a sustained attention deficit in BD that persists through periods of euthymia (Bora et al., 2005; Clark & Goodwin, 2004; Liu et al., 2002; Torres et al., 2007). Clark and colleagues (2002) observed impairments in sustained attention even after controlling for any possible interference from mood symptoms. Although this effect was associated with chronicity of illness, younger participants with relatively recent illness onsets were also observed to be impaired in this domain, suggesting that attention deficits may be a trait marker of bipolar disorder. Indeed, this conceptualization is supported by Bora and colleagues (2009), who included sustained attention deficits as part of a cognitive endophenotype

of BD, as these deficits have also been observed among first-degree relatives of individuals with BD.

One of several studies to utilize continuous performance tests (CPT) as a measure of attention, Bora et al. (2006) found that relative to controls, euthymic BD patients demonstrated significant impairments in target sensitivity as well as marked inconsistency in response times. Although several studies have utilized the CPT to measure sustained attention, there is a high degree of variability of measures in the literature that may temper some of the conclusions that can be drawn about the "purity" of attention deficits in bipolar disorder. For example, Yates et al. (2010) found that euthymic BD participants performed significantly worse than controls on the Digit Span Forward and Digit Span Backward, although these tests are also valid cognitive measures of working memory. The Robinson et al. (2006) meta-analysis includes digit span and trail making in their analyses of attention; however, there is some overlap with attention in these tests of both working memory and executive functioning, respectively. As noted earlier, executive functioning has been identified as one of the most stable cognitive deficits in bipolar disorder as well as a cognitive endophenotype, leaving the possibility that attention deficits may be better explained by executive function deficits to the extent to which the measure taps both domains.

Relationship between cognitive deficits and functional outcomes

Despite the fact that the average individual with BD possesses at least a partial college education, approximately 55% of individuals with BD are unemployed (Wingo et al., 2009). Spurred by this striking discrepancy, as well as other published and anecdotal reports of functional disability in individuals with BD, there has been considerable research into the factors associated with these poor outcomes. As touched upon previously, there is a growing literature

to suggest that cognitive impairments play a key role in generating and maintaining occupational and psychosocial functioning deficits. Martinez-Àran et al. (2004) reported that psychosocial functioning in BD patients was associated with cognitive functioning rather than with clinical variables: no relationship was found between psychosocial functioning and chronicity of illness, total episodes, types of episodes, or numbers of hospitalizations or suicide attempts in their sample. Instead, the cognitive domains of frontal executive functioning, learning and memory were significantly associated with psychosocial functioning. Gilbert et al. (2010) also reported significant associations between cognitive variables and vocational functioning in a sample of 154 patients with BD. Although limited by self-reported data, results indicated that concentration problems were significant predictors of employment status, whereas no associations between employment and mood state were observed.

O'Shea and colleagues (2010) conducted a more focused examination of the relationship between cognitive functioning and functional outcomes by utilizing ecologically valid neurocognitive assessments that more closely map onto everyday activities than more classic neuropsychological batteries (e.g., the Test of Everyday Attention (TEA), the Rivermead Behavioural Memory Test, and the Behavioral Assessment of the Dysexecutive Syndrome). BD patients performed significantly worse than a healthy control group on all measures, and results showed a significant association between impaired attention and unemployment.

In summary, there are numerous reports of persistent cognitive deficits during the euthymic phase of bipolar disorder in the domains of executive functioning, verbal learning, working memory, and sustained attention. However, as mentioned previously, cognitive functioning is not the only domain of functioning to remain impaired during periods of euthymic

mood. Research also points to persistent sleep disruption throughout all phases of bipolar disorder, including the euthymic phase.

Sleep Disruption in Bipolar Disorder

Sleep disturbance, even in the absence of BD, is associated with a number of poor outcomes including impairments in daytime functioning, increased psychosocial stress, and increases in the utilization of healthcare (Ancoli-Israel & Roth, 1999). Within the context of BD, disrupted sleep has been implicated in the pathogenesis of manic episodes (Columbo et al., 1999) and has been marked as a key prodromal symptom of depressive episodes (Jackson et al., 2003). Indeed, the sleep/wake cycle has been a key component of theoretical conceptualizations of BD that hypothesize that individuals with BD may have circadian systems that are either endogenously dysregulated or overly sensitive to disruption (Ehlers, Frank, & Kupfer, 1988; Monsour, Monk & Nimgoankar, 2005a; Monsour et al., 2005b; Wehr et al., 1987).

The characteristics of disturbed sleep in BD differ depending on affective state. Reduced need for sleep is a key DSM-5 criterion for mania, whereas both hypersomnia and insomnia may be experienced during depressive episodes (American Psychological Association, 2013). Harvey (2008) conducted a comprehensive review of 20 studies of sleep disturbance across depressed, manic and mixed phases of BD, and reported marked disturbance across all samples: 69% to 99% of individuals experienced reduced need for sleep during the manic phase, with more variable rates of hypersomnia (23% to 78%) and insomnia (varying all the way up to 100% of the sample) observed in the depressive phase (Harvey, 2008). Sleep disturbance is not relegated to depressed or manic phases, however, with examinations of sleep functioning in euthymia suggesting both a high prevalence of sleep disturbance as well as associations with episode recurrence and general impairment.

Characteristics of Sleep Disturbance in the Euthymic Phase of BD

Disturbed sleep is an oft-reported residual symptom of the inter-episode period, and many individuals in the euthymic phase of BD appear to have significantly poorer sleep relative to healthy individuals. Millar and colleagues (2004) conducted an analysis of remitted BD patients using both objective and subjective measures of sleep disturbance. One hundred percent of the BD sample reported protracted sleep disturbance, compared to only 21% in the non-BD group. Analyses of actigraph data revealed trends toward longer total sleep time, longer sleep onset latency, and less efficient sleep among bipolar participants, as well as significantly more variable sleep duration and night waking time. Subjectively, BD participants reported longer sleep onset latency, as well as greater variability in sleep duration, sleep onset latency, and sleep efficiency.

Harvey and colleagues (2005) conducted a similar analysis, but included a comparison group of individuals with primary insomnia. Seventy percent of the BD sample experienced a clinically significant sleep disturbance, and group comparisons demonstrated that the sleep of BD participants more closely resembled an insomnia profile than a healthy sleep profile. Actigraph data revealed longer total sleep times among BD participants, as well as lower average daytime activity levels. BD participants reported significantly longer sleep onset latency relative to the good sleeper group when assessed via self-report. This difference in subjective estimations in sleep variables vs. objective measurements is not inconsistent with established patterns reported in the insomnia literature, such that individuals with insomnia tend to underestimate their total sleep time as well as overestimate the time it takes to fall asleep (Carskadon et al., 1976, Mercier et al., 2002).

It is important to note that not all of the data on sleep during the euthymic phase of BD support the concept of chronic sleep disturbance. Jones et al. (2005) conducted an actigraphic assessment of sleep patterns among individuals in the euthymic phase of BD and failed to observe differences among sleep parameters when compared to healthy controls. The authors did find, however, that individuals with BD exhibited less stable and more variable daytime activity patterns, and that this variability was a significant predictor of group status. This variability in comparison to controls is consistent with aforementioned reports of circadian instability among individuals with BD. Using activity instability and irregularity as a proxy for circadian rhythm instability (which forms the central theme of the Social Zeitgeber Hypothesis; Elhers, Frank, & Kupfer, 1988) suggests that this instability may be a trait marker of the disorder rather than an episode-related phenomenon.

Cognitive Functioning in Sleep-Deprived Healthy Controls and Sleep Disordered Patients

In order to consider the potential influence of sleep disturbance on cognitive functioning in BD, it is important to understand how disrupted sleep impacts cognitive functioning in healthy individuals. By examining points of convergence and divergence in the literature on cognitive deficits in healthy individuals who have undergone experimental sleep deprivation or who suffer from insomnia vs. individuals with BD, we gain important perspective on what aspects of cognitive functioning may be most susceptible to sleep disturbance.

Cognitive Functioning in Insomnia

Cognitive deficits, both self-reported and objective, are well-documented in the insomnia literature. Insomnia is characterized by the DSM-5 as difficulty initiating or maintaining sleep or experiencing non-restorative sleep for a period of at least one month (APA, 2013). Approximately 3.9% to 22.1% of the population is estimated to carry a diagnosis of insomnia

(Roth et al., 2011). From a cognitive functioning standpoint, individuals with insomnia appear to be impaired in the domains of episodic memory, problem solving, manipulation in working memory, and retention in working memory, although effect sizes are relatively small (Fortier-Brochu et al., 2012). Moreover, individuals with insomnia often report poor concentration, poor memory, and increased problems completing work tasks (Fortier-Borchu et al., 2012). However, there is some indication that the cognitive impairment observed in insomnia may increase or decrease depending on the severity of sleep disturbance. Szelenberger and Niemcewicz (2000) conducted an analysis of cognitive functioning among insomnia patients and healthy controls and found that the degree of learning impairment on a test of immediate recall correlated significantly with participants' scores on the Athens Insomnia Scale.

Support for a cognitive deficit in insomnia can also be drawn from the fact that cognitive behavioral therapy for insomnia (CBT-I), a psychotherapeutic intervention that has been shown to improve symptoms of insomnia, may also improve cognitive functioning. In a pilot, randomized controlled trial of CBT-I and sleep hygiene in a sample of individuals with fibromyalgia, a condition characterized in part by disrupted sleep, CBT-I was associated with improvements in alertness, executive functioning, and overall daily functioning (Miró et al., 2011).

Poor occupational functioning is also not uncommon in insomnia. Impairments in daytime functioning and work performance are frequently reported among individuals with insomnia (Bonnet et al., 2000; Schweitzer et al., 1992; Stepanski et al., 1988). Additionally, research on functional outcomes in insomnia found that individuals with insomnia were absent from work twice as often as healthy sleepers, had higher rates of motor vehicle accidents (likely due to impaired attention), and were more prone to poor self-esteem, job satisfaction, and work

efficiency (Léger et al., 2006). It is important to note, however, that it remains unknown at this time if poor cognitive functioning is the driving force behind these occupational impairments.

Cognitive consequences of acute and chronic sleep deprivation in healthy individuals

Examinations of experimentally induced acute and chronic sleep deprivation in healthy sleepers may offer a clearer picture of the specific cognitive effects of sleep deprivation, one of the various forms of sleep disturbance. Relative to studies of total sleep deprivation, there have been fewer studies conducted on partial sleep deprivation (sleep restricted to less than 7 hours in a 24 hour period) and chronic partial sleep deprivation, the patterns of sleep deprivation that are most germane to BD. However, evidence suggests that mood and cognition are more impaired following partial than total sleep deprivation (Durmer & Dinges, 2005), highlighting the possibility that the chronically disrupted sleep often observed in BD may be directly related to cognitive impairments.

Durmer and Dinges (2005) conducted a comprehensive review of the literature on experimentally induced sleep deprivation and reported cognitive slowing, decreased response time, decline in short-term recall and working memory, and reduced learning as consequences. Prefrontal cortex-related executive attention and working memory abilities also appear to be affected and, notably, neurophysiological studies have identified decreased activity in the PFC during periods of sleepiness (Drummond et al., 1999; 2001). For example, short-term sleep deprivation (24 hours) was associated with a decrease in global cerebral glucose metabolism with specific effects in the thalamus and PFC (Thomas et al., 2000). Coincidentally, the thalamus has been implicated in the etiology of BD (Ng et al., 2009), while a separate examination of thalamic volumes in individuals with BD demonstrated smaller volumes of the right thalamus in BD patients compared to normal controls (Radenbach et al., 2010).

Evidence suggests that marked partial sleep deprivation is not necessary to produce cognitive impairments, but rather reductions in sleep to just 6 hours of sleep per night may have adverse effects on cognitive performance and daily living (Van Dogen et al., 2003). Van Dogen and colleagues demonstrated that a total sleep deprivation period of 72 hours was associated with more cognitive impairment than any single partial sleep-deprivation period (limited to 4, 6, or 8 hours in bed). As expected, no cognitive deficits were reported following 8 hours in bed, but after two weeks of chronic sleep restriction to 4 hours per night, performance on measures of attention and memory were comparable to that of the group that endured 72 hours of total sleep deprivation. In a similar fashion, those restricted to 6 hours of sleep per night over the same period demonstrated cognitive functioning comparable to one night's total sleep deprivation.

Summary of Findings

As discussed above, there is substantial evidence pointing to chronic and, in many cases, severe sleep disruption across all phases of BD, including the euthymic phase. Additionally, persistent cognitive impairments have been observed during the inter-episode phase. Given what is known about cognitive functioning among individuals with insomnia as well as reports of cognitive consequences of experimentally induced sleep deprivation, it is theoretically possible that the sustained sleep disruption observed in BD may play a role in the maintenance of cognitive deficits, and, by extension, poor functional outcomes.

The Present Study

The present study aimed to examine the extent to which sleep disruption may contribute to cognitive deficits in individuals with bipolar disorder, and, in turn, impact occupational functioning. Participants were males and females age 18 to 65 who carried diagnoses of either primary insomnia, bipolar I or II disorder in the euthymic phase, or no psychiatric diagnosis.

Participants were screened with a diagnostic interview and questionnaires to determine group membership (see Methods). Following screening, participants were given an actigraph, a device that is worn on the wrist that monitors sleep/wake activity, to wear for a period of one week. At the end of the one-week sleep monitoring period, participants returned to Temple University for a 90-minute testing session during which they were administered a battery of cognitive tests tapping domains of executive functioning, verbal learning and memory, working memory, and attention. They then completed questionnaires about mood symptoms and occupational functioning. Analyses examined group differences in sleep, cognitive, and occupational functioning, as well as relationships between sleep functioning and cognitive functioning and cognitive functioning and occupational functioning. Mediational analyses examining the role of sleep in any significant cognitive/occupational relationships were also conducted.

CHAPTER 2

METHODS

Participants and Procedure

Screening Procedure

Participants for this study were 72 males and females, aged 18 to 65. Participants were recruited from the Temple University campus and the greater Philadelphia community via a two-phase screening process. In Phase I, approximately 1,954 individuals aged 18 to 65 completed screening questionnaires consisting of a revised General Behavior Inventory (GBI; Depue, Krauss, Spoont, & Arbisi, 1989), a questionnaire assessing the severity and duration of affective symptoms, and the Insomnia Severity Index (ISI; Morin et al., 2011) a questionnaire assessing severity of insomnia symptoms. Participants who met specific combinations of high or low GBI cut-off scores and ISI scores (see inclusion/exclusion criteria below) were invited to participate in the Phase II screening procedure consisting of a diagnostic interview (Schedule for Affective Disorders and Schizophrenia – Lifetime Version (SADS-L; Endicott & Spitzer, 1978), an interview of current insomnia symptoms, self-reports of depression (Beck Depression Inventory [BDI]Beck, Steer, & Brown, 1996) and mania (Altman Self-Rating Mania Scale [ASRM]; Altman et al., 1997) symptoms, and a brief assessment of intellectual functioning (Kaufman Brief Intelligence Test; Kaufman & Kaufman, 1990).

To be eligible for the study, participants were required to carry a diagnosis of bipolar I or bipolar II disorder in the euthymic phase, insomnia, or no history of mood or sleep disorders, be within the ages of 18 to 65, be willing to commit to a week of actigraph assessment and be able to read, write, and speak English. Exclusion criteria included active suicidal or homicidal ideation, psychotic symptoms, baseline IQ below 70, and an uncontrolled severe medical

condition. Participants with severe suicidal and homicidal ideation and/or psychotic symptoms were considered to be inappropriate for inclusion due to the acute need for treatment of their manic or depressive episode. Participants with an IQ lower than 70 may experience additional cognitive challenges above and beyond those potentially imposed upon them by BD or insomnia. As these deficits may be difficult to tease apart, those individuals with below normal IQ were not invited to participate in the full study. Individuals with uncontrolled medical conditions may experience physical symptoms that may substantially interfere with sleep and were thus excluded from participation. While it is true that various antidepressants, mood stabilizers, and atypical antipsychotics often prescribed to individuals with bipolar disorder may play a role in cognitive functioning, attempting to test the study hypotheses on an unmedicated sample would reduce the generalizability of the results, as the majority of individuals with BD are prescribed medications. Thus, medication usage did not form the basis for exclusion from participation in this study, however medication usage and dosage was recorded for use as covariates in statistical analyses.

Participants who completed Phase I screening were invited to participate in Phase II if specific Phase I criteria were met. For potential bipolar participants, Phase I criteria included GBI scores of at least 13 on the depression index and at least 11 on the hypomania index. There were no minimum cutoffs for ISI scores for bipolar participants. Potential insomnia participants were required to score below a 7 on both GBI indices of depression and hypomania, and score at least a 10 or higher on the Insomnia Severity Index. Scores of 10 and higher have been shown to identify sleep-disrupted individuals in community samples (Morin et al., 2011). Potential control participants had to score below a 7 on both the depression and hypomania indices of the GBI and below a 7 on the Insomnia Severity Index. Scores of 7 and below represent the lower quartile of the ISI, and would thus provide a good demonstration of satisfactory sleep.

Phase II screening involved additional exclusionary criteria. As data on cognitive performance among "softer" bipolar diagnoses (e.g., bipolar NOS, cyclothymia) is sparse, including these diagnoses in the study might have limited generalizability of findings and hampered the ability to detect significant effects of cognitive variables. Thus, individuals who were diagnosed via the SADS-L with bipolar NOS or cyclothymia were excluded from participation in the Bipolar group. Those individuals with self-reported sleep disturbance as well as an ISI of 10 or higher were invited to participate in the Insomnia group. Those individuals who endorsed symptoms of insomnia but denied impairment or distress from these symptoms, or denied at least one month duration of symptoms were excluded from participation. Individuals who met inclusion criteria for insomnia but who carried diagnoses of bipolar NOS, cyclothymia, or experienced a major depressive episode in the past year were excluded from participation. Those individuals who endorsed any current or past mood diagnosis or any current sleep disruption were excluded from the control group. Individuals who reported satisfactory sleep via the use of sleeping medications were excluded from participation.

Full Study Procedure

Participants who met screening criteria were invited to participate in the full study. Those individuals then completed a Pittsburgh Sleep Quality Index (PSQI; see Measures) and were fitted with an actigraph. Research has shown that the use of actigraphy is useful in the assessment of sleep/wake activity and that data collected via actigraphy is more accurate than data collected through standard sleep/wake diaries (Ancoli-Israel, et al., 2003; Brooks et al., 1993; Sadeh, 1995; Webster et al., 1982). Actigraphs provide several important objective sleep variables including: 1) sleep efficiency (a simple ratio of hours asleep versus hours spent in bed, which gives an estimate of the amount of time an individual spends *trying* to sleep), 2) sleep

onset latency (how long it takes to fall asleep after going to bed), 3) wake time after sleep onset (the total amount of time the participant is awake following initial sleep onset; a total sum of all mid-sleep awakenings), and 4) overall daily activity patterns (periods of activity vs. rest throughout a 24 hour period).

All actigraphy data were scored by the primary investigator and compared against self-reported sleep diaries to assess for discrepancies in interval calculations. In 7 cases, rest and sleep intervals were not automatically generated by the software and needed to be created by hand. There were no significant group differences among those individuals who required hand scoring vs. those who did not. Hand placement of intervals was conducted using self-reported sleep diaries as a general guide for interval onset times. Once the general time span for intervals was pinpointed, sleep onset intervals were inserted and sleep offset intervals were marked just before the onset of new continuous activity.

Actigraphy took place for one week prior to cognitive testing. Participants received detailed instructions on how to wear the instrument and were told to wear it at all times, on their non-dominant wrist, except while bathing or engaging in any other activities during which the actigraph could get wet (e.g., swimming). Cognitive testing and occupational functioning assessment took place at Temple University at the culmination of the one-week actigraphy and sleep monitoring period. All cognitive assessments were conducted by assistants who were blind to participants' group assignment as well as the results of their actigraphy. Participants were administered five cognitive tests with breaks worked into the battery. Following a short break, participants were administered the Work Personality Profile and the Work Performance Questionnaire.

Measures

Phase I Screening Measures

The General Behavior Inventory (GBI). The GBI (Depue, Krauss, Spoont & Arbisi, 1989) was used as a screening questionnaire to select individuals likely to carry a diagnosis of Bipolar Disorder. The GBI is a 73 item questionnaire designed to assess various experiences related to depressive and/or hypomanic symptoms based on dimensions of intensity, duration, and frequency. It has been validated in undergraduates, outpatients, and relatives of individuals with bipolar I disorder. The GBI is a psychometrically strong measure, with internal consistency α's of 0.90 to 0.96, test-retest reliability *r*'s of 0.71 – 0.74, satisfactory sensitivity (0.78) and superior specificity (0.99) for bipolar spectrum disorders (Depue et al., 1981; 1989). Discriminant validity is also strong (*r* of .88 in distinguishing individuals with affective disorders from those with no diagnosis) (Mallon et al., 1986).

Insomnia Severity Index (ISI). The ISI (Morin et al., 2011) is a 7-item questionnaire used to assess the severity of insomnia symptoms utilizing a 5-point Likert-type scale. Internal consistency for this measure is excellent (α = .90) with good convergent validity (Morin et al., 2011). A study on the psychometrics of the ISI revealed a cutoff score of 10 to be adequate in community samples for the diagnosis of insomnia (Morin et al., 2011).

Phase II Screening Measures

Schedule for Affective Disorders and Schizophrenia – Lifetime. The Schedule for Affective Disorders and Schizophrenia – Lifetime (SADS-L; Endicott & Spitzer, 1978) is a semi-structured diagnostic interview used to assess current and lifetime history of Axis I disorders. The mood disorders and psychosis sections of an expanded SADS-L (exp-SADS-L;

see Alloy et al., 2008; Nusslock et al., 2007) was administered to assess for the presence of current or past major depressive disorder, bipolar spectrum disorder, or psychosis. This portion of the expanded version of the SADS-L assesses the occurrence, duration, and severity of mood and psychosis symptoms over the course of an individual's lifetime. The exp-SADS-L has demonstrated excellent inter-rater reliability, with $\kappa > .90$ for unipolar depression diagnoses based on 80 jointly rated interviews (Alloy et al., 2000) and $\kappa > .96$ for bipolar spectrum diagnoses based on 105 jointly rated interviews (Alloy et al., 2008).

Unstructured Clinical Interview for Insomnia. An unstructured clinical interview was utilized to diagnose primary insomnia. This interview collected data on sleep onset latency, total sleep time, number of mid-sleep and early-morning awakenings, symptoms of obstructive sleep apnea, symptoms of circadian sleep phase disorder, nightmares, and sleep-related behaviors. Information on medical conditions was collected to determine if medical exclusion was warranted.

Beck Depression Inventory (BDI). The Beck Depression Inventory (Beck et al., 1996) is a 21-item self-report measure of symptoms of depression, and is the gold standard of self-reported measures of the severity of depression. The scale allows the participant to report on symptoms of depressed mood, anhedonia, sleep and appetite disturbance, and suicidal ideation, among others. The BDI was administered following the 7-day actigraphy period and was used to both inform potential clinical risk and to control for any effects of mood on cognitive and occupational functioning outcomes.

Altman Self-Rating Mania Scale (ASRM). The ASRM (Altman et al., 1997) is a 5-item self-report scale designed to assess both presence and severity of manic symptoms. The ASRM correlates significantly with the Clinician Administered Rating Scale for Mania (CARS-M) and

the Young Mania Rating Scale (YMRS) and has high sensitivity and specificity (Altman et al., 1997). The ASRM was administered in conjunction with the BDI to both inform potential clinical risk and to control for any effects of mood on cognitive and occupational functioning outcomes.

Kauffman Brief Intelligence Test Second Edition (KBIT-II). The KBIT-II (Kaufman & Kaufman, 1990) was used to obtain a baseline assessment of intelligence. The KBIT-II is designed for individuals aged 4 to 90 and assesses both verbal and nonverbal abilities and is ideal for generating a reliable baseline IQ with minimal participant burden. Correlations between the KBIT and the Wechsler Adult Intelligence Scale- Revised (WAIS-R; Wechsler, 1976), a longer and more comprehensive intelligence test, were 0.83, 0.77, and 0.88 for Verbal, Nonverbal, and Composite scales, respectively (Naugle et al., 1993). WAIS-R and K-BIT scores are similar across age and educational levels, although mean K-BIT scores tend to be approximately 5 points higher than WAIS-R scores (Naugle et al., 1993).

Cognitive Functioning

The following cognitive tests assess the domains of functioning that have been shown to be impaired among individuals with BD: verbal learning, executive functioning, sustained attention, and working memory. To the greatest extent possible, this study utilized tests that have been used in previous studies of cognitive functioning in bipolar disorder. A subset of variables from each test were used in analyses (see Preliminary Analyses).

Stroop subtest of the Delis-Kaplan Executive Functioning System (DKEFS). The Stroop subtest of the DKEFS (Delis et al., 2004) is a test of an individual's ability to direct attention and provides insight into cognitive effects that result from attentional fatigue. Participants were required to name a color that is printed in a color not denoted by the name (e.g., the word "red"

printed in blue ink instead of red ink). When this is required, naming the color of the word takes longer and is more prone to errors than when the color of the ink matches the name of the color. Four conditions of this test are administered: color naming (the participant names the colors of squares on the stimulus book), color reading (the participant reads the color words from the stimulus book), inhibition (the participant names the color of the ink rather than reading the color word) and inhibition/switching (the participant switches between naming the color of the ink and reading the color word). Internal consistency of the Stroop subtest ranges from moderate to high (.62 to .86; Shunk et al., 2006). The Stroop is commonly included in executive functioning test batteries and gives a valid measure of cognitive flexibility, processing speed, and directed attention (Strauss, Sherman, & Spreen, 2006).

Ruff 2 & 7 Selective Attention Test. The Ruff 2 & 7 Selective Attention Test (Ruff et al., 1992) is a pencil-and-paper measure of sustained and selective attention consisting of 20 trials of a visual search and cancellation task. The respondent detects and marks though all occurrences of two target digits: 2 and 7. The Ruff 2 & 7 test has been standardized and normed for use in individuals ages 16 to 70, with results of reliability tests showing high internal consistency and high split-half reliability (Ruff et al., 1992).

Tower of London. The Tower of London (Shallice, 1982) task assesses executive planning and is frequently incorporated into standard executive functioning test batteries. The test consists of two boards with pegs and several discs of different colors. The object is to move the discs from one peg to another without violating a set of rules given to the subject by the test administrator. The Tower of London provides adequate discrimination between high and low-achieving subjects and provides satisfactory split-half reliability (r=.72) and internal consistency (α=.69) (Kaller, Unterrainer, & Stahl, 2011).

California Verbal Learning Test (CVLT-II). The CVLT-II (Rasmussen et al., 2001) is a learning test that has been used extensively in neuropsychology to assess auditory/verbal episodic memory. The CVLT-II measures recall, recognition, encoding strategies, learning rates, and error types. Participants are read a list of words five times, and are asked to recall these words each time to assess the participant's learning curve. Short and long-term free and cued recall trials are also administered, as are forced choice and recognition discrimination trials. Internal consistency of this measure is excellent (Rasmussen et al., 2001).

Digit Span (subtest of the Wechsler Memory Scale). In the digit span (Wechsler, 1997), participants were presented with a string of numbers and asked to repeat them verbatim. Length of strings increased with each subsequent set. Participants were then asked to repeat a list of numbers in reverse order. Similar to the letter-number sequencing task, the digit span task assesses the participants' ability to monitor and manipulate information. The digit span has been used extensively in tests of cognitive functioning in BD (Robinson et al., 2006).

Sleep Functioning

The Pittsburgh Sleep Diary (PghSD). The PghSD (Monk et al., 1994b) is a self-report instrument used to document and quantify sleep/wake behaviors. The PghSD has separate components for completion at bedtime and upon first waking, referring to the events leading up to sleep and the just-completed sleep period, respectively. The PghSD has shown good validity in agreement with actigraph data, with reported correlations of .56 and .81 for sleep timing and quality, respectively. Sleep Diaries were not included in statistical analyses for study hypotheses, but rather were collected to ensure some form of sleep monitoring in the event there were widespread errors via actigraphy (e.g. misuse, loss of actigraphs).

The Pittsburgh Sleep Quality Index (PSQI). The PSQI (Buysse, 1989) is a self-report measure that assesses sleep quality and disturbance over a one-month time interval. The measure generates component scores of subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. This measure has good internal consistency (α = .83) and test-retest reliability (r=.85).

Actigraphy. All participants were equipped with wristwatch actigraphy for 7 nights. The devices used were Actiwatch AW-64 (Mini Mitter, Philips Respironics Inc., Bend, OR, USA). This device features a sensitivity of 0.05 g and a bandwidth between 3 and 11 Hz, with a sampling frequency of 32 Hz. Actigraphy data were stored in 15-sec epochs for a continuous period of 7 days. Sleep onset data were analyzed using the Immobile Minutes algorithm in Actiware 5.57 (Mini Mitter Philips Respironics Inc.), which generated wake, rest, and sleep intervals for each participant for each night of actigraphy.

Occupational Functioning

The Work Personality Profile – Self Report (WPP-SR). The WPP-SR (Bolton & Roessler, 1986a) consists of 58 items and assesses those capabilities that satisfy fundamental work role requirements, i.e., work attitudes, values, habits, and behaviors that are considered essential to achievement and maintenance of suitable employment. Items are rated on a standard four-point rating scale. The report consists of five factors: task orientation, social skills, work motivation, continuity/persistence of work behavior and personal presentation. Scales from this measure have shown good internal consistency and validity (Bolton & Roessler, 1986b) and have been used in major reports of vocational functioning in individuals with schizophrenia (Vauth et al., 2004).

Work Performance Questionnaire. This is an original questionnaire created by the

investigator to obtain objective rather than subjective vocational data. The questionnaire assessed total months of employment, number of firings, number of times of self-terminated employment, and number of different jobs an individual has had both in the past year and in his or her lifetime.

CHAPTER 3

HYPOTHESES

Previous research has demonstrated a relationship between cognitive functioning and occupational functioning among individuals with bipolar disorder, as well as a relationship between sleep deprivation and cognitive functioning among healthy individuals. However, no study to date has integrated these established relationships to suggest a possible mechanism of poor occupational functioning in bipolar disorder. Thus, hypotheses were formed to test the degree to which these previously validated relationships may intertwine in BD.

Group Differences in Sleep, Cognitive Functioning, and Occupational Functioning

Hypothesis 1a: Sleep functioning among bipolar, insomnia, and healthy control participants.

I predicted that individuals with bipolar disorder would not differ significantly from individuals with insomnia in their objective or subjective reports of sleep disturbance. Control participants would exhibit superior sleep functioning relative to both insomnia and bipolar participants.

Hypothesis 1b: Cognitive functioning among bipolar, insomnia, and healthy control participants.

I predicted that individuals with bipolar disorder would not differ significantly from individuals with insomnia in terms of cognitive performance. Control participants would exhibit superior cognitive functioning relative to both insomnia and bipolar participants.

Hypothesis 1c: Occupational functioning among bipolar, insomnia, and healthy control participants.

I predicted that individuals with bipolar disorder would exhibit worse occupational functioning relative to individuals with insomnia and healthy controls. Control participants

would exhibit superior occupational functioning relative to both insomnia and bipolar participants.

Associations between Sleep, Cognitive, and Occupational Functioning

Hypothesis 2: Association between sleep and cognitive functioning

Disrupted sleep will significantly predict lower scores on all measures of cognitive functioning.

Hypothesis 3: Association between sleep and occupational functioning.

Disrupted sleep will significantly predict lower scores on measures of occupational functioning.

Hypothesis 4: Association between cognitive and occupational functioning.

Cognitive performance will predict occupational functioning.

Hypothesis 5: The mediational effect of sleep on cognitive and occupational functioning.

Sleep disruption will mediate the relationship between cognitive performance and occupational functioning.

Summary of Hypotheses

The present study examined five main hypotheses. Specifically, it was expected that individuals with BD would demonstrate sleep and cognitive disturbance comparable to individuals with primary insomnia, and that both individuals with insomnia and individuals with bipolar disorder would demonstrate poor sleep and cognitive functioning relative to healthy controls. Consistent with the overarching hypothesis that sleep and cognitive functioning are significantly related in bipolar disorder, it was expected that poor sleep functioning would predict poor cognitive performance, as well as poor occupational functioning. Additionally, poor

cognitive performance would predict poor occupational functioning, and sleep disturbance would mediate that relationship.

CHAPTER 4

RESULTS

Preliminary Analyses

A priori variable selection

Data collection for the study yielded a large number of potential variables of interest for analysis. To reduce the number of statistical tests and to increase generalizability of findings to the extant literature, the target variables for analysis were selected a priori. Of the numerous sleep variables collected, I chose the self-reported variables of ISI score and PSQI score, and the actigraph variables of onset latency and wake time after sleep onset. ISI scores provide a general overview of the severity of insomnia symptoms and have been shown to distinguish between healthy and disordered sleepers (Morin et al., 2011). The PSQI and actigraphy variables have been utilized in significant reports of sleep disturbance in BD (e.g., Harvey 2005), and thus, including these variables in the current study would enable greater comparability of findings. The actigraphy variables of wake time after sleep onset and sleep onset latency were specifically selected because they represent frequently reported symptoms of sleep disturbance among individuals with insomnia and bipolar disorder.

The cognitive assessments themselves were chosen for the study based on the knowledge of which domains of cognitive functioning are most affected in BD; however, further culling of variables was necessary. Utilizing results from meta-analyses of cognitive functioning in BD as a guide (e.g. Bora et al., 2009), specific variables were selected to match earlier reports of deficits in cognitive functioning. This procedure yielded the following cognitive variables: Short-term free recall, long-term free recall, recognition discrimination and number of intrusions from the California Verbal Learning Test (CVLT); Digit Span Forward and Backward; and the

Inhibition and Inhibition/Switching tasks from the Stroop Color/Word Interference test. Use of the Tower Test and the Ruff 2 & 7 Selective Attention test is relatively less frequent in the literature, but other more common tests of executive functioning and selective attention (e.g., the Wisconsin Card Sort, Conners' Continuous Performance Task) could not be obtained for the present study. Thus, target variables were selected that best assessed the core domains that they were designed to test. For the Tower test, these variables were total number of moves (indicating lack of planning) and total errors (indicative of response inhibition/set loss). For the Ruff 2 & 7, I chose Controlled Detection Accuracy and Controlled Detection Errors, as controlled detection (discriminating 2's and 7's from an array of other numbers) requires higher levels of processing than automatic detection (discriminating 2's and 7's from an array of letters).

Due to the large number of possible combinations of variables for regression analyses, further variable reduction was required to avoid type I error. For associations involving sleep functioning, three variables were selected for regression analyses: Insomnia Severity Index, Pittsburgh Sleep Quality Index (total score), and Actigraphy Sleep Disturbance. Actigraphy sleep disturbance is a computed variable consisting of the sum of awakenings and sleep onset as measured by actigraphy. Higher values on both of these measurements are indicative of poorer sleep, and the combination of these variables would encompass a wider range of sleep disruption while still keeping the total number of statistical tests relatively small.

A similar computational technique was employed to reduce the number of cognitive variables included in regression analyses. A summed CVLT variable was constructed using short delay free recall, long delay free recall, and recognition discrimination, as high scores on all of these variables indicate better performance in this domain, and are consistent with variables utilized in other published reports of CVLT measures. The Ruff 2&7 variable is a

summed variable of controlled detection accuracy and errors (reverse scored). The Tower variable is a summed variable of errors and total moves, and the Stroop variable is a summed variable of the inhibition and inhibition/switching variables, and the Digit Span variable is a summed variable of the forward and backward totals. Occupational variables were restricted to lifetime unemployment and lifetime number of firings.

Sample Description and Associations Among Study Variables

Table 1 presents demographic and clinical characteristics of the study sample. Of the 72 participants, 33.3% (*n*=24) were diagnosed with bipolar I or II disorder, 33.3% (*n* = 24) were diagnosed with primary insomnia, and 33.3% (*n*=24) were healthy control participants. The sample was 61% (*n*=44) female, 65.3% (*n*=47) Caucasian, 18.1% (*n*=13) African American, 4.2% (*n* = 3) Asian, 1.4% (*n* = 1) Hispanic, 2.8% (*n* = 2) Pacific Islander and 8.3% (*n* = 6) "other." The mean participant age was 31.46 years (*SD* = 12.37), with an average education level of 14.19 years (*SD* = 1.93). Bipolar, insomnia, and control participants did not significantly differ on gender ($\chi^2(2) = 0.117$, $p = .94$), ethnicity ($\chi^2(5) = 0.117$, $p = .53$), age ($F(2,71) = 0.16$, $p = .86$), or years of education ($F(2,71) = 0.49$, $p = .62$). Table 2 presents means and standard deviations of sleep, cognitive, and occupational outcome variables.

Some gender differences were observed in study variables: females demonstrated greater recognition discrimination on the CVLT ($F(1,70) = 8.05$, $p = .006$) and performed worse on Stroop Inhibition ($F(1,70) = 6.00$, $p = .01$). Females also had a higher number of lifetime firings than males ($F(1,70) = 4.01$, $p = .05$). No gender differences were noted among any sleep variables. Although all groups reported depression and hypomania scores in the euthymic range, groups differed significantly on these variables, such that bipolar participants had higher ASRM scores compared to control and insomnia participants, as well as higher BDI scores than control

participants, but they did not differ significantly from insomnia participants on the BDI (ASRM: $F(2,69) = 7.88$, $p = .001$; BDI: $F(2,69) = 13.681$, $p < .001$). Thus, to control for any symptom level effects on sleep and cognitive functioning, BDI and ASRM scores were entered as covariates in all analyses. As expected, groups differed significantly on medication status ($\chi^2(2) = 34.76$, $p < .001$), as only individuals in the bipolar group were taking psychiatric medications (some with sedative effects). Thus, medication status was also entered as a covariate in analyses. Groups did not differ in age; however, age related effects on sleep and cognitive functioning are well-documented (Deary et al., 2009; Ohayon et al., 2004), and thus, age was added as a covariate in all analyses to control for the wide range of ages in each group. Table 3 presents partial correlations among study variables controlling for the effects of age, medication status, and BDI and ASRM scores.

Table 1. Demographic and clinical characteristics of study sample (N=72)

	Full Sample (*n*=72)		Control (*n*=24)		Insomnia (*n*=24)		Bipolar (*n*=24)*	
Gender								
	n	*%*	*n*	*%*	*n*	*%*	*n*	*%*
Male	28	39.0	10	41.7	9	37.5	9	37.5
Female	44	61.0	14	58.3	15	62.5	15	62.5
Race								
	n	*%*	*n*	*%*	*n*	*%*	*n*	*%*
Caucasian	47	65.3	19	79.2	14	58.3	14	58.3
African American	13	18.1	2	8.3	5	20.8	6	25
Asian	3	5.5	1	4.2	1	4.2	1	4.2
Hispanic	1	1.4	0	0	1	4.2	0	0
Pacific Islander	2	1.4	1	4.2	0	0	1	4.2
Biracial/Other	6	8.3	1	4.2	2	8.3	3	12.5
Age								
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
	31.46	1.93	30.96	12.90	30.79	12.99	32.63	11.61
Education								
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
	14.19	1.93	14.50	1.96	14.13	2.03	13.96	1.85
Clinical Characteristics								
ASRM	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
	2.10	1.86	1.71	1.83	1.37	1.31	3.21	1.91
BDI	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
	4.01	4.20	0.92	1.35	6.04	4.43	5.08	4.20
Medication Status	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*
	13	0	0	0	0	0	13	54.16

**Bipolar Group consists of 66.6% (n = 16) Bipolar II and 33.3% (n = 8) Bipolar I participants. ASRM = Altman Self Rating Mania Scale; BDI = Beck Depression Inventory*

Table 2. Means and Standard Deviations of Study Variables

	Control		Insomnia		Bipolar	
Cognitive Functioning	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
CVLT Short Delay Free Recall	11.79	3.02	11.00	3.50	10.54	2.52
CVLT Long Delay Free Recall	11.67	3.35	11.58	3.08	10.92	2.47
CVLT Square Root of Intrusions	1.22	0.97	1.01	0.89	1.68	1.21
CVLT Recognition Discrimination	3.40	0.73	3.33	0.63	2.96	0.62
Digit Span Forward	11.33	1.69	11.58	2.72	9.71	1.40
Digit Span Backward	9.08	1.74	9.96	2.66	8.58	2.06
Ruff 2&7 Controlled Detection Errors	14.74	15.75	17.43	21.13	7.00	7.70
Ruff 2&7 Controlled Detection Accuracy	91.22	8.19	89.97	9.78	95.25	4.89
Stroop Inhibition	46.41	7.03	47.88	9.20	50.00	7.86
Stroop Inhibition/Switching	51.83	9.14	55.70	19.54	58.68	18.50
Tower Total Moves	142.54	36.29	142.39	45.36	120.61	45.39
Tower Rule Violations	0.63	1.38	0.92	1.74	0.83	1.30
Sleep Functioning						
Insomnia Severity Index	2.58	2.75	17.50	3.48	10.88	5.10
PSQI Total	2.46	1.38	11.48	3.34	8.00	3.94
PSQI Sleep Duration	0.21	0.51	2.04	1.11	0.79	1.02
PSQI Sleep Disturbance	0.88	0.34	1.43	0.51	1.33	0.64
PSQI Sleep Latency	0.50	0.59	2.39	0.99	1.50	1.10
PSQI Day Dysfunction	0.38	0.50	1.35	0.71	1.33	0.82
PSQI Sleep Quality	0.29	0.46	2.13	0.46	1.29	0.81
Sleep Onset Latency via Actigraphy	2.71	1.23	3.18	0.94	3.05	0.98
Number of Awakenings via Actigraphy	1.92	0.43	2.23	0.31	1.81	1.21
Occupational Functioning						
Lifetime Number of Firings	0.08	0.28	0.33	0.64	1.13	1.54
Lifetime Number of Quit Jobs	1.33	2.41	1.67	1.31	4.00	5.67
Lifetime Months of Unemployment	7.71	7.36	25.38	42.55	31.50	48.67
WPP Task Orientation	76.73	6.64	76.68	6.81	73.30	8.80
WPP Social Skills	41.55	4.78	40.90	7.14	38.49	6.68
WPP Work Motivation	28.61	3.15	29.07	2.90	26.96	3.72
WPP Work Conformance	31.18	4.12	31.81	2.56	28.74	4.93
WPP Personal Presentation	29.55	2.66	28.54	3.04	28.24	3.04

**CVLT = California Verbal Learning Test; PSQI = Pittsburgh Sleep Quality Index; WPP = Work Personality Profile*

Table 3. Partial Correlations among study variables controlling for age, medication status, and mood symptoms.

	Short Delay	Long Delay	Intru-sions	Recog. Discrim	Digit Span F	Digit Span B	Ruff Error	Ruff Acc	Stroop Inhibit	Stroop Switch	Tower Moves	Tower Error	ISI	PSQI Duration	PSQI Disturb
Short Delay	1.000														
Long Delay	.865**	1.000													
Intrusions	-.201	-.247	1.000												
Recog. Discrim.	.662**	.697**	-.372*	1.000											
Digit Span F	.019	.137	.024	.155	1.000										
Digit Span B	.203	.305*	-.029	.181	.496**	1.000									
Ruff Error	.003	-.021	.120	-.008	.012	.061	1.000								
Ruff Acc	.055	.049	-.112	.062	-.001	-.021	-.951	1.000							
Stroop Inhibition	-.394*	-.380*	-.012	-.347*	.170	-.017	-.029	-.034	1.000						
Stroop Switching	-.322*	-.311*	.077	-.306*	.083	-.095	-.097	.055	.454**	1.000					
Tower Moves	.103	.019	-.022	-.017	-.188	-.114	.204	-.184	-.126	-.305*	1.000				
Tower Error	-.106	-.089	-.083	-.030	-.063	-.059	.504**	-.470**	-.061	-.091	.138	1.000			
ISI	-.124	-.041	-.086	-.135	.117	.216	-.092	.103	.095	.045	-.176	-.101	1.000		
PSQI Duration	-.065	.095	-.251	.038	.182	.155	.058	-.021	.069	.098	-.089	.033	.359*	1.000	
PSQI Disturbance	-.122	-.208	.011	-.262*	-.073	-.020	.115	-.183	.194	-.071	.147	.096	.148	.028	1.000
PSQI Latency	.058	.082	-.202	.090	.258*	.467**	.029	-.005	.040	-.280*	.005	.095	.357*	.173	.224
PSQI Dysfunction	-.118	-.025	-.017	-.098	.206	.103	-.145	.076	.121	.035	-.246	-.176	.396*	.342*	.166
PSQI Quality	-.008	.033	-.164	.016	.204	.213	.081	-.054	.094	.028	-.134	.103	.563**	.497**	.044
Log Act Onset	-.021	-.114	-.134	.097	.116	-.015	-.110	.155	.064	-.074	.108	-.004	.270*	-.076	-.060
Sqrt Act Awakenings	.045	.055	-.150	.152	.072	.249	-.037	.045	-.195	-.033	.020	.041	.318*	.269*	-.155
Lifetime Firings	-.135	-.091	.025	-.196	-.218	.046	-.183	.216	.143	.323*	-.181	-.051	.330*	.072	.018
Lifetime Quit	.076	-.034	.073	.044	.006	-.081	-.147	.145	-.060	-.143	.146	-.210	-.064	-.146	.097
Lifetime Unemploy	.015	-.049	.110	-.151	.008	.207	.336*	-.250	-.020	.161	-.061	.189	.075	.329*	.016
Task Orientation	.040	.099	.020	.122	.150	-.128	.057	-.069	-.041	-.074	-.066	.049	.088	.240	-.017
Social Skills	.036	.193	-.310*	.252	.015	-.072	.037	-.075	.050	-.179	-.035	-.009	.217	.329*	-.052
Work Motivation	-.011	.080	-.001	.077	.202	-.050	.053	-.086	.068	-.082	-.156	-.033	.092	.270*	-.035
Conformance	.088	.154	-.070	.207	.216	-.023	.227	-.244	-.051	-.106	-.005	.076	.097	.193	-.008
Personal Presentation	-.025	.129	-.163	.154	.194	-.042	.012	-.099	.025	-.294*	.123	.001	.144	.209	.077

*** = <.001; * = <.05 Short Delay = CVLT Short Delay Free Recall; Long Delay = CVLT Long Delay Free Recall; Intrusions = CVLT Square Root Intrustions; Digit Span F = Digit Span Forward; Digit Span B = Digit Span Backward; Ruff Error = Ruff 2 & 7 Controlled Detection Errors; Ruff Acc = Ruff 2 & 7 Controlled Detection Accuracy; Stroop Inhibit = Stroop Color/Word Interference Inhibition; Stroop Switch – Stroop Color/Word Interference Inhibition/Switching; Tower Moves = Tower Total Moves; Tower Error = Tower Total Errors; ISI – Insomnia Severity Index; PSQI Duration = Pittsburgh Sleep Quality Index Sleep Duration; PSQI Disturb = Pittsburgh Sleep Quality Index Sleep Disturbance; PSQI Latency = Pittsburgh Sleep Quality Index Onset Latency; PSQI Dys = Pittsburgh Sleep Quality Index Daytime Dysfunction; PSQI Quality = Pittsburgh Sleep Quality Index Sleep Quality; Log Act Onset – Log of Sleep Onset via Actigraphy; Sqrt Act Awakenings = Square Root of Awakenings via Actigraphy; Lifetime Unemploy = Lifetime length of unemployment; Task Orient = Work Personality Profile Task Orientation; Social Skills = Work Personality Profile Social Skills; Motivation = Work Personality Profile Work Motivation; Conformance = Work Personality Profile Work Conformance; Personal Performance = Work Personality Work Personal Presentation.*

Table 3 (Continued). Partial Correlations among study variables controlling for age, medication status, and mood symptoms.

	PSQI Latency	PSQI Dys	PSQI Quality	Act Onset	Act Awake	Lifetime Firings	Lifetime Quit	Lifetime Unemp	Task Orient	Social Skills	Motiv-ation	Confor-mance	Personal Presentation
CVLT SDFR													
CVLT LDFR													
CVLT Sqrt Intrusions													
CVLT RD													
DS Forward													
DS Backward													
Ruff CD Error													
Ruff CD Acc													
Stroop Inhibition													
Stroop Switching													
Tower Total Moves													
Tower Rule Violations													
Insomnia Severity													
PSQI Duration													
PSQI Disturbance													
PSQI Sleep Latency	1.000												
PSQI Day Dysfunction	.090	1.000											
PSQI Sleep Quality	.379*	.157	1.000										
Log Act Onset	.323*	-.116	.255*	1.000									
Sqrt Act Awakenings	.178	-.045	.287*	.040	1.000								
Lifetime Firings	-.120	.021	.029	-.114	.047	1.000							
Lifetime Quit Jobs	-.160	.058	-.096	-.056	-.116	.057	1.000						
Lifetime Unemploy	.240	-.128	.409*	-.103	.113	-.043	-.096	1.000					
Task Orientation	-.067	-.008	.174	.286*	-.010	-.214	-.181	-.137	1.000				
Social Skills	.001	.204	.175	.109	-.032	-.107	-.181	-.249	.565**	1.000			
Work Motivation	.014	.177	.115	.081	-.097	-.166	-.131	-.160	.728**	.702**	1.000		
Work Conformance	.076	.011	.156	.224	.059	-.363*	-.123	-.105	.717**	.693**	.788**	1.000	
Personal Presentation	.135	.080	.191	.290*	-.014	-.302*	-.022	-.199	.657**	.712**	.705**	.748**	1.000

*** = <.001; * = <.05 Short Delay = CVLT Short Delay Free Recall; Long Delay = CVLT Long Delay Free Recall; Intrusions = CVLT Square Root Intrustions; Digit Span F = Digit Span Forward; Digit Span B = Digit Span Backward; Ruff Error = Ruff 2 & 7 Controlled Detection Errors; Ruff Acc = Ruff 2 & 7 Controlled Detection Accuracy; Stroop Inhibit = Stroop Color/Word Interference Inhibition; Stroop Switch – Stroop Color/Word Interference Inhibition/Switching; Tower Moves = Tower Total Moves; Tower Error = Tower Total Errors; ISI – Insomnia Severity Index; PSQI Duration = Pittsburgh Sleep Quality Index Sleep Duration; PSQI Disturb = Pittsburgh Sleep Quality Index Sleep Disturbance; PSQI Latency = Pittsburgh Sleep Quality Index Onset Latency; PSQI Dys = Pittsburgh Sleep Quality Index Daytime Dysfunction; PSQI Quality = Pittsburgh Sleep Quality Index Sleep Quality; Log Act Onset – Log of Sleep Onset via Actigraphy; Sqrt Act Awakenings = Square Root of Awakenings via Actigraphy; Lifetime Unemploy = Lifetime length of unemployment; Task Orient = Work Personality Profile Task Orientation; Social Skills = Work Personality Profile Social Skills; Motivation = Work Personality Profile Work Motivation; Conformance = Work Personality Profile Work Conformance; Personal Performance = Work Personality Work Personal Presentation.*

Examination of the distribution of study variables revealed significant deviations from normality in three variables: CVLT Intrusions, Sleep Onset via Actigraphy, and Number of Awakenings via Actigraphy. Logarithmic (for actigraphy variables) and square root (for CVLT) transformations were successful in remediating these violations, and the transformed variables were utilized in main analyses.

Tests of Study Hypotheses

Group Differences in Sleep, Cognitive Functioning, and Occupational Functioning

Hypothesis 1a: Sleep functioning among bipolar, insomnia, and healthy control participants.

Hypothesis 1a stated that bipolar participants would not differ significantly from insomnia participants on any measure of sleep disruption, but would exhibit significantly worse sleep than control participants. Tests were conducted using ANCOVA controlling for age, medication status, BDI and ASRM scores. Post-hoc contrasts were conducted for each significant omnibus test, utilizing a Bonferroni alpha correction with a significance threshold of $p = .016$. Tests of this hypothesis yielded mixed findings. Omnibus ANCOVA analyses yielded significant group differences in insomnia severity ($F(2, 65) = 60.7$; $p < .001$). Consistent with hypotheses, bipolar participants demonstrated significantly greater levels of insomnia severity than healthy controls when assessed via the Insomnia Severity Index ($t(69) = -2.36$, $p < .001$). However, contrary to hypotheses, bipolar participants exhibited lower levels of insomnia severity relative to participants in the insomnia group ($t(69) = -5.88$; $p < .001$). It is notable, however, that the mean ISI score in the bipolar group was 10.81, which has been an indicator of insomnia in community samples (Morin et al., 2011).

Univariate ANCOVAs, controlling for age, medication status, BDI, and ASRM scores, yielded significant group differences on several PSQI variables (PSQI Duration: $F(2,65) = 15.72$,

p <.001; PSQI Sleep Latency: $F(2,65) = 9.86$, p <.001; PSQI Day Dysfunction: $F(2,65) = 5.26$, p = .008; PSQI Sleep Quality: $F(2,65) = 32.62$, p <.001). Again, results were mixed relative to hypotheses. Pairwise contrasts revealed bipolar participants exhibited significantly longer sleep onset latency than control participants ($t(69) = 3.77$; p, <.001); however, contrary to hypotheses, bipolar participants exhibited shorter sleep latency than insomnia participants ($t(69) = -3.32$; p <.001). The same pattern of findings was observed with PSQI Sleep Quality, with bipolar participants reporting significantly poorer quality of sleep compared to control participants ($t(69) = 5.78$, p <.001), but significantly better quality of sleep compared to insomnia participants ($t(69) = -4.79$, p <.001). In terms of PSQI Sleep Duration, bipolar participants slept longer than insomnia participants ($t(69) = 4.69$, p <.001); however, pairwise comparisons demonstrating bipolar participants slept less than controls failed to reach a significance threshold of p = .016 after Bonferroni correction ($t(69) = -2.21$, p =.03). However, the hypothesized pattern emerged in analyses of PSQI Day Dysfunction, with bipolar participants exhibiting greater daytime effects of sleep disturbance than controls ($t(69) = 4.81$; p <.001), but no significant difference in daytime effects relative to insomnia participants ($t(69) = .07$; p = .94). A trend toward significance was observed in PSQI Sleep Disturbance ($F(2,65) = 3.01$, p = .06).

Analyses of sleep variables measured by actigraphy also produced mixed findings. No significant group differences were observed via univariate ANCOVA for the variables of sleep onset and sleep duration. A significant group difference was observed for the square root of awakenings ($F(2, 65) = 5.17$; p = .008); however, pairwise contrasts showed only a trend toward significance between insomnia and control participants (following Bonferroni correction), with insomnia participants demonstrating a greater square root of awakenings relative to controls ($t(69) = 2.02$, p=.047). Table 4 presents full ANCOVA analyses of sleep variables.

Table 4. *Group Differences in Sleep Functioning*

Source	*Df*	*F*	Partial η²	*p*	Significant Group Comparisons
Insomnia Severity Index					
Age	1	5.535	.078	.022	
Med Status	1	2.508	.037	.118	
ASRM	1	.633	.010	.429	
BDI	1	.686	.010	.410	
Group	2	60.704	.651	.000	IN>BD>HC
Source	***Df***	***F***	**Partial η²**	***p***	**Significant Group Comparisons**
PSQI Sleep Duration					
Age	1	5.154	.075	.027	
Med Status	1	.033	.001	.856	
ASRM	1	.570	.009	.453	
BDI	1	1.108	.017	.296	
Group	2	15.716	.329	.000	BD<IN
PSQI Sleep Disturbance					
Age	1	.230	.004	.633	
Med Status	1	.040	.001	.842	
ASRM	1	.067	.001	.797	
BDI	1	1.592	.024	.212	
Group	2	3.008	.086	.056	--
PSQI Sleep Latency					
Age	1	.032	.001	.858	
Med Status	1	1.490	.023	.227	
ASRM	1	3.110	.046	.083	
BDI	1	6.979	.098	.010	
Group	2	9.856	.235	.000	IN>BD>HC
PSQI Day Dysfunction					
Age	1	4.484	.065	.038	
Med Status	1	1.591	.024	.212	
ASRM	1	.002	.000	.966	
BDI	1	2.982	.045	.089	
Group	2	5.263	.141	.008	BD>HC
PSQI Sleep Quality					
Age	1	.786	.012	.379	
Med Status	1	1.876	.028	.176	
ASRM	1	.785	.012	.379	
BDI	1	2.897	.043	.094	
Group	2	32.621	.505	.000	HC>BD>IN
Source	***Df***	***F***	**Partial η²**	***p***	**Significant Group Comparisons**
Actigraph Log of Sleep Onset					
Age	1	3.335	.052	.073	
Med Status	1	.024	.000	.878	
ASRM	1	.846	.014	.361	
BDI	1	.020	.000	.887	
Group	2	.976	.031	.382	--
Actigraph Square Root Number of Awakenings					
Age	1	.213	.003	.646	
Med Status	1	3.305	.050	.074	
ASRM	1	1.622	.025	.208	
BDI	1	1.540	.024	.219	
Group	2	5.165	.141	.008	IN>HC*
Actigraph Sleep Duration					
Age	1	.132	.002	.717	
Med Status	1	.095	.002	.759	
ASRM	1	.004	.000	.952	
BDI	1	1.705	.026	.196	
Group	2	.670	.021	.515	--

**ASRM = Altman Self Rating Mania Scale; BDI = Beck Depression Inventory *statistical trend after Bonferroni correction (p < .10)*

Hypothesis 1b: Cognitive functioning among bipolar, insomnia, and healthy control participants.

Hypothesis 1b stated that individuals with bipolar disorder would not differ significantly from individuals with insomnia in terms of cognitive performance, and that control participants would exhibit superior cognitive functioning relative to both insomnia and bipolar participants. Results were mixed for this group of comparisons. Analyses of CVLT variables yielded significant group differences for square root of intrusions ($F(2, 65) = 4.51$; $p = .015$) and recognition discrimination ($F(2, 65) = 3.16$; $p = .05$). Bonferroni corrected post-hoc contrasts failed to yield significant findings, but there was a trend for larger square root of intrusions among bipolar participants compared to insomnia participants ($t(69) = 2.27$, $p = .03$). No significant differences were observed between bipolar and control participants ($t(69) = 0.70$, $p = .48$). Pairwise contrasts of recognition discrimination were marginally significant in the hypothesized direction following Bonferroni correction, bipolar participants demonstrating poorer recognition discrimination compared to controls ($t(69) = 2.32$, $p = .023$), and marginally poorer recognition discrimination compared to insomnia participants ($t(69) = 1.93$; $p = .06$). No significant group differences were observed for short or long delay free recall (Short Delay: $F(2, 65) = 0.46$, $p = .64$; Long Delay: $F(2, 65) = 0.64$, $p = .53$).

Significant group differences were observed for digit span forward ($F(2, 65) = 3.79$; $p = .028$). Consistent with hypotheses, bipolar participants performed worse than control participants ($t(69) = 2.79$; $p = .007$); however, they also performed worse than insomnia participants on this measure ($t(69) = 3.22$, $p = .002$). A trend toward significance was observed in digit span backward ($F(2,65) = 2.8$, $p = .07$).

Contrary to hypotheses, no other test of cognitive functioning yielded significant group differences. Table 5 presents full ANCOVA results for all group comparisons of cognitive functioning variables.

Table 5. Group Differences in Cognitive Functioning.

Source	*Df*	*F*	Partial η^2	*p*	Significant Group Comparisons
CVLT Short Delay Free Recall					
Age	1	8.213	.112	.006	
Med Status	1	.523	.008	.472	
ASRM	1	2.012	.030	.161	
BDI	1	.110	.002	.742	
Group	2	.455	.014	.636	--
CVLT Long Delay Free Recall					
Age	1	9.764	.131	.003	
Med Status	1	1.927	.029	.170	
ASRM	1	1.057	.016	.308	
BDI	1	.013	.000	.911	
Group	2	.636	.019	.533	--
CVLT Square Root Intrusions					
Age	1	13.577	.173	.000	
Med Status	1	5.676	.080	.020	
ASRM	1	.351	.005	.556	
BDI	1	.441	.007	.509	
Group	2	4.512	.122	.015	BD>IN*
CVLT Recognition Discrimination					
Age	1	20.122	0.236	0	
Med Status	1	2.735	0.04	0.103	
ASRM	1	2.312	0.034	0.133	
BDI	1	0.26	0.004	0.612	
Group	2	3.162	0.089	0.049	BD<HC*
Digit Span Forward					
Age	1	.227	.003	.635	
Med Status	1	.066	.001	.798	
ASRM	1	.120	.002	.730	
BDI	1	2.087	.031	.153	
Group	2	3.791	.104	.028	IN>HC>BD
Digit Span Backward					
Age	1	1.136	.017	.290	
Med Status	1	.360	.006	.551	
ASRM	1	.443	.007	.508	
BDI	1	2.945	.043	.091	
Group	2	2.801	.079	.068	--
Ruff 2& 7 Controlled Detection Errors					
Age	1	.945	.015	.335	
Med Status	1	.034	.001	.854	
ASRM	1	.018	.000	.895	
BDI	1	1.406	.022	.240	
Group	2	1.299	.040	.280	--
Ruff 2& 7 Controlled Detection Accuracy					
Age	1	1.085	.017	.302	
Med Status	1	.003	.000	.955	
ASRM	1	.044	.001	.834	
BDI	1	1.898	.029	.173	
Group	2	1.700	.051	.191	--

**ASRM = Altman Self Rating Mania Scale; BDI = Beck Depression Inventory *statistical trend after Bonferroni correction (p < .10)*

Table 5 (Continued). Group Differences in Cognitive Functioning.

Source	*Df*	*F*	Partial η^2	*p*	Significant Group Comparisons
Stroop Inhibition					
Age	1	9.008	.122	.004	
Med Status	1	.343	.005	.560	
ASRM	1	2.508	.037	.118	
BDI	1	2.716	.040	.104	
Group	2	1.254	.037	.292	--
Stroop Inhibition/Switching					
Age	1	1.931	.029	.169	
Med Status	1	1.497	.023	.226	
ASRM	1	.048	.001	.827	
BDI	1	3.358	.049	.071	
Group	2	1.440	.042	.244	--
Tower Total Number of Moves					
Age	1	3.439	.052	.068	
Med Status	1	2.285	.035	.136	
ASRM	1	.472	.007	.495	
BDI	1	1.551	.024	.218	
Group	2	.305	.010	.738	--
Tower Rule Violations					
Age	1	4.709	.069	.034	
Med Status	1	.046	.001	.831	
ASRM	1	5.149	.074	.027	
BDI	1	6.544	.093	.013	
Group	2	2.615	.076	.081	--

**ASRM = Altman Self Rating Mania Scale; BDI = Beck Depression Inventory*

Hypothesis 1c: Occupational functioning among BD, insomnia, and healthy control participants.

Hypothesis 1c was that individuals with BD would exhibit worse occupational functioning relative to individuals with insomnia and healthy controls, and that control participants would exhibit superior occupational functioning relative to both insomnia and bipolar participants. Results were mixed for these analyses. A univariate ANCOVA revealed significant group differences for number of lifetime firings (F (2,65) = 3.20, p = .047*)*. Consistent with hypotheses, bipolar participants exhibited greater lifetime firings than both controls (t(69) = 3.69, p <.001) and insomnia participants (t(69) = 2.81, p = .006) after post-hoc correction. No significant differences were observed in length of unemployment or number of quit jobs. Analyses of the Work Personality Profile failed to yield significant group differences

via univariate ANCOVAs. Table 6 presents full ANCOVA results for all group comparisons of occupational variables.

Table 6. Group Comparisons of Occupational Functioning.

Source	*Df*	*F*	partial η^2	*p*	*Significant Group Comparisons*
Work Performance Profile					
Lifetime Unemployed					
Age	1	0.386	.006	.536	
Med Status	1	1.853	.028	.178	
ASRM	1	.214	.003	.645	
BDI	1	.465	.007	.498	
Group	2	1.475	.043	.236	--
Lifetime Quit					
Age	1	1.307	.020	.257	
Med Status	1	4.466	.064	.038	
ASRM	1	1.358	.020	.248	
BDI	1	1.873	.028	.176	
Group	2	0.356	.011	.702	--
Lifetime Fired					
Age	1	4.671	.067	.034	
Med Status	1	6.772	.094	.011	
ASRM	1	1.007	.015	.319	
BDI	1	4.521	.065	.037	
Group	2	3.209	.090	.047	BD>IN>HC
Work Personality Profile					
Task Orientation					
Age	1	3.309	.048	.074	
Med Status	1	0.020	.000	.889	
ASRM	1	1.376	.021	.245	
BDI	1	.012	.000	.912	
Group	2	0.343	.010	.711	--
Work Conformance					
Age	1	0.139	.002	.710	
Med Status	1	0.160	.002	.690	
ASRM	1	.009	.000	.924	
BDI	1	.166	.003	.685	
Group	2	2.359	.068	.103	--
Personal Presentation					
Age	1	.253	.004	.617	
Med Status	1	.725	.011	.398	
ASRM	1	.095	.001	.759	
BDI	1	1.770	.027	.188	
Group	2	.549	.017	.580	--
Work Motivation					
Age	1	0.067	.001	.796	
Med Status	1	0.271	.004	.604	
ASRM	1	.025	.000	.875	
BDI	1	.119	.002	.731	
Group	2	0.884	.026	.418	--
Social Skills					
Age	1	0.398	.006	.530	
Med Status	1	0.206	.003	.651	
ASRM	1	.055	.001	.815	
BDI	1	.351	.005	.556	
Group	2	0.831	.025	.440	--

**ASRM = Altman Self Rating Mania Scale; BDI = Beck Depression Inventory*

Associations between Sleep, Cognitive, and Occupational Functioning

Hypothesis 2: Association between sleep and cognitive functioning

Hypothesis 2 was that disrupted sleep would significantly predict lower scores on all measures of cognitive functioning. Analyses did not yield any significant associations between any combination of sleep and cognitive functioning variables. Full analyses are listed in Table 7.

Table 7. Sleep Disturbance Predicting Cognitive Functioning

Predicting CVLT Performance				
Insomnia Severity Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	-.189	.06	-.368	-3.151*
Medication Status	1.20	1.965	.075	0.610
Step 2				
Altman Self Rating Mania Scale	-.651	.436	-.191	-1.492
Beck Depression Inventory	-0.092	.209	-.061	-.439
Step 3				
Insomnia Severity Index	-.013	.116	-.015	-.115
Pittsburgh Sleep Quality Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	-.216	.060	-.406	-3.572*
Medication Status	1.810	2.034	.114	.890
Step 2				
Altman Self Rating Mania Scale	-.718	.449	-.211	-1.59
Beck Depression Inventory	-.027	.236	-.018	-.115
Step 3				
Pittsburgh Sleep Quality Index	-.088	.202	-.067	-.437
Actigraphy Sleep Disturbance	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	-.219	.065	-.397	-3.387*
Medication Status	1.44	2.02	.089	.716
Step 2				
Altman Self Rating Mania Scale	-.645	.443	-.187	-1.45
Beck Depression Inventory	-.082	.180	-.055	-.456
Step 3				
Actigraphy Sleep Disturbance	.000	.028	.001	.012
Predicting Digit Span Performance				
Insomnia Severity Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	-.019	.053	-.044	-.358
Medication Status	-1.443	1.73	-.108	-.833
Step 2				
Altman Self Rating Mania Scale	-.356	.385	-.125	-.926
Beck Depression Inventory	-.216	.184	-.171	-1.18
Step 3				
Insomnia Severity Index	.147	.102	.199	1.44
Pittsburgh Sleep Quality Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	-.040	.052	-.092	-.769
Medication Status	-2.20	1.74	-.169	-1.26

Table 7 (continued). Sleep Disturbance Predicting Cognitive Functioning.

Step 2				
Altman Self Rating Mania Scale	-.207	.385	-.075	-.538
Beck Depression Inventory	-.340	.202	-.276	-1.68
Step 3				
Pittsburgh Sleep Quality Index	.349	.173	.323	2.015
Actigraphy Sleep Disturbance	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	-.060	.054	-.138	-1.113
Medication Status	-1.679	1.692	-.131	-.992
Step 2				
Altman Self Rating Mania Scale	-.358	.371	-.131	-.964
Beck Depression Inventory	-.038	.151	-.032	-.253
Step 3				
Actigraphy Sleep Disturbance	.029	.023	.151	1.223
Predicting Ruff 2&7 Selective Attention Performance				
Insomnia Severity Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.119	.145	.101	.821
Medication Status	5.43	4.75	.150	1.14
Step 2				
Altman Self Rating Mania Scale	.202	1.07	.027	.189
Beck Depression Inventory	.830	.509	.240	1.63
Step 3				
Insomnia Severity Index	-.431	.282	-.215	-1.53
Pittsburgh Sleep Quality Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.057	.150	.047	.381
Medication Status	7.87	5.01	.218	1.57
Step 2				
Altman Self Rating Mania Scale	.015	1.12	.002	.013
Beck Depression Inventory	.853	.587	.247	1.45
Step 3				
Pittsburgh Sleep Quality Index	-.545	.501	-.180	-1.089
Actigraphy Sleep Disturbance	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.140	.147	.122	.955
Medication Status	6.18	4.58	.184	1.35
Step 2				
Altman Self Rating Mania Scale	-.021	1.03	-.003	-.020
Beck Depression Inventory	.326	.412	.104	.792
Step 3				
Actigraphy Sleep Disturbance	-.009	.063	-.019	-.145
Predicting Tower Test Performance				
Insomnia Severity Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	-.618	.408	-.179	-1.52
Medication Status	-30.46	14.05	-2.77	-2.17*
Step 2				
Altman Self Rating Mania Scale	-2.18	3.10	-.09	-.702
Beck Depression Inventory	2.15	1.49	.210	1.45
Step 3				
Insomnia Severity Index	-.984	.833	-.163	-1.18

Table 7 (continued). Sleep Disturbance Predicting Cognitive Functioning.

Predicting Tower Test Performance				
Pittsburgh Sleep Quality Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	-.618	.418	-.174	-1.48
Medication Status	-26.411	15.24	-.242	-1.733
Step 2				
Altman Self Rating Mania Scale	-2.68	3.31	-.117	-.810
Beck Depression Inventory	2.31	1.71	.228	1.36
Step 3				
Pittsburgh Sleep Quality Index	-1.45	1.43	-.165	-1.013
Actigraphy Sleep Disturbance	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	-.662	.447	-.182	-1.483
Medication Status	-32.25	14.82	-.29	-.217*
Step 2				
Altman Self Rating Mania Scale	-.644	3.20	-.028	-.201
Beck Depression Inventory	1.09	1.26	.109	.862
Step 3				
Actigraphy Sleep Disturbance	.162	.193	.103	.842
Predicting Stroop Color/Word Interference Performance				
Insomnia Severity Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.403	.211	.225	1.91†
Medication Status	12.12	6.88	.218	1.76†
Step 2				
Altman Self Rating Mania Scale	.726	1.53	.061	.475
Beck Depression Inventory	-1.19	.732	-.227	-1.63
Step 3				
Insomnia Severity Index	.514	.406	.168	1.27
Pittsburgh Sleep Quality Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.489	.218	.263	2.24*
Medication Status	10.0	7.32	.180	1.37
Step 2				
Altman Self Rating Mania Scale	.736	1.61	.062	.455
Beck Depression Inventory	-1.03	.849	-.194	-1.21
Step 3				
Pittsburgh Sleep Quality Index	.391	.727	.084	.538
Actigraphy Sleep Disturbance	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.601	.226	.312	2.66*
Medication Status	12.71	7.08	.224	1.79
Step 2				
Altman Self Rating Mania Scale	.288	1.55	.024	.185
Beck Depression Inventory	-.834	.632	-.159	-1.32
Step 3				
Actigraphy Sleep Disturbance	-.056	.098	-.068	-.578

** = <.05, ** = <.001, † = <.10*

Hypothesis 3: Association between sleep and occupational functioning.

Hypothesis 3 stated that disrupted sleep would significantly predict lower scores on measures of occupational functioning. Sleep disturbance as measured by the Pittsburgh Sleep Quality Index significantly predicted greater lifetime unemployment in the sample ($\beta = .381$, $p = .018$). No other relationship between sleep disturbance and occupational functioning was statistically significant. Table 8 presents full results for all associations between sleep and occupational functioning variables.

Hypothesis 4:Association between cognitive and occupational functioning.

Hypothesis 4 stated that cognitive performance would predict occupational functioning. Consistent with hypotheses, performance on the Stroop task predicted increased number of lifetime firings ($\beta = .014$, $p = .005$). Additionally, there was a trend toward significance for poor performance on the CVLT to predict greater number of lifetime firings ($\beta = -.185$, $p = .095$). Contrary to hypotheses, no other relationship between cognitive and occupational functioning was significant. Table 9 presents full results for all associations between cognitive and occupational variables.

Table 8. Sleep Disturbance Predicting Occupational Functioning.

Predicting Lifetime Number of Firings				
Insomnia Severity Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.015	.009	.172	1.67
Medication Status	1.42	.290	.532	4.89**
Step 2				
Altman Self Rating Mania Scale	-.06	.064	-.105	-.932
Beck Depression Inventory	-.060	.031	-.238	-1.95
Step 3				
Insomnia Severity Index	.031	.017	.212	1.82
Pittsburgh Sleep Quality Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.020	.009	.226	2.18*
Medication Status	1.26	.309	.473	4.08**
Step 2				
Altman Self Rating Mania Scale	-.053	.068	-.093	-.778
Beck Depression Inventory	-.057	.036	-.226	-1.59
Step 3				
Pittsburgh Sleep Quality Index	.033	.031	.147	1.06
Actigraphy Sleep Disturbance	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.025	.009	.274	2.68*
Medication Status	1.47	.293	.542	5.00**
Step 2				
Altman Self Rating Mania Scale	-.084	.064	-.146	-1.29
Beck Depression Inventory	-.037	.026	-.147	-1.40
Step 3				
Actigraphy Sleep Disturbance	-.005	.004	-.117	-1.15
Predicting Lifetime Unemployment				
Insomnia Severity Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.226	.384	.073	.588
Medication Status	26.8	12.6	.278	2.13*
Step 2				
Altman Self Rating Mania Scale	-2.24	2.79	-.108	-.802
Beck Depression Inventory	.098	1.34	.011	.073
Step 3				
Insomnia Severity Index	.278	.740	.053	.376
Pittsburgh Sleep Quality Index	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.203	.378	.063	.536
Medication Status	17.7	12.71	.184	1.39
Step 2				
Altman Self Rating Mania Scale	-.251	2.81	-.012	-.089
Beck Depression Inventory	-2.02	1.47	-.221	-1.37
Step 3				
Pittsburgh Sleep Quality Index	2.06	1.26	.381	2.42*

** = <.05, ** = <.001, † = <.10*

Table 8 (continued). Sleep Disturbance Predicting Occupational Functioning.

Actigraphy Sleep Disturbance	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.362	.420	.107	.861
Medication Status	27.74	13.14	.279	2.11*
Step 2				
Altman Self Rating Mania Scale	-2.24	2.88	-.106	-.779
Beck Depression Inventory	.262	1.172	.028	.223
Step 3				
Actigraphy Sleep Disturbance	.027	.181	.018	.147

** = <.05, ** = <.001, † = <.10*

Table 9. Cognitive Functioning Predicting Occupational Functioning.

Predicting Number of Lifetime Firings				
Stroop Color/Word Interference	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.012	.009	.134	1.33
Medication Status	1.22	.285	.459	4.28**
Step 2				
Altman Self Rating Mania Scale	-.083	.061	-.146	.179
Beck Depression Inventory	-.021	.026	-.082	.422
Step 3				
Stroop Color/Word Interference	.014	.005	.301	2.92*
California Verbal Learning Test	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.012	.009	.143	1.31
Medication Status	1.42	.291	.534	4.89**
Step 2				
Altman Self Rating Mania Scale	-.097	.065	-.170	-1.49
Beck Depression Inventory	-.034	.026	-.135	-1.29
Step 3				
California Verbal Learning Test	-.031	.018	-.185	-1.69†
Ruff 2 & 7 Selective Attention	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.018	.009	.203	.197†
Medication Status	1.32	.300	.496	4.39**
Step 2				
Altman Self Rating Mania Scale	-.087	.067	-.150	-1.30
Beck Depression Inventory	-.037	.027	-.144	-1.35
Step 3				
Ruff 2 & 7 Selective Attention	.013	.008	.177	1.69
Tower Test	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.013	.009	.157	1.51
Medication Status	1.46	.318	.535	4.60**
Step 2				
Altman Self Rating Mania Scale	-.121	.067	-.210	-1.81†
Beck Depression Inventory	-.017	.027	-.068	-.647
Step 3				
Tower Test	-.004	.003	-.149	-1.369
Digit Span	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.018	.009	.211	2.05*
Medication Status	1.35	.296	.508	4.57**
Step 2				
Altman Self Rating Mania Scale	-.086	.065	-1.51	-1.32
Beck Depression Inventory	-.033	.027	-.129	-1.22
Step 3				
Digit Span	-.021	.021	-.104	-1.01

** = <.05, ** = <.001, † = <.10*

Table 9 (Continued). Cognitive Functioning Predicting Occupational Functioning.

Predicting Lifetime Unemployment				
Stroop Color/Word Interference	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.137	.385	.044	.356
Medication Status	23.52	12.67	.244	1.85
Step 2				
Altman Self Rating Mania Scale	-2.51	2.74	-.121	-.915
Beck Depression Inventory	.545	1.13	.060	.479
Step 3				
Stroop Color/Word Interference	.260	.220	.150	1.182
California Verbal Learning Test	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.187	.404	.060	.462
Medication Status	26.97	12.57	.280	2.14*
Step 2				
Altman Self Rating Mania Scale	-2.62	2.81	-.127	-.935
Beck Depression Inventory	.323	1.140	.035	.283
Step 3				
California Verbal Learning Test	-.365	.786	-.060	-.464
Ruff 2 & 7 Selective Attention	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.293	.380	.093	.773
Medication Status	29.60	12.77	.307	2.32*
Step 2				
Altman Self Rating Mania Scale	-2.32	2.83	-.111	-.818
Beck Depression Inventory	.639	1.160	.069	.551
Step 3				
Ruff 2 & 7 Selective Attention	-.505	.327	-.189	-1.55
Tower Test	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.163	.389	.052	.419
Medication Status	30.66	13.85	.309	2.21*
Step 2				
Altman Self Rating Mania Scale	-3.57	2.91	-.17	-1.23
Beck Depression Inventory	.694	1.17	.075	.593
Step 3				
Tower Test	-.052	.118	-.057	-.437
Digit Span	***B***	**S. E. *B***	**β**	***t***
Step 1				
Age	.258	.374	.083	.690
Medication Status	27.54	12.58	.286	2.19*
Step 2				
Altman Self Rating Mania Scale	-2.11	2.78	-.102	-.760
Beck Depression Inventory	.410	1.13	.045	.361
Step 3				
Digit Span	.631	.876	.088	.721

** = <.05, ** = <.001, † = <.10*

Hypothesis 5: The mediational effect of sleep on cognitive and occupational functioning.

Hypothesis 5 was that sleep disruption would mediate the relationship between cognitive performance and occupational functioning. In this sample, poorer performance on the Stroop Color/Word Interference was associated with a greater number of lifetime firings. However, analyses revealed no significant mediational effect when sleep disturbance (either via ISI, PSQI or actigraphy) were added to the model as potential mediators. Table 10 presents full results for all tests of mediation.

Table 10. Sleep as a Mediator of the Relationship Between Stroop Color/Word Interference and Number of Lifetime Firings

Insomnia Severity Index	*B*	S. E. *B*	β	*t*
Step 1				
Age	.009	.009	.109	1.079
Medication Status	1.25	.283	.472	4.43**
Altman Self Rating Mania Scale	-.070	.062	-.122	-1.13
Beck Depression Inventory	-.044	.030	-.176	-1.48
Stroop Color/Word Interference	.014	.005	.301	2.917*
Step 2				
Stroop Color/Word Interference	.013	.005	.277	2.68*
Insomnia Severity Index	.024	.017	.166	1.47
Pittsburgh Sleep Quality Index	*B*	S. E. *B*	β	*t*
Step 1				
Age	.013	.009	.150	.148
Medication Status	1.122	.298	.421	3.76**
Altman Self Rating Mania Scale	-.063	.065	-.111	-.971
Beck Depression Inventory	-.043	.034	-.170	-1.24
Stroop Color/Word Interference	.014	.005	.289	2.77*
Step 2				
Stroop Color/Word Interference	.014	.005	.289	2.77*
Pittsburgh Sleep Quality Index	.027	.029	.123	.929
Actigraphy Sleep Disturbance	*B*	S. E. *B*	β	*t*
Step 1				
Age	.018	.010	.198	1.89†
Medication Status	1.32	.291	.488	4.54**
Altman Self Rating Mania Scale	-.087	.062	-.151	-1.39
Beck Depression Inventory	-.027	.026	-.108	-1.05
Stroop Color/Word Interference	.012	.005	.252	2.36*
Step 2				
Stroop Color/Word Interference	.012	.005	.244	2.82*
Actigraphy Sleep Disturbance	-.004	.004	-.101	-1.02

** = <.05, ** = <.001, † = <.10*

CHAPTER 5

DISCUSSION

Summary and Conclusions

The present study aimed to examine the relationship between sleep disruption and deficits in cognitive and occupational functioning in BD. We expected BD participants to demonstrate greater sleep disturbance via both subjective and objective measurement compared to controls, and equivalent sleep disturbance relative to individuals with insomnia. We hypothesized that individuals with BD also would demonstrate greater cognitive and occupational impairment compared to controls, but not significantly different from insomnia participants. We expected sleep disturbance to be significantly associated with poor cognitive performance; cognitive impairment to be significantly associated with occupational impairment, and for sleep disturbance to mediate the relationship between cognitive and occupational functioning.

Findings from the present study were mixed with respect to their support for study hypotheses. Bipolar participants demonstrated more disrupted sleep than controls only on self-reported symptoms. Actigraphic assessment of sleep did not yield any significant differences between bipolar and control participants on key markers of sleep disturbance. Bipolar participants demonstrated better sleep than insomnia participants on all measures except for self-reported symptoms of daytime dysfunction, in which bipolar participants did not differ significantly from insomnia participants. Insomnia participants reported significantly greater severity of insomnia symptoms than bipolar participants; however, bipolar participants' mean levels of insomnia severity were above cutoff scores for identifying insomnia in community samples.

Results of analyses of cognitive and occupational functioning data were also mixed. Bipolar participants demonstrated significantly worse cognitive performance than control participants on measures of working memory (Digit Span Forward) and marginally worse verbal learning (CVLT recognition discrimination), but were not significantly different from controls on any other cognitive measure. Bipolar participants demonstrated a trend toward higher square root of intrusions on the CVLT task relative to insomnia participants, but not control participants. In line with hypotheses, bipolar participants reported being fired from their jobs more frequently compared to insomnia and control participants; however, significant group differences were not observed in any other measure of occupational functioning.

Regression analyses examining associations between sleep, cognitive, and occupational variables also yielded mixed findings. Sleep disturbance as measured by the Pittsburgh Sleep Quality Index was significantly associated with a longer history of lifetime unemployment, but no other combination of sleep disturbance and occupational functioning was significant. Cognitive impairment was significantly associated with occupational impairment only in the domain of executive functioning as measured by the Stroop Color/Word Interference task. Impairment on this task was associated with a greater number of lifetime firings; however, sleep disturbance failed to mediate this significant relationship.

Analyses of sleep data supported previous findings of disturbed sleep throughout the euthymic phase of BD. The present findings were consistent particularly with results from Harvey et al. (2005), which utilized the same participant groupings (insomnia, euthymic bipolar, healthy sleepers) and nearly the same subjective and objective measures. Both reports found significant differences between bipolar participants and controls on PSQI variables of onset latency, daytime dysfunction, and sleep quality, and both reports found nonsignificant

differences in the variable of PSQI sleep disturbance. Some differences were noted in that the current study found insomnia participants reported worse functioning in sleep latency than bipolar participants and controls, whereas the Harvey et al. report observed no significant differences between bipolar and insomnia participants on this variable. Also identical to this study, the Harvey et al. report failed to observe significant differences in actigraphy assessments of sleep onset latency and awakenings after sleep onset. However, Harvey and colleagues noted significantly longer sleep duration among bipolar participants compared to insomnia and control participants, whereas the current report found no significant differences among groups. Despite these differences, however, findings from the current study continue to suggest that sleep disturbance remains a significant problem among individuals with bipolar disorder even during periods of euthymic mood.

Some discrepancy was observed in this study between subjective and objective reports of sleep disturbance both among insomnia and bipolar participants. This discrepancy is not novel, and, in fact, also is consistent with published reports of sleep patterns of individuals with insomnia and with BD. Studies have shown that individuals with insomnia tend to overestimate the length of time it takes to fall asleep, as well as underestimate the overall duration of their nights' sleep (Carskadon et al., 1976). Although differences between prospective self-report and prospective actigraphy estimates of these sleep parameters were not analyzed in this study, differences emerged in retrospective self-report and prospective actigraphy that are consistent with these established findings. Both insomnia and bipolar participants reported various aspects of sleep disturbance on the PSQI that were not captured via objective measurement, thus suggesting a similar sleep related cognitive component may be operating in both insomnia and bipolar disorder. However, dysfunctional attitudes and beliefs about sleep were not assessed in

this study as they were in the Harvey et al. report, so this hypothesis could not be formally tested with this sample.

Importantly, the current study utilized a bipolar sample that was comprised of an uneven distribution of bipolar disorder type: 66.6% (n=16) were diagnosed with bipolar II disorder, whereas 33.3% (n=8) were diagnosed with bipolar I. Of the examinations of sleep parameters in euthymic bipolar samples in the extant literature, the majority have been conducted on homogenous samples of individuals with bipolar I. Only two studies (Sylvia et al., 2011, and Brill et al., 2011) conducted analyses on mixed samples of bipolar I and II disorder. The fact that this study adds to a relatively small number of studies examining sleep disruption among samples including participants with bipolar II disorder supports the generalizability of sleep disturbance across the spectrum of BD in the euthymic phase.

Results of assessments of cognitive functioning also yielded mixed findings. Relative to healthy controls, bipolar participants exhibited a statistical trend for worse performance on two indices of verbal learning and performed significantly worse on one assessment of working memory. These findings are consistent with established reports of cognitive deficits among individuals with bipolar disorder. Indeed, results are similar to Cavanagh et al.'s (2002) report of significant impairment in verbal learning, as well as with multiple meta-analyses documenting verbal learning deficits among individuals with bipolar disorder (Robinson et al., 2006; Arts et al., 2008). Our finding that bipolar participants performed worse on the digit span relative to controls is consistent with Yates et al. (2010), who found euthymic bipolar participants exhibited worse performance on both digit span forward and backward relative to healthy controls.

Inconsistent with the extant literature on cognitive functioning in euthymic bipolar patients is the fact that several expected findings were not obtained in this sample. Despite large

effect sizes across multiple meta-analyses, each executive functioning measure in this sample failed to yield significant results relative to either insomnia or control participants. Additionally, measures of attention and working memory (e.g., the Ruff 2 & 7 and the digit span backward), which could be conceptualized as tests of executive functioning due to their respective emphasis on set-shifting and mental manipulation, also produced null findings when compared across groups. One possible explanation for these null findings may be heterogeneity of the bipolar group noted above. Cognitive functioning in individuals with bipolar II is relatively understudied compared to cognitive functioning in bipolar I. Torrent et al. (2006) reported that bipolar II participants exhibited impairment in the same cognitive domains, but with reduced severity relative to participants with bipolar I. Solé et al. (2012) reported cognitive deficits in bipolar participants relative to controls in the domains of sustained attention, verbal learning and memory, and executive functioning. However, the authors utilized different tests of executive functioning than the current study (e.g., Wisconsin Card Sort Task, Trail making Task). They too utilized the Stroop Color/Word Interference task, but similar to the present study, the authors also reported no significant differences between controls and bipolar participants on that measure. It is possible, then, that the heterogeneity of the bipolar sample, with potentially varying levels of severity of cognitive deficit and/or different types of cognitive deficits, may have yielded null findings in this sample.

Also unexpected was the significant difference in bipolar participants' performance on the digit span forward, but not the digit span backward. One would expect that the additional mental manipulation required to reverse digits would be especially taxing on an already challenged executive functioning system, thus leading to significantly poorer performance on the backward measure. Again, it is possible that the high proportion of bipolar II participants may

have contributed to null findings in this domain. Additionally, Torrent et al.'s (2006) study indicated that the strength of the effects for executive functioning in bipolar II participants was less than for the domains of verbal learning and working memory when compared to bipolar I participants (Torrent et al., 2006). It is possible that in addition to the high percentage of bipolar II participants, the overall size of the bipolar sample may have been too small to detect smaller executive functioning effects. The Torrent et al. and Solé et al. reports included samples of 33 and 43 bipolar II participants respectively, which is an increase of 9 to 19 participants, respectively, over the present study's bipolar sample size. Thus, the current study may have been adequately powered to detect the large executive functioning effect sizes noted in bipolar I samples but not large enough to detect smaller effects observed in bipolar II samples.

The goal of making direct comparisons of cognitive functioning between insomnia and bipolar participants was to examine the degree to which both groups may share similar cognitive deficits. Contrary to hypotheses, there was no comparison of cognitive functioning in which bipolar and insomnia participants did not differ significantly while also performing worse than control participants. Technically, this hypothesis was supported in analyses of recognition discrimination; however, there was a statistical trend for bipolar participants to perform worse on this measure, yielding lackluster support for the hypothesis.

Contrary to hypotheses, sleep disturbance was not associated with cognitive functioning in this sample. However, it is important to note that, although analyses in the present study were conducted while participants were euthymic, the euthymic phase is not necessarily a window into a phenotype of bipolar disorder. In other words, an absence of a significant relationship between sleep disturbance and cognitive functioning during the euthymic phase does not rule out the possibility that these systems are related. It is possible that there is a threshold of sleep

disturbance that must be met in order for cognitive functioning to be affected. Thus, examinations of this study's central hypotheses across phases of bipolar disorder may reveal different relationships.

The lack of significant associations between sleep and cognitive functioning in this sample also suggests that perhaps a key component of the central hypothesis may be missing, namely the role of emotion processing and regulation. Evidence suggests that poor emotional regulation may hinder executive problem solving (Zelazo & Cunningham, 2007), and may temporarily interfere with executive control (Schmeichel, 2007). Moreover, the orbital prefrontal cortex has been shown to play key roles in emotion regulation (Cardinal et al., 2002) as well as impulse control and maintenance of set (Lezak, Howieson, & Loring, 2004). From behavioral observations, lack of sleep has been shown to increase negative mood, affective volatility, and irritability (Murray & Harvey, 2010). In the other direction, emotional stimuli (both negative and positive) have been associated with increased sleep disturbance among individuals with bipolar disorder (Dahl et al., 2002). Additionally, key brain structures involved in sleep regulation are also key components of emotion regulation circuitry (e.g., amygdala, limbic system). Thus, by examining associations between sleep and cognitive functioning in the absence of emotional dysregulation (i.e., during periods of euthymia), we may be missing a key mediating or moderating component. Further research would be necessary to test these highly complex relationships.

Results of tests of occupational functioning were mixed regarding study hypotheses. Although bipolar participants experienced a greater number of firings in their lifetimes, they did not demonstrate differential levels of occupational functioning on any other measure. Results were limited in that only self-reported data were collected. Collection of important objective data

(e.g., social security disability status, reports from employers/professors, grade point averages) was either not feasible or was difficult to incorporate into analyses. For example, several participants consented to releasing their college transcripts, thus providing objective information about scholastic performance. However, not all participants were enrolled in college, thus making it difficult to compare objective scholastic data with either subjective or objective reports of work performance.

Only one cognitive variable, Stroop Color/Word Interference, was associated with occupational functioning. However, as demonstrated in Tables 8, 9 and 10, medication status was significant in nearly every model. Importantly, only individuals with bipolar disorder were taking medications, and only half of the bipolar sample was presently medicated. Thus, it may be important to consider the role of medication in both cognitive and occupational functioning. It is possible that cognitive deficits may be temporally associated with episodes of depression or mania and may not exist endogenously to a debilitating degree, but that side effects from medications may impact cognitive and occupational functioning. Recruiting an unmedicated sample, especially a sample of purely bipolar I participants is difficult at best, and withholding medications simply for the purpose of testing cognitive effects is potentially quite harmful to the patient. Medication effects continue to be problematic for assessments of cognitive functioning (as well as sleep), and the present study is no exception. Future studies may benefit from specific focus on cognitive effects of medications, perhaps by examining differential cognitive performance before and after clinically indicated medication changes (in the event that the medications in question have different side effect profiles).

Clinical Implications

Findings from the present study have important clinical implications for the treatment of bipolar spectrum disorders. Consistent with previous reports, the current study confirms that sleep disturbance continues to be a significant problem for individuals with bipolar disorder through periods of euthymic mood. However, sleep disturbance, as well as daytime dysfunction associated with this disturbance, was only observed on self-report, with actigraph data failing to demonstrate objective evidence of sleep disruption. These differential findings suggest that individuals with bipolar disorder may benefit from psychotherapies that address the cognitive maintenance factors of insomnia (e.g., negative beliefs about sleep, anxiety about sleeplessness). Cognitive Behavioral Therapy for Insomnia (CBT-I) has been shown to improve insomnia symptoms, although with an emphasis on behavioral changes (e.g., adherence to sleep hygiene rules, strengthening positive associations to the sleeping area, reducing time in bed attempting to sleep). The sleep restriction component of CBT-I, which aims to eliminate prolonged mid-night awakenings, is contraindicated for individuals with bipolar disorder due to evidence that reduced sleep can bring about episodes of mania. Augmenting the stimulus control portion of CBT-I with special emphasis on cognitive restructuring of negative beliefs about sleep may be particularly beneficial to individuals with bipolar disorder.

Additionally, psychotherapies that also incorporate an emphasis on psychoeducation about sleep medications may be especially important. In addition to mood stabilizers, individuals with bipolar disorder are frequently prescribed medications either formulated specifically for sleep or that have sedating side effects. The time in which these medications are taken is often crucially important to their effectiveness, as is their regular use. Interpersonal and Social Rhythm Therapy (IPSRT; Frank et al., 2008) contains a psychoeducation component

about bipolar disorder that provides special emphasis on medication adherence. For these reasons, as well as others, this intervention may be helpful even for individuals not in an active episode of depression or hypomania. Indeed, the euthymic phase of the disorder may be a prime time for engaging patients in interventions aimed at increasing the length of well intervals.

Some cognitive impairments were noted in the present study (e.g., difficulties with set shifting as demonstrated by poorer performance on the Stroop task). Executive functioning has been shown to be impaired via multiple examinations of cognitive functioning in bipolar disorder, thus suggesting that cognitive remediation may be beneficial for affected individuals. Numerous remediation protocols exist for addressing various elements of executive functioning (e.g., problem solving skills, attention training, emotional regulation), and may be helpful as an adjunct to traditional psychotherapy and medication management.

Strengths and Limitations

The present study had several important strengths. First, the study had several methodological strengths. Data were collected using a multi-method approach. Self-report as well as objective measurements of sleep were collected, allowing for a fine tuned examination of real vs. perceived sleep disruption among participants. Moreover, data were collected both prospectively and retrospectively, allowing for a more comprehensive snapshot of sleep disturbance. Administrators of cognitive testing were blind to participants' group assignments, which reduced the likelihood that testing results would be influenced by their potential expectations of participant performance. With regard to participant selection, great care was taken to define euthymic status (e.g., via cutoff scores on mood symptom measures as well as through diagnostic interviewing to ensure participants were not exhibiting evidence of even

minor affective episodes) as well as to exclude participants who were not bipolar but whose sleep disturbance symptoms appeared to be rooted in psychological phenomena.

An additional strength of the present study is its novel approach. To date, this study is the only one to examine possible causal pathways to both cognitive and occupational dysfunction that are not rooted in either affective symptomatology or genetics. Although initial results provided limited support for study hypotheses, the integration of sleep disturbance with other affected systems in BD is in its infancy, and this study may pave the way for more focused and advanced examinations of how these important variables may interconnect.

Despite these strengths, the present study suffered from a number of limitations. From a methodological standpoint, the fact that the bipolar sample contained a mixture of bipolar I and bipolar II participants may have impacted study findings. Although similar cognitive profiles have been observed among bipolar I and II samples in a number of studies, others have demonstrated differential cognitive profiles, as well as differences in intensity of cognitive deficits. Thus, the heterogeneity of the bipolar sample may have made it more difficult to detect the hypothesized effects. Future studies that examine the proposed relationships among bipolar I *or* bipolar II participants would clarify the effects of this sample's heterogeneity.

Another limitation of the study was that many analyses suffered from a lack of statistical power. This lack of power has a few different causes. First, recruitment of the insomnia and bipolar groups proved to be markedly difficult, given that the study did not take place in a major medical center with greater access to participants who would more readily fit into one of these two groups. The use of the euthymic phase of BD as well as the requirement that insomnia participants not be experiencing an episode of major depression further impacted recruitment. Thus, the final study sample (n = 72) is smaller than the original proposed sample of 84, which

would have better allowed for impacts of attrition and missing data. Moreover, the heterogeneity of the bipolar sample, noted earlier, may also have impacted the anticipated strength of effects for cognitive variables. The study was adequately powered to detect the presence of large effect sizes (as are often observed in bipolar I), but may have been insufficient to detect the smaller effect sizes observed among bipolar II participants.

Issues with collection of occupational functioning data as well as sample recruitment may have led to the abundance of null findings in analyses of occupational functioning. First, the study sample may have been too high functioning, and thus strong effects may not have been detected. Approximately 50% of the study sample was recruited from Temple University, and while recruitment did not differ significantly across groups, the fact that half of the sample were functioning well enough to maintain good standing in college may not have been representative. Given the fact that participants were being tasked with the responsibility of caring for expensive equipment (e.g., actigraphs), care was taken to ensure participants were able to demonstrate some level of responsibility and could be more easily located in the event equipment was lost (e.g., had stable housing, internet access, own phone, no current drug/alcohol problems). However, a good proportion of individuals with bipolar disorder may not fall into the above categories, and thus the present analyses may not capture the level of occupational functioning that is more representative of the population. From a data collection standpoint, analyses were limited by the fact that all data was obtained via self-report. Objective measurements were difficult to obtain for several reasons. As noted earlier, there was a mixture of individuals who were currently enrolled in college as well as those who were either unemployed or active in the workforce. Given this heterogeneity, it was difficult to devise a single metric on which to compare functioning. In other words, creating a well-validated method to compare functioning

in a job to academic functioning was inherently difficult, and no method has been utilized and published to date. Objective data on academic functioning (e.g., unofficial transcripts) were collected for a subset of participants who consented, but obtaining similar objective information from individuals who were working or who had completed school long ago posed problems in terms of maintaining confidentiality as well as combining data.

Finally, results may have been limited by the large number of analyses required. Grouping of variables as well as a-priori variable selection was conducted to limit the number of statistical tests performed. It is possible that significant effects may have been obtained via different combinations of variables, however these effects would likely have been washed out after post-hoc corrections. Thus, future studies of the role of sleep and cognitive functioning in BD may require more streamlined data collection to reduce the number of tests while maximizing likelihood of detecting significant findings.

Directions for Further Research

Although the theoretical underpinnings of the present study -- namely that sleep disruption plays a mediating role in the maintenance of cognitive and, by extension, occupational functioning deficits in bipolar disorder – were not confirmed, results nevertheless revealed several avenues for further research. First, given that results of the present study may have been complicated by a heterogeneous bipolar sample, examining the proposed relationships between sleep and cognitive functioning among a sample of solely bipolar I participants would be beneficial. It is possible that any association between sleep disruption and cognitive functioning may differ across the spectrum of bipolar disorder. As noted previously, the literature on cognitive functioning in bipolar disorder demonstrated cognitive deficits among individuals with both bipolar I and II disorder, but noted differences in severity of impairment (with more severe

impairments noted among individuals with bipolar I). Direct comparisons of the sleep/cognitive functioning association between bipolar I and bipolar II samples may lead to better understanding of the mechanisms behind differential cognitive performance across the spectrum of bipolar disorder.

Whereas research on sleep architecture in bipolar disorder has uncovered areas of disruption (e.g., reduced stage I sleep (Thase et al., 1989), increased fragmentation of REM (Duncan, Pettigrew, & Gillin, 1979)), little is known about how or whether these disruptions contribute to functional impairment or how they may relate to the genesis or maintenance of affective episodes. Examining relationships between sleep architecture and cognitive functioning may help fill some of these gaps in understanding. Moreover, examining these relationships with groups of individuals in various phases of bipolar disorder may help determine whether episode specific disruptions may have different effects on cognitive and occupational functioning.

Further research on the underlying mechanisms of functional impairment in bipolar disorder is clearly needed. Although deficits in cognitive functioning, over and above clinical variables, have been associated with poor functional outcomes, little is known about how these deficits directly translate into difficulties obtaining and maintaining stable employment. Executive functioning has been the only cognitive variable to consistently predict occupational deficits, but executive functioning is universally understood to be a fairly large category of cognitive functions that can include working memory, attention, response inhibition, and set shifting, among others. More research should be conducted to understand the specific domains of cognitive functioning that are affected in bipolar disorder. Moreover, more longitudinal analyses are needed to gain a more focused understanding of how episodic changes affect overall

functioning. Cross sectional designs fail to uncover temporal relationships that may be crucial to understanding the progression of functional impairment among individuals with bipolar disorder.

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