The role of circadian timing and sleep disturbance in obsessive-compulsive disorder: A multimethod approach.

By

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To the women who paved the way

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Chapter I

Introduction

The high degree of sleep loss in the US has been called a public health crisis (Barnes & Drake, 2015). Although the Centers for Disease Control (CDC) recommend 7-8 hours of sleep per night for adults, almost 30% of US adults report getting 6 or less hours of sleep per night on average (CDC, 2009). The high rate of adults who get less than the recommended amount of sleep is particularly alarming given the well-documented effects of sleep loss across multiple systems, including negative effects for physiological, cognitive, and emotional functioning. For example, sleep loss impairs immune system function (Dinges et al., 1995) and alters cortisol secretion (Omisade et al., 2010). Similarly, sleep loss impairs higher-order cognitive function, such as attention and decision-making (Horne & Harrison, 2000) and leads to deficits in inhibition (Drummond et al., 2006). Finally, sleep disturbance is linked to impaired emotional function, including increased negative affect (Dinges et al., 1997), problems with emotion regulation (Mauss et al., 2013), and increased stress reactivity (Minkel et al., 2014). Sleep disturbance is also highly comorbid with most psychiatric disorders (Baglioni et al., 2016; Benca et al., 1992) and is linked to risk for suicidal ideation and suicide attempts (Pigeon et al., 2012). High rates of comorbidity between sleep problems and psychopathology, as well as overlap between neurobiological systems that support sleep and affective function, have led to the proposal of sleep as a transdiagnostic factor that may mechanistically contribute to psychopathology (Harvey et al., 2011) and suggest that understanding the basic mechanisms of sleep may yield insight into mental health outcomes.

How is Sleep Defined?

Sleep is defined as a reversible state of decreased engagement with and responsivity to the environment with behavioral correlates such as closed eyes, recumbence, and diminished observable activity (Carskadon & Dement, 2011). Physiologically, sleep can be classified into two categories: non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. NREM sleep can be further classified into four stages[1] (stage 1, stage 2, stage 3, stage 4) reflecting progression into deeper sleep (Siegel, 2004). NREM sleep is characterized by synchronous electroencephalogram (EEG) activity that is marked by distinct features including sleep spindles, K-complexes, and high amplitude, low frequency "slow waves" (Carskadon & Dement, 2011). As sleepers move from stage 1 to stage 4, faster frequency, lower amplitude waveforms such as alpha and beta waves decrease and higher amplitude, lower frequency theta and delta waves increase (Moorcroft, 2003). Slow wave sleep (SWS) or delta sleep refers to stages 3 and 4, during which highest amplitude delta waves occur (Siegel, 2004). NREM sleep is typically associated with the potential for muscle movement and limited mentation or dreams (Carskadon & Dement, 2011). In contrast, REM sleep is characterized by low amplitude, fast frequency EEG activity similar to that observed during wakefulness and is therefore commonly referred to as paradoxical sleep (Siegel, 2004). REM sleep is also distinguished by rapid eye movements, muscle atonia, dreams, irregular heart rate, and increased blood pressure, respiratory rate, and pupil diameter (Carskadon & Dement, 2011; Siegel, 2004).

Sleep architecture describes the distribution of time spent in each stage of sleep in a given night. Healthy adults cycle through the stages of NREM and REM sleep in a largely stable

[1] Note that the American Academy of Sleep Medicine (AASM) terminology combines stages 3 and 4 (N3; Iber, Ancoli-Israel, & Quan, 2007).

fashion. The first sleep cycle of the night typically progresses as follows: 1 to 7 minutes of stage 1, 10 to 25 minutes of stage 2, 20 to 40 minutes of SWS, and 1 to 5 minutes of REM (Carskadon & Dement, 2011). This cycle is then repeated over the course of the night with decreasing time spent in SWS and increasing time spent in REM sleep with each subsequent cycle (Brown, Basheer, McKenna, Strecker, & McCarley, 2012; Carskadon & Dement, 2011) for an average of 4-5 cycles (Moorcroft, 2003). In a given night, approximately 5% of sleep is spent in stage 1, 50% in stage 2, 20% in SWS, and 25% in REM (Moorcroft, 2003). Previous research has found evidence for variability in sleep architecture in the anxiety-related disorders, including decreased REM latency in OCD (Insel et al., 1982), increased stage 1% in OCD and panic disorder (Ferini-Strambi et al., 2002; Insel et al., 1982), and decreased SWS% in posttraumatic stress disorder (PTSD) (Fuller et al., 1994).

Neural Mechanisms of Sleep

Understanding the neurobiology of sleep first requires an understanding of the mechanisms of wakefulness. Wakefulness is achieved through a grouping of excitatory pathways originating in the reticular formation in the brainstem and extending to the cortex known as the ascending reticular activating system (ARAS; Siegel, 2004). The ARAS consists of two branches, the dorsal and ventral pathways, with distinct neurotransmitter activity (Brown et al., 2012). The dorsal pathway originates in the laterodorsal and pedunculopontine tegmental nuclei (LDT/PPT), which innervate the thalamus via acetylcholine (Schwartz & Roth, 2008). The thalamus then projects excitatory signals widely to the cortex (Brown et al., 2012). The ventral pathway includes noradrenergic projections from the locus coeruleus and serotonergic projections from the raphe nuclei (Brown et al., 2012). These regions send excitatory signals directly to the cortex (Jones, 2011), as well as indirectly through the tuberomamillary nucleus

and lateral hypothalamus, which in turn send arousal signals to the cortex through the basal forebrain via histamine, orexin, and acetylcholine, respectively (Brown et al., 2012).

NREM sleep is achieved through inhibition of wake-promoting pathways. The ventral lateral preoptic nucleus of the hypothalamus contains a group of neurons that utilize GABA and galanin to inhibit the ARAS (Brown et al., 2012), and these neurons fire most frequently during NREM sleep (España & Scammell, 2011). Likewise, the median preoptic area contains GABAergic neurons that inhibit the ARAS (Brown et al., 2012), which begin firing just before NREM sleep (España & Scammell, 2011). Importantly, the VLPO is also inhibited by wake-promoting regions (Schwartz & Roth, 2008). This mutually inhibitory link between NREM sleep and wake is known as the "flip-flop" switch (Saper et al., 2001), which describes the rapid transitions between wake and NREM sleep where the activation of one system turns the other "off" and vice versa.

REM sleep is generated by "REM-on" cells in the pons, which are observed to have their highest firing rate during REM sleep (Moorcroft, 2003; Siegel, 2004). Cholinergic neurons in the LDT/PPT are thought to produce the paradoxical wake-like EEG activity and muscle atonia evident in REM, the latter of which is mediated by glycine signaling from the medulla (España & Scammell, 2011). Notably, many LDT/PPT nuclei are also active during wakefulness, though a subpopulation is selectively active during REM (España & Scammell, 2011). Classic formulations proposed that REM sleep was regulated by inhibitory interactions between these cholinergic pathways and monoaminergic systems (McCarley & Hobson, 1975). However, recent findings have also implicated other regions in REM regulation. GABAergic and glutamatergic signaling in the sublaterodorsal nucleus is linked to REM EEG activity and muscle atonia, and this region may participate in a reciprocal inhibitory loop with GABAergic neurons

in the ventral periaqueductal grey and lateral pontine tegmentum to regulate NREM/REM transitions (Saper et al., 2011). Finally, neurons in the lateral hypothalamus which are highly active during REM and quiescent during wake are thought to utilize GABA and melanin-concentrating hormone to inhibit the same wake promoting regions that are activated by orexin (España & Scammell, 2011).

How is Sleep Measured?

Sleep measurement can be broadly grouped into objective and subjective methods. While objective assessment is unbiased and more precise, subjective measures are also critical, as polysomnography (PSG) indices explain limited variance in subjective sleep quality (Kaplan et al., 2017). Thus, both objective and subjective methods are necessary to capture the sleep experience and may similarly be necessary to fully characterize sleep in psychopathology.

Sleep is a complex process represented by multiple indicators. Sleep continuity reflects the consistency of sleep and includes the following parameters: total sleep time (TST), sleep onset latency (SOL), sleep efficiency (SE), number of awakenings (NWAK), and wake after sleep onset (WASO). Sleep architecture is percentage of time spent in a given stage during the sleep period (i.e., stage 1%, rapid eye movement [REM]%, etc.). Additional REM parameters include REM onset latency, or the time from sleep onset to first REM period, and REM density, or the frequency of rapid eye movements (Baglioni et al., 2016).

Objective Sleep Methods

Polysomnography (PSG)

PSG is the most comprehensive objective measure of sleep and consists of electroencephalogram recordings (EEG), electrooculogram recordings (EOG), and electromyogram recordings (EMG) (Bastien, 2011). Though considered gold-standard, PSG is

limited by its relative expense, burden to the participant (Ancoli-Israel et al., 2003), and lack of ecological validity (Buysse et al., 2006).

Actigraphy

Actigraphy measures motion using accelerometers, allowing for estimation of sleep/wake patterns (Ancoli-Israel et al., 2003). Actigraphy correlates highly with PSG (Cellini et al., 2013) but is less consistent with sleep diaries (Lockley et al., 1999). Actigraphy has increased ecological validity, low expense, and minimal invasiveness relative to PSG (Ancoli-Israel et al., 2003) but detects wakefulness less reliably (Paquet et al., 2007).

Subjective Sleep Methods

Sleep diary

Sleep diaries capture the subjective perception of the previous night's sleep, typically over one week (Carney et al., 2012). Sleep diaries commonly include self-reported sleep continuity and sleep quality (Buysse et al., 2006) and are considered the gold-standard for subjective sleep assessment (Carney et al., 2012). Sleep diaries are ecologically valid, low burden, and low cost but are limited by reliance on the participant's ability to accurately estimate their sleep (Buysse et al., 2006).

Sleep Questionnaires

Sleep questionnaires assess global subjective sleep quality and disturbances over a specified time period (Buysse et al., 2006). Sleep questionnaires are the lowest cost and burden option for measuring sleep and are unique in sampling sleep-related impairment. However, like sleep diaries, they are vulnerable to inaccuracy, as well as increased retrospective bias.

Summary

Each mode of assessment samples a different facet of sleep that may be dysregulated in psychopathology. However, extant research in this area has largely utilized a single-method approach, which precludes identifying distinct patterns of sleep disturbance across psychiatric conditions that may provide novel insight into underlying physiology. Thus, a multi-method approach that integrates subjective and objective assessment is necessary to fully characterize sleep in psychopathology, including anxiety-related disorders.

Linking Sleep and Obsessive-Compulsive Disorder (OCD)

Despite considerable evidence for the widespread impact of sleep disturbance, sleep remains an understudied factor in psychopathology (Harvey, 2008). Sleep disturbance has typically been considered an epiphenomenon, and limited research has addressed how sleep disturbance may actually contribute to psychopathology (Harvey, 2008). Considering extant research showing that sleep loss impairs physiological, cognitive, and emotional function, it is critical to move beyond the typical framework of sleep disturbance as a symptom of psychopathology to examine how sleep disturbance may contribute to the development of these disorders and identify specific mechanisms that account for this relationship. This novel approach to the link between sleep disturbance and psychopathology may highlight important new targets for intervention.

A literature review conducted by our lab indicates that sleep disturbance may be important for understanding multiple anxiety-related disorders (Cox & Olatunji, 2016a), including obsessive-compulsive disorder (OCD). OCD is a chronic and debilitating disorder characterized by obsessions, or intrusive distressing thoughts, and compulsions, or repetitive behaviors intended to reduce the distress of the obsessions. Common themes in OCD include contamination, symmetry, harm, and religiosity (American Psychiatric Association, 2013). OCD

is one of the least common anxiety-related disorders, with 12-month and lifetime prevalence rates of 1% and 1.9%, respectively (Kessler, Berglund, et al., 2005; Kessler, Chiu, et al., 2005). OCD can be subtyped into early onset (11 years old) and late onset (23 years old). Early onset OCD represents 76% of cases, is more common in males, and is linked to increased symptom severity (S. Taylor, 2011). Current models of OCD posit a diathesis-stress model in which the interaction of genetic vulnerabilities and environmental stressors results in hyperactivity in cortico-striato-thalamo-cortical circuitry (Chamberlain et al., 2005; Pauls et al., 2014). Results from our lab indicate that in a nationally representative sample, individuals with sleep disturbance report increased OCD symptoms compared to individuals without sleep disturbance (see Figure 1; Cox & Olatunji, 2016b), and extant research links both subjective and objective sleep disturbance with OCD symptoms (Cox & Olatunji, 2016a).

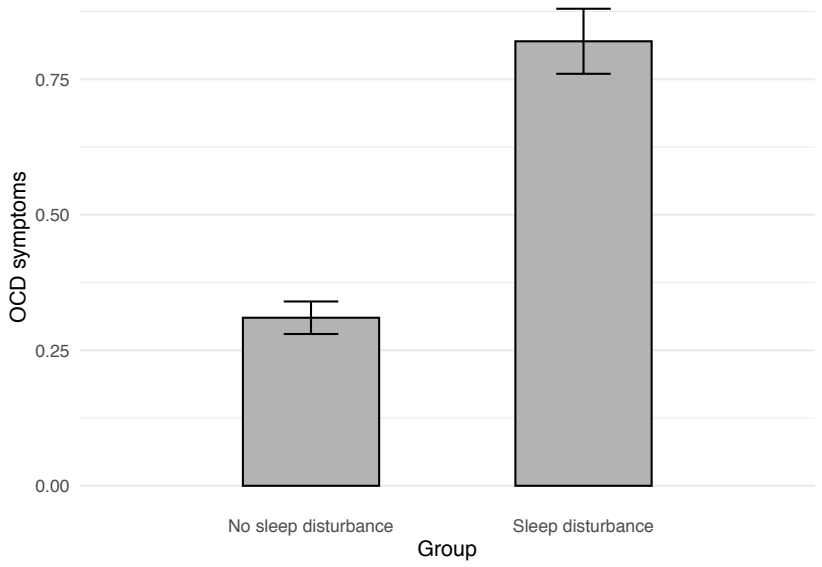

Figure 1. Obsessive-compulsive disorder (OCD) symptoms in those with and without sleep disturbance from Cox & Olatunji, 2016b.

Likewise, objective sleep studies have found evidence for decreased TST (Voderholzer et al., 2007) and variability in REM sleep parameters in OCD (Insel et al., 1982; Rapoport et al.,

1981). In contrast, limited research has examined subjective sleep in OCD, with the one extant study indicating no differences between those with OCD and healthy controls (Bobdey et al., 2002). Interestingly, our meta-analysis of sleep in anxiety-related disorders found a unique pattern of sleep disturbance in OCD. Specifically, OCD was characterized by shorter TST and REM pressure (i.e., decreased REM latency, increased REM%, increased REM density) but not the disturbed sleep continuity evident in other anxiety-related disorders (Cox & Olatunji, 2020). Thus, further delineation of the role of sleep in OCD may yield new insight into unique biopsychological mechanisms. Given the debilitating nature of OCD (Ruscio et al., 2010), it is critical to identify novel targets for intervention that may improve treatment outcome, such as sleep disturbance.

The Role of Circadian Rhythms

Importantly, sleep is partly regulated by circadian rhythms (Borbély et al., 2016). Circadian rhythms are autonomous 24-hours cycles in processes ranging from gene expression to behavior that occur independent of environmental input, and misalignment in these rhythms results in pathology (Roenneberg & Merrow, 2016). Accumulating evidence implicates disruptions in circadian rhythms to psychopathology (e.g., McClung, 2013; Wulff, Gatti, Wettstein, & Foster, 2010). Alterations in diurnal cortisol secretion are evident in multiple disorders, including PTSD (Morris et al., 2012), depression (Vreeburg et al., 2010), and anxiety disorders (Kallen et al., 2008; Vreeburg et al., 2013). Likewise, decreased melatonin is linked to affective disorders more broadly (Carpenter et al., 2017; Naismith et al., 2012). The overlap between circadian rhythms, sleep, and psychopathology is most evident in studies linking delayed sleep timing to psychopathology (Robillard et al., 2015), with a particularly robust effect in OCD (Nota et al., 2015). Further, one recent study found increased OCD prevalence at more

northern latitudes (Coles et al., 2018), suggesting circadian dysregulation due to decreased light exposure may contribute to OCD pathology. The potential role of sleep and circadian rhythms in OCD may have important treatment implications, as recent findings show that inpatient OCD treatment facilities with consistent lights out times yield higher rates of treatment response (Coles & Stewart, 2019). Together these findings call for additional examination of circadian processes within the context of OCD.

One such circadian process that has received recent attention is chronotype. Chronotype represents a spectrum from morningness to eveningness, such that individuals who trend towards eveningness have a later sleep-wake schedule and later peaks in circadian processes such as cortisol, core body temperature, and subjective alertness and vice versa (Bailey & Heitkemper, 2001; Kerkhof & Van Dongen, 1996). Importantly, eveningness may be indicative of desynchrony in circadian rhythms and environmental demands (Duffy et al., 2001). In addition to findings linking chronotype and psychopathology more broadly (Antypa et al., 2016; Lemoine et al., 2013), recent results from our lab utilizing a structural equation modeling approach suggest that eveningness may be uniquely linked to anxiety symptoms (Cox & Olatunji, 2019; see Figure 2).

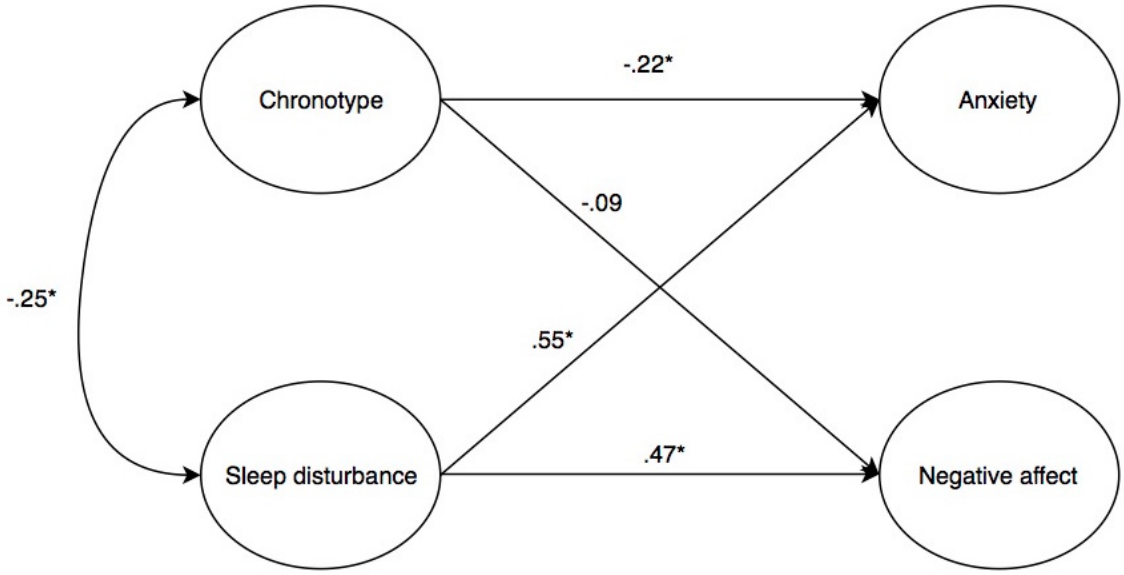

Figure 2. Unique associations between latent chronotype, sleep disturbance, anxiety, and negative affect from Cox & Olatunji, 2019.

This finding is consistent with previous circadian rhythm research delineating the negative effects of "living against the circadian clock" (Roenneberg & Merrow, 2016). Social jetlag, or a misalignment between the internal circadian clock and environmental demands (Wittmann et al., 2006), can be conceptualized as a milder form of shift work and has been linked to poor mental health (see Taylor & Hasler, 2018 for a review). A consistent mismatch between desired sleep/wake timing and daily schedules may result in chronic sleep disturbance (e.g., increased sleep onset latency, decreased total sleep time, insomnia symptoms), which may then confer vulnerability for OCD. Indeed, we recently published evidence for a prospective relationship between eveningness and OCD symptoms that was partially mediated by insomnia symptoms (Cox, Tuck, & Olatunji, 2018; see Figure 3). However, as with sleep disturbance, few studies have examined the role of circadian processes, such as chronotype, as contributing factors to OCD, and other intervening processes remain unknown. The proposed studies will use OCD as a case example to examine specific mechanisms that may link chronotype and sleep

disturbance to psychopathology. The results of these studies will inform future research examining how sleep and circadian processes contribute to various psychopathological processes and their treatment.

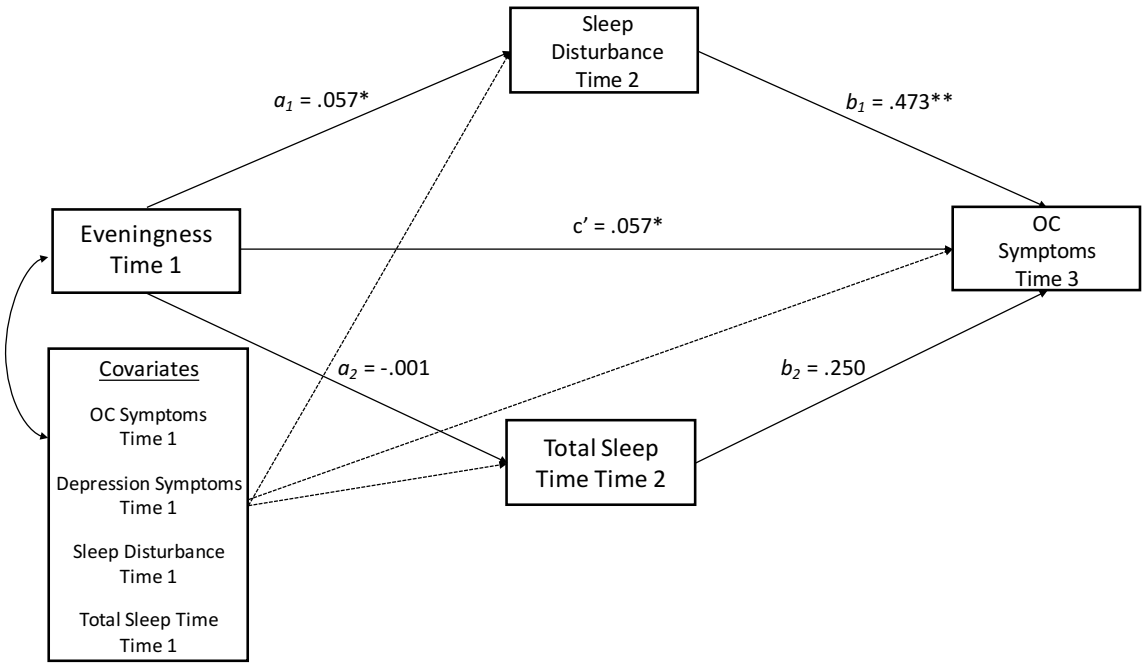

Figure 3. The mediating role of sleep disturbance in the prospective association between eveningness and OCD symptoms from Cox, Tuck, & Olatunji, 2018.

Potential Mechanisms Linking Sleep and Circadian Rhythm Disturbance to OCD

Inhibition

One candidate mechanism that may explain the relationship between sleep disturbance and OCD is inhibition, or the use of cognitive control to withhold a prepotent response (Wiecki & Frank, 2013). Extant research indicates that sleep deprivation impairs inhibition (Drummond et al., 2006), even when controlling for potential time of day effects (Bocca et al., 2014). Likewise, habitual patterns of sleep duration and variability are also associated with cognitive control (Whiting & Murdock, 2016; Wilckens et al., 2014). Findings from neuroimaging

research indicate that sleep loss leads to decreased functional connectivity between prefrontal regions (Verweij et al., 2014), as well as decreased activation of these regions (Ma et al., 2015). Given the links between inhibitory control and prefrontal activity (Verbruggen & Logan, 2008), insufficient sleep may disrupt prefrontal cortex's top-down control capability, which then leads to impaired inhibition.

Preliminary results of a structural equation model of self-report data from our lab indicate that deficits in executive function partially account for the relationship between sleep disturbance and repetitive negative thinking, even with general distress included in the model (see Figure 4; Cox, Ebesutani, & Olatunji, 2016). Thus, problems with executive function, such as inhibitory deficits, due to sleep disturbance may be a unique factor that contributes to the development of psychopathological processes, such as intrusive thought. This interpretation is consistent with recent findings indicating links between habitual sleep duration and cognitive control among individuals with elevated repetitive negative thinking (Nota & Coles, 2018).

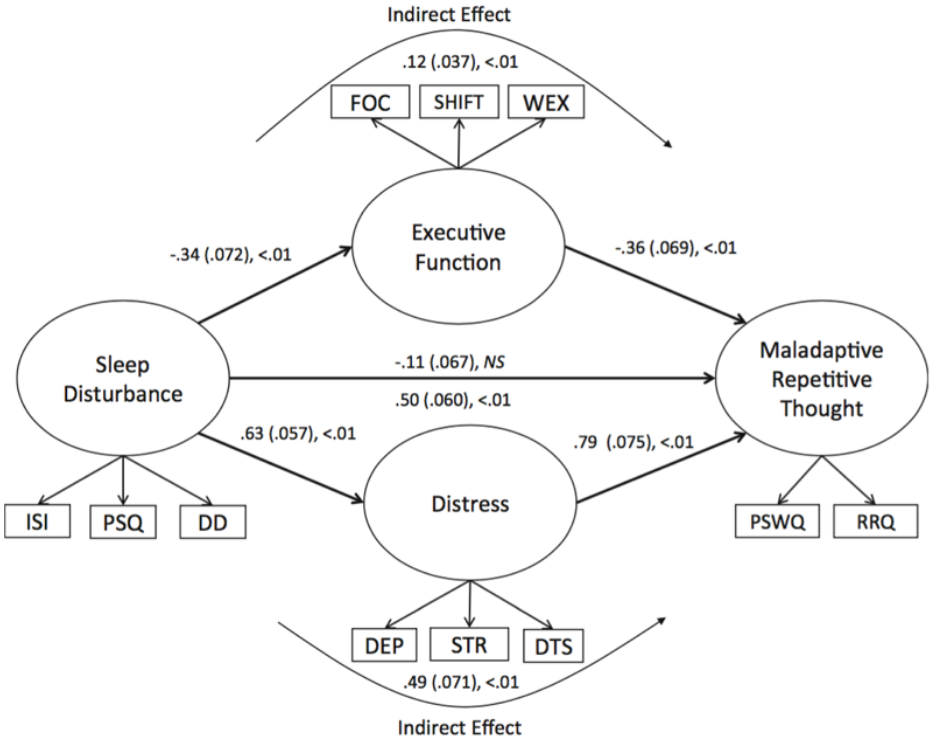

Figure 4. The mediating role of executive function in the association between sleep disturbance and maladaptive repetitive thought from Cox, Ebesutani, & Olatunji, 2016.

Likewise, individuals with OCD exhibit consistent deficits in cognitive functions regulated by prefrontal control (Snyder et al., 2015). Inhibitory deficits linked to frontal cortex abnormalities may underlie the inability to control or regulate obsessions and and/or compulsions (Chamberlain et al., 2005). Indeed, recent evidence indicates that individuals with OCD exhibit inhibitory deficits compared to healthy controls (Kang et al., 2013; McLaughlin et al., 2016), and impaired inhibitory function is associated with decreased activity in frontal regions (Kang et al., 2013). Consistent with the inclusion of cognitive control in the Research Domain Criteria (RDoC) matrix set forth by the National Institutes of Mental Health for studying psychopathology (Insel et al., 2010), it is critical to understand how deficits in cognitive control processes, such as inhibition, may contribute to OCD.

Stress

Another candidate mechanism in the relationship between sleep disturbance and OCD is stress. Although stress is an adaptive response to threat, a stress response that is excessive, blunted, and/or prolonged can contribute to physiological and psychological disorder (McEwen & Karatsoreos, 2015). Stressful life events are linked OCD onset (Rosso et al., 2012), and daily stressors are linked to increased daily OCD symptoms (Macatee et al., 2013). While few studies have examined stress reactivity in OCD, one study found increased subjective and physiological stress reactivity in women with postpartum OCD compared to healthy postpartum women (Lord et al., 2012). Notably, this study also found evidence for increased subjective sleep disturbance in the postpartum OCD sample. However, no study to date has examined how stress reactivity may link sleep disturbance to OCD symptoms. This gap in the literature is notable given previous findings that both acute sleep loss (Minkel, Moreta, et al., 2014) and chronic poor sleep (Massar et al., 2017; Mrug et al., 2016) predict increased stress reactivity. Likewise, poor executive function abilities are associated with increased stress reactivity (Hendrawan et al., 2012), possibly due to diminished top-down control from the prefrontal cortex (Taylor et al., 2008). Taken together, results from the extant literature suggest that sleep disturbance may impair inhibitory control, which may then result in increased stress reactivity.

Towards a Comprehensive Model of Sleep and Circadian Rhythm Disturbance in OCD

Our comprehensive review of the literature (Cox & Olatunji, 2016a) points to inhibition and stress as two candidate mechanisms that may link sleep disturbance to OCD. The proposed model (see Figure 5) integrates disconnected lines of research and hypothesizes that later circadian timing, such as evening chronotype, contributes to OCD through sleep disturbance, and sleep disturbance contributes to OCD through decreased inhibition and increased stress

reactivity. More specifically, acute sleep disturbance may lead to acute OCD symptoms in the short term, and over time, chronic sleep disturbance due to underlying circadian rhythm abnormalities may contribute to the development of OCD.

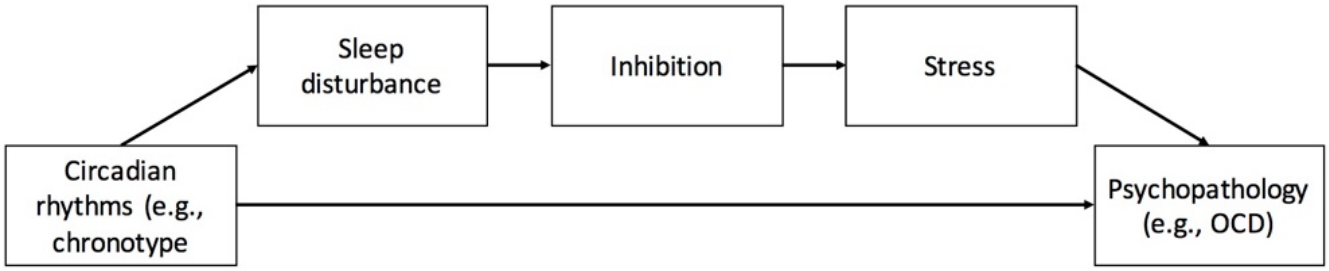

Figure 5. Conceptual model of the pathway from delayed circadian rhythms to psychopathology through the serial effects of sleep disturbance, inhibition, and stress.

The proposed studies will test this model by utilizing multiple levels of analysis to combine subjective and objective measures, as well as laboratory and ambulatory assessment to fully examine the role of later circadian timing and sleep disturbance in OCD. Study 1 will examine the impact of acute sleep restriction on inhibition and OCD symptoms and the moderating role of daily stressors in healthy sleepers. Study 2 will compare individuals with OCD to healthy controls on indicators of circadian timing, sleep, inhibition, and stress reactivity, test a model by which sleep disturbance mediates the relation between later circadian timing and OCD symptoms, and examine the impact of daily sleep duration and timing on OCD symptoms. The results of these studies will provide insight into whether acute sleep loss *causes* OCD symptoms in the short term and how later circadian timing and sleep disturbance are linked to OCD through downstream dysregulated processes, including decreased inhibition and increased stress reactivity. The goal of this research program is to apply this model to other disorders and processes to understand how sleep and circadian processes contribute to psychopathology.

Chapter II

Study 1

As reviewed above, accumulating evidence suggests that sleep disturbance is highly comorbid with anxiety-related disorders, including OCD (see Cox & Olatunji, 2016 for a review) and is associated with increased disability (Ramsawh et al., 2009). In fact, increasing research indicates that sleep disturbance may causally contribute to anxiety-related symptoms and disorders. Indeed, sleep disturbance predicts increased general anxiety symptoms across a range of sampling periods, from 1 day (Cox, Sterba, et al., 2018) to over 6 months (Doane et al., 2014). Longitudinal studies have also found a prospective link between sleep disturbance and increased OCD symptoms (Cox, Tuck, et al., 2018) broadly, as well as increased obsessions, specifically (Cox, Cole, et al., 2018). Interestingly, one cross-sectional study found that only obsessions, but not other facets of OCD, are associated with sleep disturbance (Timpano et al., 2014), suggesting that sleep disturbance may uniquely influence facets of OCD characterized by intrusive cognition. However, the impact of acute sleep loss on these symptoms remains unclear. Although previous research has found that total sleep deprivation increases state anxiety, relatively few studies have examined the impact of partial sleep restriction on anxiety (Pires et al., 2016), and no study to date has examined the effect of sleep restriction on OCD symptoms. This is an important gap in the literature, as partial sleep restriction is more similar to the insufficient sleep individuals are likely to experience in daily life, and findings from total sleep deprivation paradigms may not extend to day-to-day sleep disruptions. Further, testing the effect of acute

sleep loss on OCD symptoms is an important first step in testing a causal link between sleep disturbance and OCD.

Sleep restriction designs may be more ecologically valid for examining the effects of partial sleep loss on OCD symptoms. Extant sleep restriction studies have used one of two paradigms: shorter sleep duration with a shorter sampling period (e.g., 4 hours sleep opportunity for one night; Sadeh, Dan, & Bar-Haim, 2011; Wu et al., 2008) or longer sleep duration with a longer sampling period (e.g., 5-6.5 hours sleep opportunity for 5-7 nights; (Baum et al., 2014; Cousins et al., 2018). The few studies examining sleep restriction indicate a subsequent increase in state anxiety in adults (Irwin et al., 2012; Wu et al., 2008) and adolescents (Reddy et al., 2017) using both paradigms. These findings highlight the deleterious effects of sleep restriction on the transitory emotional state consisting of feelings of apprehension, nervousness, and physiological sequelae such as an increased heart rate or respiration. However, the impact of sleep restriction on obsessions specifically and other OCD symptoms more broadly (i.e., checking, ordering, contamination) remains unclear. Such symptoms offer more specific insight into the role of sleep loss in OCD relative to state anxiety, which can be acutely elevated in the absence of anxiety pathology (Botella & Parra, 2003) and does not reliably distinguish between individuals with high and low OCD symptoms (Abramovitch et al., 2015).

What is also unclear in the existing literature is the mechanism by which sleep loss exerts its potential effects on OCD symptoms. As reviewed previously, one possible mechanism is inhibition. In addition to total sleep deprivation, deficits in inhibition are also found in studies implementing sleep restriction paradigms (Demos et al., 2016; Lo et al., 2016), suggesting that even partial sleep curtailment negatively impacts cognitive control abilities. Given evidence for inhibitory deficits in OCD (Kang et al., 2013; McLaughlin et al., 2016; Penadés et al., 2007),

effective inhibition may limit intrusive anxious cognition and behaviors, such as obsessions and compulsions; however, when inhibition is impaired by sleep loss, such symptoms may occur in excess.

Stress may also contribute to the effects of sleep loss on OCD symptoms. As discussed previously, stressful life events are associated with OCD onset (Rosso et al., 2012) and daily stressors are associated with increased daily OCD symptoms (Macatee et al., 2013). Previous research also indicates that sleep deprivation impacts affective response to stress, such that mild stressors are perceived as more distressing when sleep deprived (Minkel, Banks, et al., 2014). These findings link both sleep loss and stressors to adverse emotional outcomes, such as OCD symptoms, and suggest that experiencing a stressor following sleep restriction may amplify the negative emotional effects of sleep loss.

Taken together, extant findings suggest that inhibition may be one mechanism by which poor sleep results in increased OCD symptoms, and stress may moderate this effect. Study 1 tested this mechanism using a partial sleep restriction design. We hypothesized that inhibition would decrease (Hypothesis 1a) and OCD symptoms would increase (Hypothesis 1b) following sleep restriction, decreased inhibition due to sleep restriction would predict increased OCD symptoms following sleep restriction (Hypothesis 2), and stress would increase the effects of sleep restriction on inhibition and OCD symptoms (Hypothesis 3). We also conducted exploratory analyses to extend Hypothesis 2 to obsessions and non-obsession OCD symptoms and repetitive negative thinking to further probe the predictive value of post-sleep restriction inhibition on specific OCD symptoms. We then conducted additional exploratory analyses to examine the effect of baseline objective and subjective sleep efficiency on the relations between post-sleep restriction inhibition and post-sleep restriction OCD symptoms.

Methods

Participants

The sample consisted of undergraduates and community adults identified as healthy sleepers, indicated by the absence of insomnia symptoms on the Insomnia Severity Index (N = 113). Undergraduate students were recruited from psychology courses and were compensated with course credit. Community adults were recruited from flyers, a university research email notification system, and ResearchMatch, a national health volunteer registry created by several academic institutions and supported by the U.S. National Institutes of Health as part of the Clinical Translational Science Award (CTSA) program, and were compensated with $75. Two participants withdrew prior to the second laboratory session, and one participant was withdrawn by study personnel for noncompliance in the first laboratory session. Participants who were identified as noncompliant with the sleep restriction protocol (i.e., actigraphy data indicated 60 or more minutes of continuous sleep between time of awakening the morning prior to the sleep restriction night and laboratory session 2, excluding the instructed 4:00am to 8:00am sleep period; n = 14), identified as noncompliant with wearing the actigraph (i.e., device detected non-wear time that was not logged in the participant's sleep diary; n = 8), and/or identified as non-responders to the sleep restriction procedure (i.e., sleepiness measured via the Stanford Sleepiness Scale following sleep restriction was less than or equal to sleepiness prior to sleep restriction; n = 18) were excluded from analyses for a final sample of 73 participants.

The mean age of the final sample was 24.23 years (SD = 10.82), ranging from 18 to 64 years (69.9% female). The ethnicity composition was as follows: Caucasian (n = 42; 57.5%), African American (n = 7; 9.6%), Asian (n = 17; 23.3%), Hispanic/Latino (n = 4; 5.5%), Other (n

= 3; 4.1%). Participants who were excluded from analysis did not differ from those included on age, race, gender, or baseline sleep measures.

Measures

Sleep

Actigraphy is an objective sleep measure that estimates sleep and wake from motion (Ancoli-Israel et al., 2003). The present study utilized ActiGraph wGT3X-BT activity monitors (ActiGraph, Pensacola, FL). Previous research indicates that actigraphy is highly accurate when compared to polysomnography (Marino et al., 2013) and that the ActiGraph wGT3X-BT is reliable and valid for estimating sleep (Cellini et al., 2013). Objective sleep efficiency was calculated with the Sadeh algorithm (Sadeh et al., 1994). Sleep periods were entered manually using participant-reported time into bed and time out of bed.

The *Consensus Sleep Diary* (CSD; Carney et al., 2012) is a 9-item sleep diary that asks participants about their last night of sleep. The CSD was developed by a panel of sleep experts to create a standard sleep diary for the assessment of daily sleep. Subjective sleep efficiency was calculated as the ratio of total sleep time to time in bed multiplied by 100.

The *Insomnia Severity Index* (ISI; Bastien, Vallieres, & Morin, 2001) is a 7-item self-report measure of insomnia symptoms over the past two weeks and is used to detect cases of insomnia and assess treatment response. Items on the ISI are rated on a Likert scale from 0 (*none*) to 4 (*very severe*), and higher scores indicate a higher severity of insomnia. A score of 7 or below indicates the absence of insomnia symptoms.

The *Stanford Sleepiness Scale* (SSS; Hoddes, Dement, & Zarcone, 1972) is a self-report scale asking participants to rate their current level of sleepiness on a scale from 1 (*Feeling active*

and vital; alert; wide awake) to 7 (*Almost in reverie; sleep onset soon; lost struggle to remain awake*), and a higher score indicates highest degree of sleepiness.

Inhibitory control

The *Stop Signal task* (Logan, 1994) is a widely used measure of response inhibition that requires participants to respond quickly and accurately to a go signal and inhibit their response when they receive the stop signal. The task is titrated to participant performance, such that participants will successfully inhibit on 50% of stop trials. This is achieved by increasing or decreasing the stop signal delay (SSD) between the go signal onset and the stop signal onset on the subsequent stop trial by 50ms if the participant successfully inhibited or failed to inhibit, respectively, on the previous stop trial. This titration ensures that the task is equally challenging for all participants and creates a mean SSD for each participant. Inhibitory control is indicated by stop signal reaction time (SSRT), or latency to inhibit a response to the stop signal. Thus, *increased* SSRT is indicative of *decreased* inhibition.

Stressors

The *Daily Inventory of Stressful Events* (DISE; Almeida, Wethington, & Kessler, 2002) is a semi-structured interview that assesses 7 categories of stressors in the past 24 hours. A modified self-report version of the DISE was utilized in the present study (Macatee, Capron, Guthrie, Schmidt, & Cougle, 2015). Items are endorsed on a dichotomous Yes/No scale and ask participants if they experienced specific types of stressors during the day ("Did you have an argument or disagreement with anyone today?"). Higher scores indicate more stressors were experienced during the day.

OCD Symptoms

The *daily OCD symptoms scale* (Macatee et al., 2013) is a 15-item scale that includes items from other validated OCD symptom measures modified for daily assessment and includes checking, contamination, ordering, and obsessing symptoms. Items on the daily OCD symptoms scale are rated on a Likert scale from 0 (*not at all*) to 4 (*extremely*), and higher scores indicate a higher severity of daily OCD symptoms. The obsessions subscale ("I got nasty thoughts and had difficulty in getting rid of them") and other OCD symptoms subscales (12 items), including checking ("I checked things quite a bit"), ordering (I felt compelled to arrange my possessions until it felt 'just right'"), and contamination ("I worried about germs"), were examined separately given previous research suggesting a unique link between sleep disturbance and obsessions (Timpano et al., 2014). The combined other OCD symptoms subscales demonstrated good internal consistency (α = .86) in the present sample. In contrast, the daily obsessions subscale demonstrated marginal internal consistency (α = .67).

Repetitive Negative Thinking (RNT)

The *Perseverative Thinking Questionnaire* (PTQ; Ehring et al., 2011) is a 15-item self-report measure of RNT. Items are rated on a Likert scale from 1 (*never*) to 4 (*almost always*), and higher scores indicate higher RNT. Item wording was modified for daily use in the present study (e.g., "The same thoughts kept going through my mind again and again"). The PTQ demonstrated good internal consistency in the present sample (α = .95).

Procedure

Prior to enrollment in the study, participants were screened for sleep health with the ISI. Those scoring an 8 or higher, indicating subthreshold or higher insomnia symptoms (Morin, Belleville, Belanger, & Ivers, 2011), were not enrolled (n = 804 including both individuals who responded to recruitment ads and undergraduate students who were screened in classrooms).

Data collection occurred over 3 consecutive days. On day 1, participants attended a laboratory session that included informed consent and administration of the baseline Stop Signal. Participants then received an actigraph, a CSD, and instructions for the next two days. Participants were instructed to maintain their typical sleep schedule on night one and complete day 1 of the CSD on the morning of study day 2. At 4pm on day 2, participants received an email with a link to a survey containing baseline administration of the OCD, RNT and stress measures and were instructed to complete the survey before 7:00pm. On night 2, participants were instructed to remain awake until 4:00am, sleep from 4:00am to 8:00am, and complete day 2 of the CSD upon awakening on the morning of study day 3. Participants returned to the laboratory for session 2 between 4:00pm and 7:00pm to complete post-sleep restriction administrations of the Stop Signal and OCD, RNT, and stress measures. Participants were instructed to not nap between awakening on study day 2 and laboratory session 2 and maintain their typical caffeine usage. Participants were also instructed to not drink alcohol or drive during or following sleep restriction. To ensure compliance with study instructions when participants were outside of the lab, participants were informed that their sleep timing would be monitored with the actigraph and were asked to call the laboratory every hour beginning at 10:00pm and record their name via voicemail (Babson et al., 2009).

Data analytic strategy

Data analysis was conducted in SPSS 25. Within subjects t-tests were conducted to assess change in inhibition and OCD symptoms following sleep restriction (Hypotheses 1a and 1b). A hierarchical multiple regression analysis was conducted to the assess the relationship between post-sleep restriction inhibition and OCD symptoms, controlling for baseline levels of inhibition and OCD symptoms (Hypothesis 2). A between subjects t-test was conducted to assess the effect

of experiencing a stressor post-sleep restriction on inhibition and OCD symptoms (Hypothesis 3). Exploratory hierarchical multiple regression analyses were then conducted to extend hypothesis 2 to obsessions and non-obsession OCD symptoms and RNT to further probe the predictive value of post-sleep restriction inhibition on specific OCD symptoms. Six moderation models were tested using the PROCESS macro (Hayes, 2013) to examine whether pre-sleep restriction subjective and objective sleep efficiency influenced the relationship between post-sleep restriction inhibition and post-sleep restriction anxiety symptoms, controlling for pre-sleep restriction inhibition and anxiety symptoms. Predictor variables were mean-centered prior to analysis. Significant interactions were probed with both a simple slopes analysis (Aiken & West, 1991) and regions of significance analysis using the Johnson-Neyman technique (Johnson & Neyman, 1936).

Results

Descriptive statistics and associations between study variables

Descriptive statistics and associations between study variables are shown in Table 1.

Measure	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.
1. Pre SSRT	--											
2. Pre subj SE	.01	--										
3. Pre obj SE	.19	.27*	--									
4. Pre OCS	.17	-.04	-.07	--								
5. Pre Obs	-.001	.05	-.12	.67**	--							
6. Pre non-Ob OCS	.20	-.06	-.04	.98**	.50**	--						

7. Pre PTQ	.22	-.11	-.11	.63**	.72**	.54**	--					
8. Post SSRT	.60**	-.04	-.10	.11	.07	.11	.23*	--				
9. Post OCS	.19	-.08	-.14	.72**	.43**	.72**	.57**	.27*	--			
10. Post Obs	.19	-.16	-.15	.40**	.57**	.31**	.58**	.37**	.59**	--		
11. Post non-Ob OCS	.15	-.05	-.11	.70**	.32**	.73**	.47**	.19	.97**	.36**	--	
12. Post PTQ	.15	-.22	-.23	.35**	.48**	.28*	.63**	.40**	.47**	.67**	.32**	--
M	301.57	86.60	81.61	3.49	.48	3.01	5.51	300.52	3.08	.67	2.42	7.73
SD	65.18	8.89	8.75	4.60	1.06	3.98	7.77	74.78	4.07	1.14	3.52	8.89
Range	208.65-470.32	60.47 - 98.9	57.8 - 100	0-20	0-6	0-15	0-37	206.54-513.68	0-15	0-5	0-13	0-37

Note. Pre SSRT = Pre sleep restriction Stop Signal reaction time, Pre subj SE = pre sleep restriction subjective sleep efficiency, Pre obj SE = pre sleep restriction objective sleep efficiency, Pre OCS = pre sleep restriction daily OCD symptoms, Pre Obs = pre sleep restriction daily obsessions, Pre non-Ob OCS = pre sleep restriction daily non-obsession OCD symptoms, Pre PTQ = pre sleep restriction daily Perseverative Thinking Questionnaire, Post SSRT = post sleep restriction Stop Signal reaction time, Post OCS = post sleep restriction daily OCD symptoms, Post Obs = post sleep restriction daily obsessions, Post non-Ob OCS = post sleep restriction daily non-obsession OCD symptoms, Post PTQ = post sleep restriction daily Perseverative Thinking Questionnaire
*$p < .05$ **$p < .01$

Table 1. Descriptive statistics and correlations for study measures ($n = 73$).

Hypothesis 1: Main effects of sleep restriction on inhibition and OCD symptoms

Results of within subject t-tests did not indicate significant changes in inhibition or OCD symptoms following sleep restriction. Specifically, there was not a significant difference in inhibition from pre-sleep restriction ($M = 301.57$, $SD = 65.18$) to post-sleep restriction ($M = 300.52$, $SD = 74.78$), $t(72) = .14$, $p = .89$, $d = .01$. Likewise, there was not a significant difference in OCD symptoms from pre-sleep restriction ($M = 3.54$, $SD = 4.62$) to post-sleep restriction ($M = 3.08$, $SD = 4.07$), $t(71) = 1.18$, $p = .24$, $d = .07$.

Hypothesis 2: Predictive effect of OCD symptoms by inhibition following sleep restriction

In the model predicting post-sleep restriction OCD symptoms, pre-sleep restriction inhibition and OCD symptoms significantly contributed to the model, $F(2,69) = 37.68$, $p < .001$ and accounted for 52% of the variance. Introducing post-sleep restriction inhibition to the model explained an additional 4% of the variance in post-sleep restriction OCD symptoms, and the R^2 change was significant ($p < .05$). When pre-sleep restriction inhibition and OCD symptoms and post-sleep restriction inhibition were included in the model, post-sleep restriction inhibition was significantly associated with post-sleep restriction OCD symptoms (B = .01, β = .25, $p < .01$), and pre-sleep restriction inhibition was unrelated (B = -.01, β = -.08, $p = .43$). See Table 2 for the results of the regression model.

		Post OCD symptoms			
Predictor	**B**	**Std. Error**	**β**	***t***	***p***
Step 1					
Pre OCD Symptoms	.62	.07	.71	8.39	<.001
Pre SSRT	.004	.01	.08	.80	.43
Step 2					
Pre OCD Symptoms	.62	.07	.71	8.69	<.001
Pre SSRT	-.01	.01	.08	-.79	.43
Post SSRT	.01	.01	.25	2.48	<.05

Note. OCD = obsessive-compulsive disorder; SSRT = Stop Signal reaction time; pre = pre-sleep restriction; post = post-sleep restriction

Table 2. Model coefficients for the hypothesized model predicting post-sleep restriction OCD symptoms from post-sleep restriction inhibitory control, controlling for pre-sleep restriction OCD symptoms and inhibitory control ($n = 71$).

Hypothesis 3: Effects of stress on inhibition and OCD symptoms following sleep restriction

Results of between subject t-tests did not indicate significant differences in inhibition or OCD symptoms between those who experienced a stressor following sleep restriction compared to those who did not. Specifically, there was not a significant difference in inhibition between those who experienced a stressor following sleep restriction (M = 311.11, SD = 81.07) compared to those who did not (M = 288.37, SD = 65.94), $t(71) = -1.30$, $p = .20$, $d = .31$. Likewise, there was not a significant difference in OCD symptoms between those who experienced a stressor following sleep restriction (M = 3.74, SD = 4.29) compared to those who did not (M = 2.35, SD = 3.73), $t(70) = -1.45$, $p = .15$, $d = .35$.

Exploratory analyses: Interactive effects on post-sleep restriction OCD symptoms

Subjective sleep efficiency. There was a trend-level interaction between subjective pre-sleep restriction sleep efficiency and post-sleep restriction inhibition to predict post-sleep restriction OCD symptoms, $\Delta R^2 = .03$, $F = 3.82$, $p = .06$. Conditional effects analysis revealed that there was a significant relation between post-sleep restriction inhibition on post-sleep restriction OCD symptoms at low, $B = .02$, $t = 3.22$, $p < .01$, and moderate levels of subjective pre-sleep restriction sleep efficiency, $B = .02$, $t = 2.72$, $p < .05$. However, at high levels of subjective pre-sleep restriction sleep efficiency, post-sleep restriction inhibition was unrelated to post-sleep restriction OCD symptoms, suggesting a protective effect of high sleep efficiency prior to acute sleep loss (see Figure 6). A regions of significance analysis identified 90.09% sleep efficiency as the point at which the effect of post-sleep restriction inhibition on post-sleep restriction OCD symptoms is no longer significant. That is, those with 90.09% subjective sleep efficiency or higher prior to sleep restriction exhibited no link between post-sleep restriction inhibition and OCD symptoms; in contrast, for those with subjective sleep efficiency lower than

90.09% prior to sleep restriction, post-sleep restriction OCD symptoms increases with decreasing post-sleep restriction inhibition.

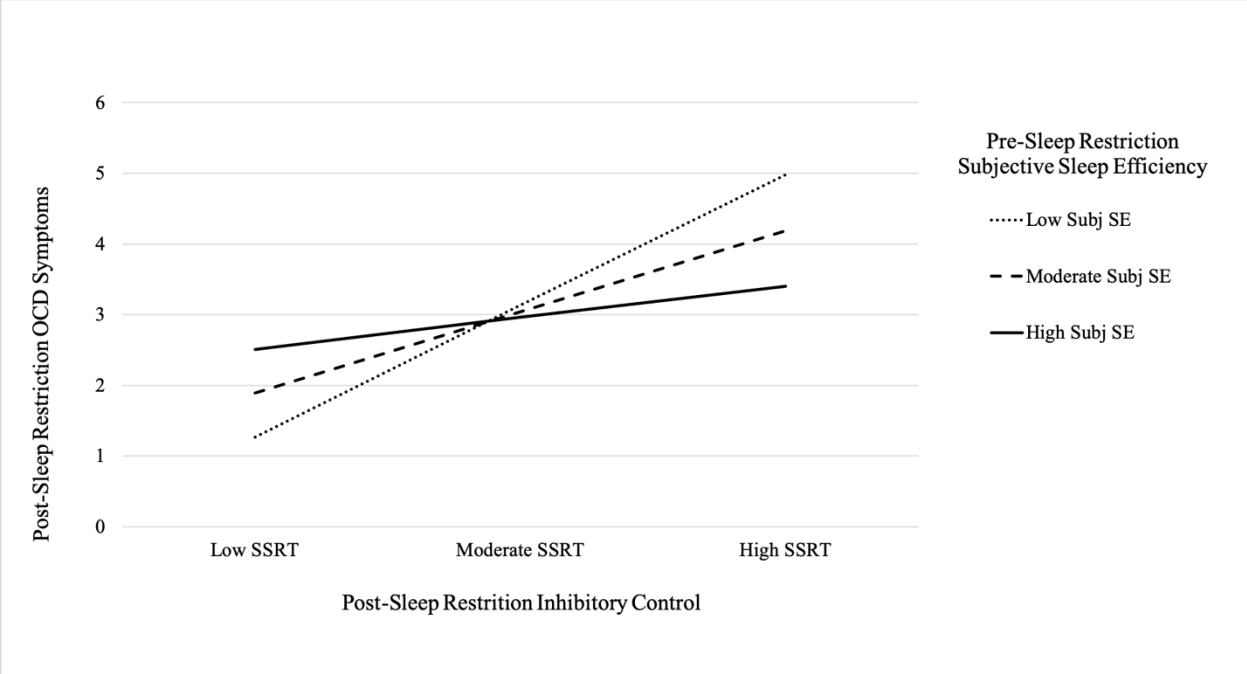

Figure 6. Simple regression slopes of inhibition predicting OCD symptoms following sleep restriction at values of pre-sleep restriction subjective sleep efficiency, controlling for pre-sleep restriction inhibition and OCD symptoms. Inhibition and subjective sleep efficiency were mean-centered prior to analysis, such that low, medium, and high represent the mean +/- one standard deviation.

Objective sleep efficiency. A similar effect was observed for objective pre-sleep restriction sleep efficiency, such that there was a trend-level interaction between objective pre-sleep restriction sleep efficiency and post-sleep restriction inhibition to predict post-sleep restriction OCD symptoms, $\Delta R^2 = .02$, $F = 3.67$, $p = .06$. Conditional effects analysis revealed that there was a significant relation between post-sleep restriction inhibition on post-sleep restriction OCD symptoms at low, $B = .02$, $t = 3.30$, $p < .01$, and moderate levels of objective pre-sleep restriction sleep efficiency, $B = .01$, $t = 2.56$, $p < .05$. However, at high levels of objective pre-sleep restriction sleep efficiency, post-sleep restriction inhibition was unrelated to post-sleep restriction OCD symptoms, suggesting a protective effect of high sleep efficiency

prior to acute sleep loss (see Figure 7). A regions of significance analysis identified 84.04% sleep efficiency as the point at which the effect of post-sleep restriction inhibition on post-sleep restriction OCD symptoms is no longer significant. That is, those with 84.04% objective sleep efficiency or higher prior to sleep restriction exhibited no link between post-sleep restriction inhibition and OCD symptoms; in contrast, for those with objective sleep efficiency lower than 84.04% prior to sleep restriction, post-sleep restriction OCD symptoms increases with decreasing post-sleep restriction inhibition.

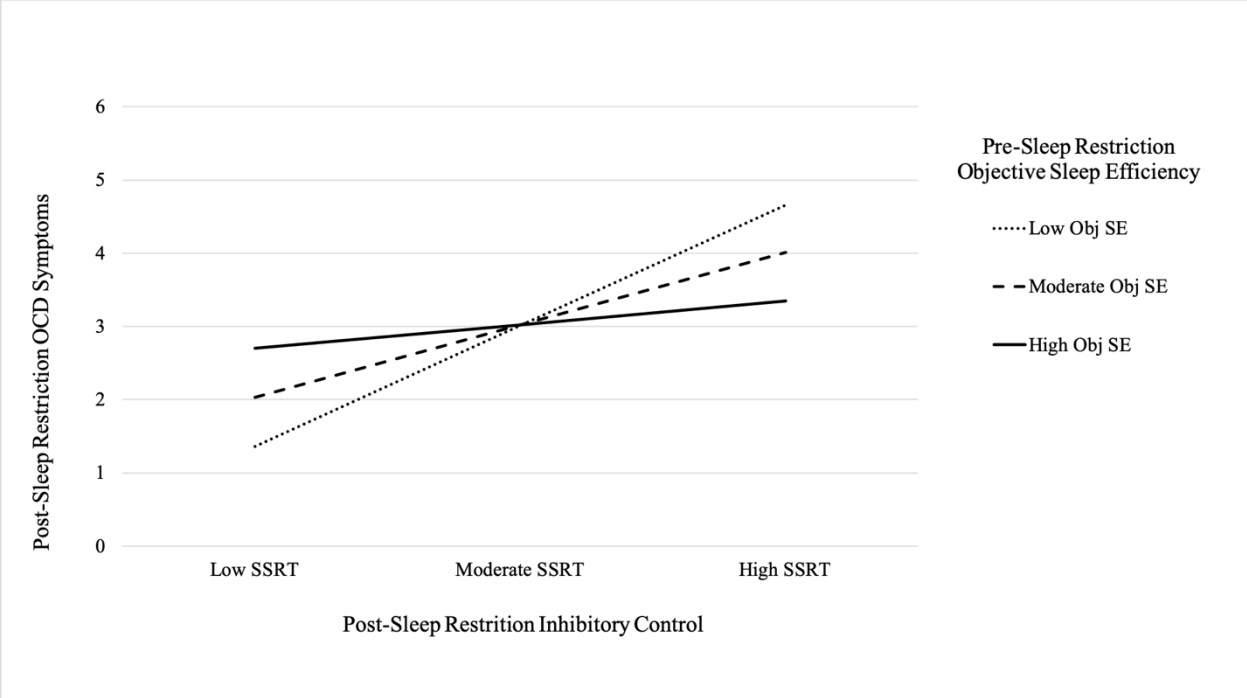

Figure 7. Simple regression slopes of inhibition predicting OCD symptoms following sleep restriction at values of pre-sleep restriction objective sleep efficiency, controlling for pre-sleep restriction inhibition and OCD symptoms. Inhibition and objective sleep efficiency were mean-centered prior to analysis, such that low, medium, and high represent the mean +/- one standard deviation.

Exploratory analyses: Predictive effect of obsessions by inhibition following sleep restriction

In the model predicting post-sleep restriction obsessions, pre-sleep restriction inhibition and obsessions significantly contributed to the model, $F(2,69) = 19.34$, $p < .001$ and accounted for 36% of the variance. Introducing post-sleep restriction inhibition to the model explained an additional 7% of the variance in post-sleep restriction obsessions, and the R^2 change was significant ($p < .01$). When pre-sleep restriction inhibition and obsessions and post-sleep restriction inhibition were included in the model, post-sleep restriction inhibition was significantly associated with post-sleep restriction obsessions (B = .01, β = .34, $p < .01$), and pre-sleep restriction inhibition was unrelated (B = -.0002, β = -.01, $p = .92$). See Table 3 for the results of the exploratory regression models.

Exploratory analyses: Predictive effect of non-obsession OCD symptoms by inhibition following sleep restriction

In the model predicting post-sleep restriction non-obsession OCD symptoms, pre-sleep restriction inhibition and non-obsession OCD symptoms significantly contributed to the model, $F(2,69) = 39.38$, $p < .001$ and accounted for 53% of the variance. Introducing post-sleep restriction inhibition to the model explained an additional .02% of the variance in post-sleep restriction non-obsession OCD symptoms, and the R^2 change was not significant ($p = .08$). When pre-sleep restriction inhibition and non-obsession OCD symptoms and post-sleep restriction inhibition were included in the model, post-sleep restriction inhibition was not significantly associated with post-sleep restriction non-obsession OCD symptoms (B = .01, β = .18, $p = .08$), and pre-sleep restriction inhibition was unrelated (B = -.01, β = -.10, $p = .36$). See Table 3 for the results of the exploratory regression models.

Exploratory analyses: Predictive effect of repetitive negative thinking by inhibition following sleep restriction

In the model predicting post-sleep restriction RNT, pre-sleep restriction inhibition and daily RNT significantly contributed to the model, $F(2,69) = 22.51$, $p < .001$ and accounted for 40% of the variance. Introducing post-sleep restriction inhibition to the model explained an additional 9% of the variance in post-sleep restriction RNT, and the R^2 change was significant ($p < .01$). When pre-sleep restriction inhibition and RNT and post-sleep restriction inhibition were included in the model, post-sleep restriction inhibition was significantly associated with post-sleep restriction RNT (B = .05, β = .39, $p < .01$), and pre-sleep restriction inhibition was associated only at trend level (B = -.03, β = -.21, $p = .06$). See Table 3 for the results of the exploratory regression models.

	Anxiety Outcome														
	Post RNT					Post obsessions					Post non-obsession OCD symptoms				
Predictor	**B**	**Std. Error**	**β**	***t***	***p***	**B**	**Std. Error**	**β**	**t**	**p**	**B**	**Std. Error**	**β**	***t***	***p***
Step 1															
Pre Anxiety Outcome	.70	.11	.63	6.51	<.001	.61	.10	.57	5.90	<.001	.64	.07	.73	8.68	<.001
Pre SSRT	.002	.01	.02	.17	.87	.003	.002	.19	2.00	.05	.001	.01	.01	.14	.39
Step 2															
Pre Anxiety Outcome	.66	.10	.58	6.55	<.001	.58	.10	.54	5.94	<.001	.64	.07	.73	8.85	<.001
Pre SSRT	-.03	.02	-.21	-1.94	.06	-.0002	.002	-.01	-.10	.92	-.01	.01	-.10	-.93	.36
Post SSRT	.05	.01	.39	3.63	<.01	.01	.002	.34	3.01	<.01	.01	.01	.18	1.76	.08

Note. RNT = repetitive negative thinking; OCD = obsessive-compulsive disorder; SSRT = Stop Signal reaction time; pre = pre-sleep restriction; post = post-sleep restriction

Table 3. Model coefficients for the exploratory models predicting post-sleep restriction anxiety outcomes from post-sleep restriction inhibitory control, controlling for pre-sleep restriction anxiety and inhibitory control (n = 71).

Exploratory analyses: Interactive effects on post-sleep restriction obsessions

Subjective sleep efficiency. There was a significant interaction between subjective pre-sleep restriction sleep efficiency and post-sleep restriction inhibition to predict post-sleep restriction obsessions, $\Delta R^2 = .09$, $F = 5.66$, $p < .05$. Conditional effects analysis revealed that there was a significant relation between post-sleep restriction inhibition on post-sleep restriction obsessions at low, $B = .01$, $t = 3.29$, $p < .01$, and moderate levels of subjective pre-sleep restriction sleep efficiency, $B = .01$, $t = 3.26$, $p < .01$. However, at high levels of subjective pre-sleep restriction sleep efficiency, post-sleep restriction inhibition was unrelated to post-sleep restriction obsessions, suggesting a protective effect of high sleep efficiency prior to acute sleep loss (see Figure 8). A regions of significance analysis identified 91.17% sleep efficiency as the point at which the effect of post-sleep restriction inhibition on post-sleep restriction obsessions is no longer significant. That is, those with 91.17% subjective sleep efficiency or higher prior to sleep restriction exhibited no link between post-sleep restriction inhibition and obsessions; in contrast, for those with subjective sleep efficiency lower than 91.17% prior to sleep restriction, post-sleep restriction obsessions increases with decreasing post-sleep restriction inhibition.

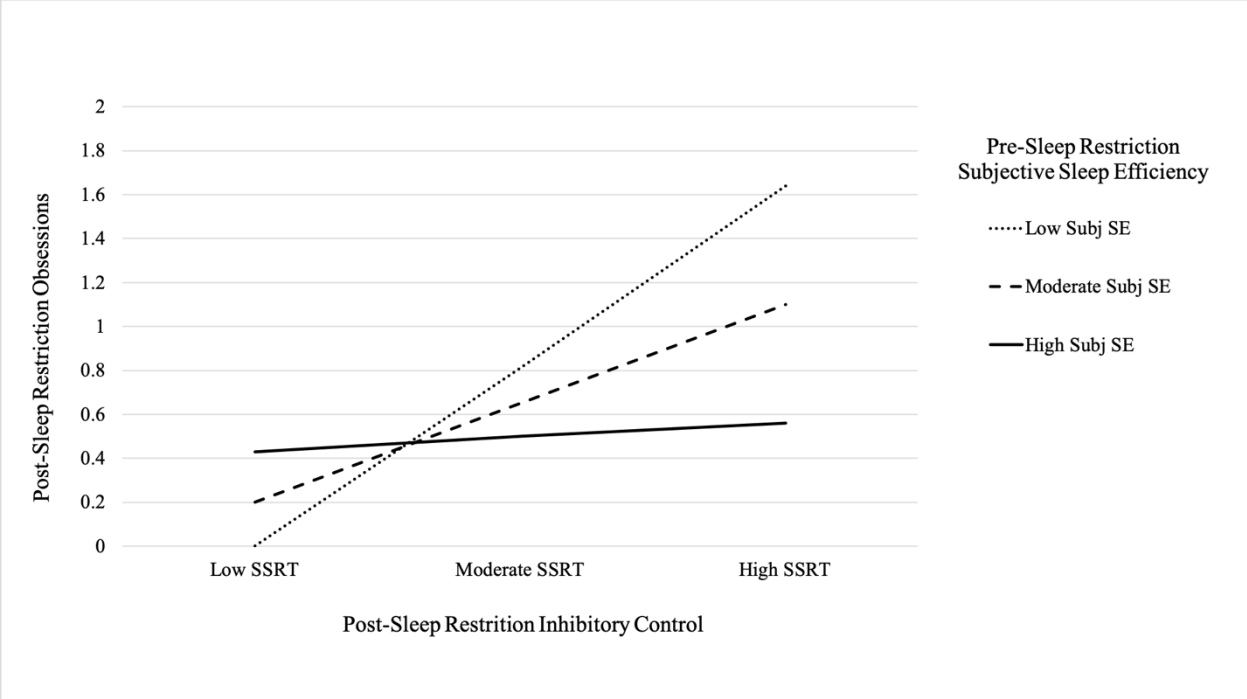

Figure 8. Simple regression slopes of inhibition predicting obsessions following sleep restriction at values of pre-sleep restriction subjective sleep efficiency, controlling for pre-sleep restriction inhibition and obsessions Inhibition and subjective sleep efficiency were mean-centered prior to analysis, such that low, medium, and high represent the mean +/- one standard deviation.

Objective sleep efficiency. A similar effect was observed for objective pre-sleep restriction sleep efficiency, such that there was a significant interaction between objective pre-sleep restriction sleep efficiency and post-sleep restriction inhibition to predict post-sleep restriction obsessions, $\Delta R^2 = .05$, $F = 6.46$, $p < .05$. Conditional effects analysis revealed that there was a significant relation between post-sleep restriction inhibition on post-sleep restriction obsessions at low, $B = .01$, $t = 4.13$, $p < .01$, and moderate levels of objective pre-sleep restriction sleep efficiency, $B = .01$, $t = 3.52$, $p < .01$. However, at high levels of objective pre-sleep restriction sleep efficiency, post-sleep restriction inhibition was unrelated to post-sleep restriction obsessions, suggesting a protective effect of high sleep efficiency prior to acute sleep loss (see Figure 9). A regions of significance analysis identified 86.22% sleep efficiency as the

point at which the effect of post-sleep restriction inhibition on post-sleep restriction obsessions is no longer significant. That is, those with 86.22% objective sleep efficiency or higher prior to sleep restriction exhibited no link between post-sleep restriction inhibition and obsessions; in contrast, for those with objective sleep efficiency lower than 86.22% prior to sleep restriction, post-sleep restriction obsessions increases with decreasing post-sleep restriction inhibition.

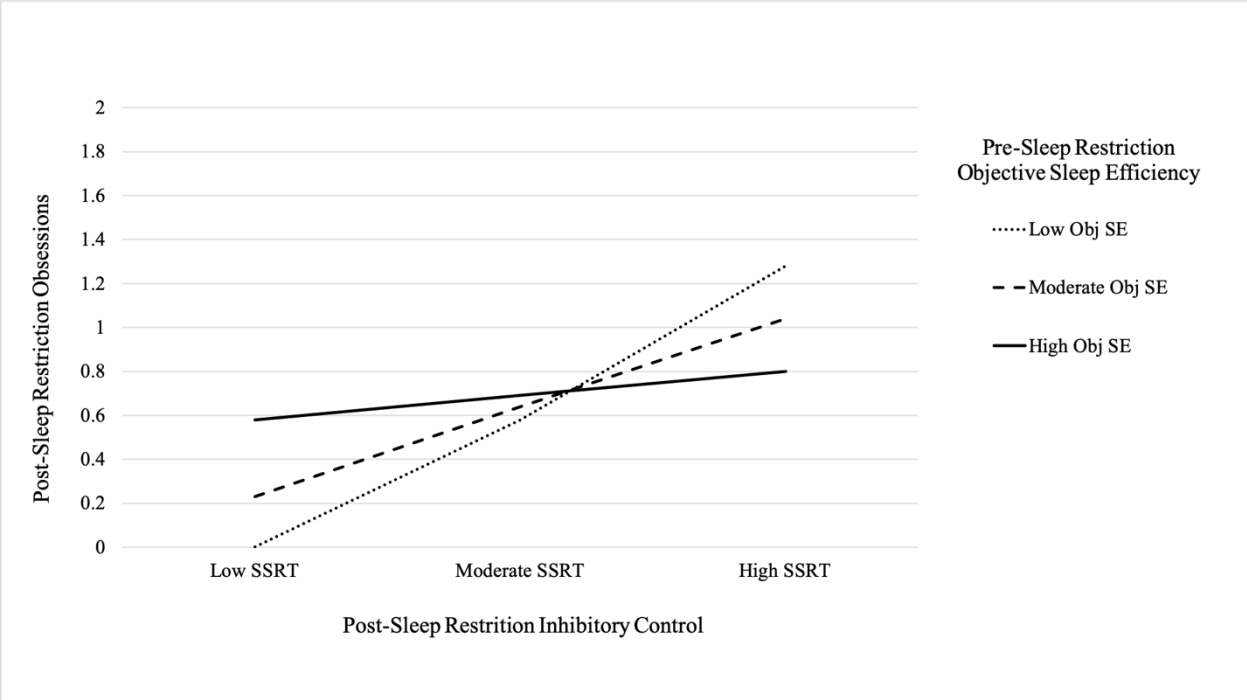

Figure 9. Simple regression slopes of inhibition predicting obsessions following sleep restriction at values of pre-sleep restriction objective sleep efficiency, controlling for pre-sleep restriction inhibition and obsessions. Inhibition and objective sleep efficiency were mean-centered prior to analysis, such that low, medium, and high represent the mean +/- one standard deviation.

Exploratory analyses: Interactive effects on post-sleep restriction non-obsession OCD symptoms

There were no significant interactions between post-sleep restriction inhibition and pre-sleep restriction subjective (p = .23) or objective sleep efficiency (p = .20) to predict post-sleep restriction non-obsession OCD symptoms.

Exploratory analyses: Interactive effects on post-sleep restriction repetitive negative thinking

Subjective sleep efficiency. There was a significant interaction between subjective pre-sleep restriction sleep efficiency and post-sleep restriction inhibition to predict post-sleep restriction RNT, $\Delta R^2 = .06$, $F = 7.07$, $p < .05$. Conditional effects analysis revealed that there was a significant relation between post-sleep restriction inhibition on post-sleep restriction RNT at low, $B = .08$, $t = 3.68$, $p < .01$, and moderate levels of subjective pre-sleep restriction sleep efficiency, $B = .05$, $t = 3.18$, $p < .01$. However, at high levels of subjective pre-sleep restriction sleep efficiency, post-sleep restriction inhibition was unrelated to post-sleep restriction RNT, suggesting a protective effect of high sleep efficiency prior to acute sleep loss (see Figure 10). A regions of significance analysis identified 91.98% sleep efficiency as the point at which the effect of post-sleep restriction inhibition on post-sleep restriction RNT is no longer significant. That is, those with 91.98% subjective sleep efficiency or higher prior to sleep restriction exhibited no link between post-sleep restriction inhibition and RNT; in contrast, for those with subjective sleep efficiency lower than 91.98% prior to sleep restriction, post-sleep restriction RNT increases with decreasing post-sleep restriction inhibition.

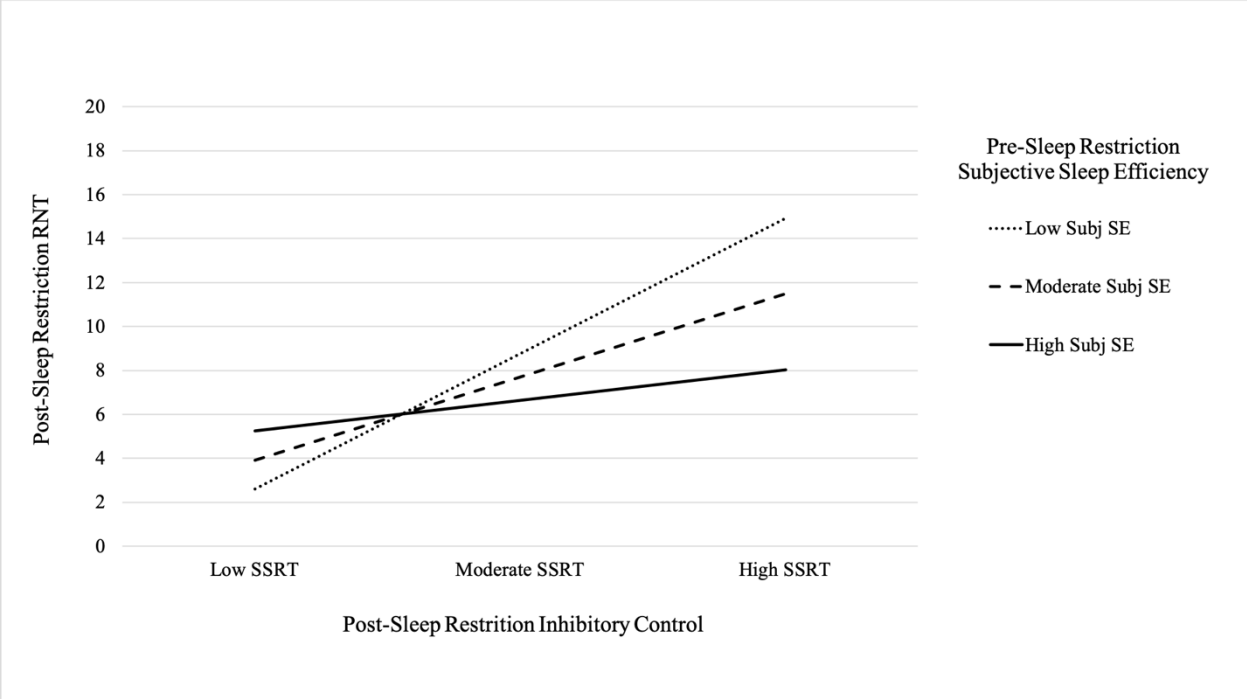

Figure 10. Simple regression slopes of inhibition predicting repetitive negative thinking (RNT) following sleep restriction at values of pre-sleep restriction subjective sleep efficiency, controlling for pre-sleep restriction inhibition and RNT. Inhibition and subjective sleep efficiency were mean-centered prior to analysis, such that low, medium, and high represent the mean +/- one standard deviation.

Objective sleep efficiency. A similar effect was observed for objective pre-sleep restriction sleep efficiency, such that there was a significant interaction between objective pre-sleep restriction sleep efficiency and post-sleep restriction inhibition to predict post-sleep restriction RNT, $\Delta R^2 = .06$, $F = 5.75$, $p < .05$. Conditional effects analysis revealed that there was a significant relation between post-sleep restriction inhibition on post-sleep restriction RNT at low, $B = .08$, $t = 3.56$, $p < .01$, and moderate levels of objective pre-sleep restriction sleep efficiency, $B = .05$, $t = 3.25$, $p < .01$. However, at high levels of objective pre-sleep restriction sleep efficiency, post-sleep restriction inhibition was unrelated to post-sleep restriction RNT, suggesting a protective effect of high sleep efficiency prior to acute sleep loss (see Figure 11). A regions of significance analysis identified 86.48% sleep efficiency as the point at which the

effect of post-sleep restriction inhibition on post-sleep restriction RNT is no longer significant. That is, those with 86.48% objective sleep efficiency or higher prior to sleep restriction exhibited no link between post-sleep restriction inhibition and RNT; in contrast, for those with objective sleep efficiency lower than 86.48% prior to sleep restriction, post-sleep restriction RNT increases with decreasing post-sleep restriction inhibition.

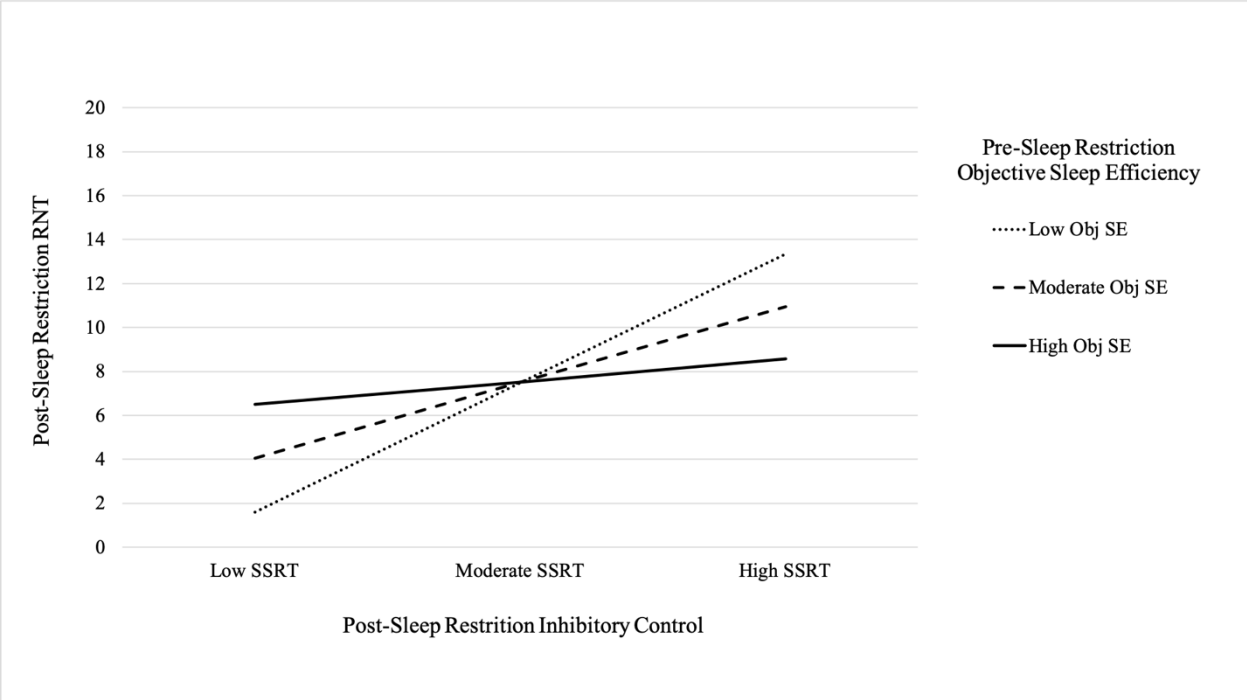

Figure 11. Simple regression slopes of inhibition predicting repetitive negative thinking (RNT) following sleep restriction at values of pre-sleep restriction objective sleep efficiency, controlling for pre-sleep restriction inhibition and RNT. Inhibition and objective sleep efficiency were mean-centered prior to analysis, such that low, medium, and high represent the mean +/- one standard deviation.

Study 1 Discussion

The present study did not find support for the hypothesis that sleep restriction would result in decreased inhibition. The null finding for inhibition is inconsistent with considerable extant research showing sleep deprivation impairs inhibition (Anderson & Platten, 2011; Bocca et al., 2014; Chuah et al., 2006; Drummond et al., 2006), including one study utilizing the Stop-

Signal task (Zhao et al., 2019). Notably, these studies all used total sleep deprivation procedures (i.e., 24 or more hours of sustained wakefulness). Thus, inhibition may be robust to more mild sleep loss procedures like that utilized in this study. Relatedly, a single night of sleep restriction may be too brief a period to detrimentally impact inhibition. Indeed, previous research has found inhibitory deficits on the Stop Signal task in patients with sleep apnea (Peer et al., 2019) and insomnia (Covassin et al., 2011), suggesting the inhibitory consequences of partial sleep loss may accumulate over time. Together with the extant literature, the present findings suggest that inhibition is robust to one night of 4-hour sleep restriction, and inhibitory deficits may only emerge with more substantial sleep deprivation and/or sleep loss over a longer period of time.

Results also did not support the hypothesis that sleep restriction would result in increased OCD symptoms. Although this is the first study to examine the effect of sleep loss on OCD symptoms specifically, previous work has found that sleep loss has a detrimental effect on a range of outcomes linked to affective disorders, including increased anxiety (Babson et al., 2010; Talbot et al., 2010), decreased positive affect (Finan et al., 2017; Franzen et al., 2008; Reddy et al., 2017), panic symptoms (Babson et al., 2009), and perceived stress (Minkel, Banks, et al., 2014). Extant work also links sleep disturbance to OCD symptoms (Timpano et al., 2014), and results from our meta-analysis indicate reduced sleep duration in OCD (Cox & Olatunji, 2020). Therefore, similar to the null finding for inhibition, it may be that the sleep manipulation employed here was too mild to impact OCD symptoms.

Similarly, the present study did not find support for the hypothesis that those who experienced a stressor following sleep restriction would exhibit decreased inhibition and increased OCD symptoms compared to those who did not experience a stressor. It is possible that the 52% of the sample who reported experiencing at least 1 stressor following sleep restriction

experienced relatively minor stressors. That is, given the naturalistic design, it is possible that our sampling period captured few, if any, significant stressors that could have amplified the effects of sleep loss. Future research implementing a laboratory stressor is needed to fully examine the possible moderating effects of stressors following sleep loss.

Still, support was found for the hypothesis that decreased inhibitory control following sleep restriction would predict increased OCD symptoms. Given the heterogeneous nature of OCD symptoms and previous research linking sleep disturbance to obsessions, but not compulsions (Timpano et al., 2014), as well as findings showing elevated RNT in those with OCD (Wahl et al., 2019), planned analyses were followed up with exploratory analyses examining obsessions individually, non-obsession OCD symptoms, and repetitive negative thinking to determine if the observed effect was specific to intrusive cognition. As with OCD symptoms as a whole, decreased inhibition following sleep restriction was associated with increased symptoms of anxious intrusive cognition, including RNT and obsessions, controlling for baseline levels of inhibition and anxiety symptoms. These findings support and extend previous literature delineating the impact of sleep loss on inhibition (Drummond et al., 2006) and anxiety (Babson et al., 2010) by showing that decreased inhibition due to sleep loss predicts increased anxiety symptoms. This finding is consistent with previous research linking inhibition to RNT (Hallion et al., 2014; Whitmer & Banich, 2007), as well as research showing that aspects of cognitive control prospectively mediate the relation between sleep disturbance and RNT and obsessions (Cox, Cole, et al., 2018). Together these findings suggest that intact inhibition may limit the intrusion of anxious cognition, such as RNT and obsessions. However, when inhibition is impaired by sleep loss, intrusive cognition increases. These results represent the first

experimental evidence for decreased inhibition as one mechanism by which sleep loss increases anxiety symptoms.

The discrepancy between the main effects (i.e., no mean change in inhibition or OCD symptoms following sleep restriction) and the regression effects (i.e., decreased post-sleep restriction inhibition predicts increased obsessions and RNT) suggest the potential presence of moderating processes. That is, sleep restriction may result in increased intrusive cognition via decreased inhibition for some individuals, but not others. Prior sleep history is one factor that may amplify or offset brief acute sleep loss. Indeed, extending sleep opportunity prior to one night of total sleep deprivation limits the impact of acute sleep loss on attention and alertness (Arnal et al., 2015; Rupp et al., 2009). This is consistent with the homeostatic regulation of sleep, such that sleep pressure increases with prolonged wakefulness and diminishes with sleep (Borbély et al., 2016). Thus, the impact of acute sleep loss should be highest among individuals who have slept less prior to sleep deprivation. Likewise, prior healthy sleep may buffer the consequences of a night of acute sleep loss. Notably, previous studies have utilized sleep extension procedures, which increase time in bed but do not necessarily increase sleep duration. An alternative approach to estimate the effect of prior sleep on the consequences of acute sleep loss is to measure sleep efficiency, which is the ratio of total sleep time to time in bed. Exploratory moderation analyses revealed that both subjective and objective sleep efficiency on the night prior to sleep restriction moderated the effect of inhibition on RNT and obsessions. There was a trend level moderation effect for total OCD symptoms, but not non-obsession OCD symptoms, suggesting the former effect is likely driven by the obsession items.

The highest levels of anxiety symptoms were reported by those with the most impaired inhibition after sleep restriction and the lowest sleep efficiency prior to sleep restriction, and this

effect was consistent across subjective and objective measures of sleep efficiency. Extant research indicates that sleep extension prior to sleep deprivation buffers the negative effects of sleep loss on cognitive function (Rupp et al., 2009; Van Dongen et al., 2004). The present study extends these findings to sleep efficiency, which suggests that facets of sleep continuity prior to sleep loss is also important for determining the degree of impact one experiences following sleep restriction. This finding also suggests that habitual sleep efficiency may have important implications for anxiety outcomes, such as intrusive cognition. That is, those with low habitual sleep efficiency may be particularly vulnerable to the effects of acute sleep loss, as evidenced by high levels of anxiety symptoms in conjunction with impaired inhibition following sleep loss. In contrast, high habitual sleep efficiency may function as a protective factor against the consequences of acute sleep loss on anxiety outcomes, as evidenced by relative resiliency regardless of levels of inhibition following sleep loss.

The present study found a relation between decreased inhibition and increased intrusive cognition characteristic of OCD following sleep loss and a moderating effect of prior sleep efficiency. These findings offer preliminary evidence for a pathway by which sleep loss may contribute to OCD. Specifically, repeated bouts of acute sleep loss may lead to accumulating deficits in inhibition, which may then result in increased OCD symptoms. Over time, persistent repetition of this pattern, particularly in combination with habitual poor sleep efficiency, may confer vulnerability for OCD and other disorders characterized by anxious intrusive cognition. In contrast, high habitual sleep efficiency may buffer these effects, such that healthy sleepers may be less likely to develop OCD. These findings highlight the importance of future research examining the impact of cumulative sleep loss on the onset of OCD and the possible protective effect of healthy interim sleep.

The present study has several strengths, including the first experimental manipulation of sleep when examining inhibition as a mechanism in the relation between sleep and OCD symptoms, the use of subjective and objective monitoring of sleep, and the enhanced ecological validity of the at-home sleep restriction procedure. However, the implications of the present findings must be considered within the context of the study limitations. First, participants were not recruited based on habitual sleep duration. Thus, it is possible that some participants in this sample were naturally short sleepers and therefore less likely to be affected by the manipulation. Though the exclusion of non-responders may have addressed this limitation, it will be informative to replicate this study among individuals with confirmed 7-8 hour habitual sleep duration. Second, though the present design permits assessment of the moderating effect of prior night's sleep efficiency, at least a week of sleep monitoring is necessary to determine habitual sleep efficiency. Thus, the present findings may not precisely reflect the effect of habitual sleep on the consequences of acute sleep loss. Relatedly, sleep efficiency as operationally defined here is a pragmatic way to describe sleep quality, but it doesn't fully capture other aspects of sleep that have been thought to provide psychophysiological benefits. Third, the present findings are limited to OCD symptoms, and additional research is needed to determine whether the present effects contribute to the onset of OCD. Relatedly, the present sample was not selected for OCD symptoms, which may limit generalizability to OCD. Fourth, though several compliance checks were put in place, it is possible that some degree of noncompliance with the sleep restriction procedure was undetected, which may limit the ability to detect the hypothesized effects. Fifth, the overrepresentation of females in the sample limits the ability to generalize these findings to males. Sixth, the daily obsessions subscale exhibited marginal internal consistency, which may impact scale validity. This issue highlights the need for validated measures of daily

psychopathology symptoms for use in ecological momentary assessment designs. Finally, non-responders were excluded from analyses in order to prevent a masking effect by those resilient to a relatively mild sleep manipulation; thus, it will be important to replicate these findings with a sleep restriction procedure that is tailored to individual habitual sleep duration in order to eliminate this potential confound.

Despite these limitations, the present study offers the first experimental evidence for a role of decreased inhibition in increased OCD symptoms, particularly obsessions, following sleep restriction and a moderating effect of prior sleep efficiency. These findings support the proposal of sleep disturbance as a mechanistic transdiagnostic factor in psychopathology (Harvey et al., 2011) and suggest the utility of further delineation of the role of sleep in OCD. While Study 1 is strengthened by the experimental manipulation of sleep, it remains unclear how habitual sleep disturbance and circadian timing impact the daily experience of OCD symptoms. That is, how might the effects identified in Study 1 develop into chronic pathology? In order to address this question, Study 2 utilized an ecological momentary assessment approach to examine daily sleep duration and timing as predictors of daily OCD symptoms, as well as mediation modeling to test the relationships between circadian timing, sleep, and OCD symptoms.

Chapter III

Study 2

Study 1 highlighted the role of sleep loss in OCD symptoms. Increasing evidence suggests that circadian rhythm disturbance may contribute to the etiology of psychopathology. Several mechanisms for a circadian-affective disorder link have been proposed in addition to disrupted sleep/wake activity, including alterations to monoamine signaling, HPA axis function, and immune system function (McClung, 2013). There has likewise been increasing interest in the role of circadian rhythms in OCD. Early studies largely found increased cortisol and decreased melatonin output with intact circadian rhythms (Catapano et al., 1992; Monteleone et al., 1995), though one study did find evidence for increased overnight cortisol output (Kluge et al., 2007). Notably, these studies utilized small sample sizes ($N < 10$), and there have been no recent studies examining the rhythms of circadian processes, such as cortisol, melatonin, and temperature in OCD compared to healthy controls. Recent studies have utilized alternative, non-physiological circadian metrics to examine the role of circadian rhythms in OCD, and findings largely implicate delayed circadian rhythms to OCD. Indeed, those with delayed sleep-wake phase disorder (DSWPD) report increased OCD symptoms compared to healthy controls (Schubert and Coles, 2013). Further, rates of DSWPD are elevated among those with severe, treatment resistant OCD (Drummond et al., 2012), and those with comorbid treatment resistant OCD and DSWPD report increased OCD symptoms compared to those with treatment resistant OCD without DSWPD (Turner et al., 2007). Studies of OCD inpatients have also pointed to a role of delayed circadian rhythms. One recent study found that delayed bedtimes were associated with increased OCD symptoms among those in residential OCD treatment (Nota et al., 2020). Further, a meta-

analysis of treatment outcomes in residential OCD programs found increased treatment response in programs with consistent schedules and lights out times, suggesting circadian entrainment may facilitate OCD treatment response (Coles & Stewart, 2019). Together these findings implicate delayed circadian rhythms in OCD and suggest circadian entrainment may be an effective treatment target.

Another alternative to physiological indicators of circadian rhythms is chronotype. As reviewed previously, chronotype is an individual difference factor that describes time of day preferences in sleep/wake activity and peak alertness, such that evening types prefer a later sleep onset and offset schedule and feel their "best" later in the day and vice versa in morning types. Notably, chronotype is associated with the timing of circadian processes, such as melatonin, cortisol, and body temperature (Bailey & Heitkemper, 2001; Kerkhof & Van Dongen, 1996). Studies examining links between chronotype and OCD have been mixed. One cross-sectional study found that evening types report increased intrusive cognition compared with morning types (Nota & Coles, 2015). In contrast, two other cross-sectional studies found that the association between eveningness and OCD symptoms was better accounted for by depression (Alvaro et al., 2014; Cox, Tuck, et al., 2018). Still, there is also evidence that eveningness predicts increased OCD symptoms over 4 months, controlling for both baseline OCD symptoms and depression (Cox, Tuck, et al., 2018). Finally, a recent study compared chronotype in individuals with OCD and healthy controls and found a trend-level effect for more evening types and fewer morning types among those with OCD (Kani et al., 2018). Taken together with the literature on delayed sleep timing, these findings point to a role of eveningness in OCD.

Findings from Study 1 suggest acute sleep loss negatively impacts inhibitory control of anxious intrusive cognition. While the 4-hour sleep restriction paradigm has enhanced ecological

validity over total sleep deprivation procedures, it remains unknown whether more normative nightly variability in sleep impacts next day OCD symptoms. Prospective monitoring of sleep and anxiety through ecological momentary assessment provides the ability to examine the association between last night's sleep and next day OCD symptoms. Though ecological momentary assessment offers diminished internal validity compared to experimental sleep restriction, the increased ecological validity of daily sampling may provide more information about how chronic subtle sleep disturbance may contribute to OCD. Indeed, recent ecological momentary assessments studies have found a link between last night's sleep and next day anxiety-related symptoms. One study found that worse subjective sleep quality predicts increased anxious arousal the following day in healthy women, whereas anxious arousal does not predict next day sleep quality (Kalmbach et al., 2017). Findings from our lab expand on this result and indicate that decreased objective and subjective total sleep time predicts increased next day anxiety, but not vice versa, and the former effect is strongest in the morning (Cox, Sterba, et al., 2018). Together these findings suggest multiple aspects of sleep predict next day anxiety and suggest the strength of this effect varies by time of day.

Ecological momentary assessment studies have also examined the links between daily sleep and symptoms of specific anxiety-related disorders. A study of individuals with generalized anxiety disorder found a bidirectional relation between daily sleep and worry (Thielsch et al., 2015), whereas studies of individuals with PTSD found unidirectional relations between decreased subjective sleep quality, efficiency (Short et al., 2017), and duration (Deviva et al., 2019) and increased PTSD symptoms the following day. Importantly, one recent study examined the relations between daily sleep duration and timing and OCD symptoms in a sample of individuals with OCD, individuals with subthreshold symptoms, and healthy controls. This

study found that later subjective sleep timing predicted both increased obsessions and compulsions the following day in those with OCD, but not in the subthreshold sample or controls (Schubert et al., 2019). Interestingly, no effect was found for sleep duration, and there was no evidence of an impact of OCD symptoms on next night's sleep. This study represents an important first step in characterizing the prospective relations between daily sleep and OCD symptoms; however, this study has several notable limitations, including the use of an unstandardized sleep diary and the absence of an objective sleep measure, such as actigraphy. Further, this study sampled OCD symptoms once/day in the evening. Given evidence for both a time of day effect for OCD symptoms (i.e., peak in the afternoon; Nota, Gibb, & Coles, 2014) and a time of day effect on the relation between last night's sleep duration and next day anxiety (i.e., strongest in the morning; Cox, Sterba, et al., 2018), a single assessment in the evening may not be an appropriate sampling window. Study 2 aims to address these limitations.

An additional aim of Study 2 is to examine mechanisms by which daily sleep may predict increased OCD symptoms. The observed relation between decreased inhibition and increased anxious intrusive cognition following acute sleep loss in Study 1 suggests the utility of further examination of the mechanistic role of decreased inhibition in the relation between sleep disturbance and OCD. In addition to findings from the sleep deprivation literature, extant research also links habitual sleep disturbance to reduced executive function. Studies of healthy young adults indicate shorter and more variable sleep duration is associated with diminished performance on executive function tasks (Kuula et al., 2018; Whiting & Murdock, 2016). Further, a study of younger and older adults found decreased objective sleep duration and increased wake after sleep onset were associated with worse executive function performance, independent of age (Wilckens et al., 2014). Finally, subjective sleep quality is associated with

worse performance on a sustained attention task (Gobin et al., 2015). These findings indicate that the sleep-executive function link is not limited to significant acute sleep loss and suggest the utility of examining the association between habitual objective and subjective sleep and inhibitory control.

There is also preliminary, though mixed, evidence for a link between circadian rhythms and impaired cognitive function. In a sample of depressed inpatients, evening chronotypes performed worse on a measure of inhibitory control than morning chronotypes (Cabanel et al., 2019). Likewise, performance on category fluency, which is one measure of executive function, was worse among older women with a later peaking activity rhythm compared to those with an earlier peaking rhythm (Walsh et al., 2014). However, a study of executive function in young adults found that although delayed sleep timing is associated with poorer self-reported executive function, it is not associated with task-based performance (Kuula et al., 2018). Further, a recent study found no association between chronotype and performance on an executive function task (McGowan et al., 2020). Still, findings from the basic circadian literature indicate a circadian rhythm to inhibition (Burke et al., 2015), suggesting additional research on the links between circadian timing and inhibition is needed.

Habitual sleep disturbance may also contribute to increased stress. Results from a study utilizing a chronic mild sleep restriction paradigm found that sustained sleep curtailment resulted in chronic dysregulation in stress systems (Simpson et al., 2016). Further, a recent study using an ecological momentary assessment design found that decreased sleep duration and quality predicted increased perceived stress the following day (Lee et al., 2017). Together these findings suggest that chronic sleep disturbance may increase both physiological and perceived stress, which may set the stage for the development of OCD.

Circadian rhythms may also influence the stress response. The circadian rhythm of cortisol is well-established, such that cortisol peaks after awakening (i.e., the cortisol awakening response) and declines over the course of the day (Désir et al., 1980; Pruessner et al., 1997). Likewise, experimental circadian misalignment results in decreased cortisol output (Wright et al., 2015). Interestingly, studies of chronotype indicate decreased morning cortisol levels in evening types compared to morning types (Kudielka et al., 2006, 2007; Petrowski et al., 2020), as well as decreased total daily cortisol output (Petrowski et al., 2013). Together these findings suggest that circadian misalignment, perhaps via eveningness, may blunt diurnal cortisol output, which may in turn alter reactivity to an acute stressor. Though limited work has been conducted in this area, extant findings indicate that, compared to morning types, evening types exhibit increased cortisol reactivity (de Punder et al., 2019) and decreased heart rate variability (Roeser et al., 2012) in response to a stressor. Thus, circadian factors, such as chronotype, may contribute to excessive stress reactivity, such as that recently observed in postpartum women with OCD (Lord et al., 2011, 2012).

Extant research suggests both sleep and circadian rhythms may be linked to OCD. Study 2 sought to examine associations between sleep and circadian rhythms in OCD using a combined case-control and ecological momentary assessment approach. It was hypothesized that individuals with OCD will exhibit later circadian timing (Hypothesis 1a), increased sleep disturbance (Hypothesis 1b), decreased inhibition (Hypothesis 1c), and increased stress reactivity (Hypothesis 1d) compared to healthy controls. Decreased daily sleep duration (Hypothesis 2a) and later daily sleep timing (Hypothesis 2b) will predict increased next day OCD symptoms, and this effect will be moderated by OCD status, inhibition, and daily stressors (Hypotheses 2c-e).

The relationship between later circadian timing and OCD symptoms will be serially mediated by sleep disturbance, inhibition, and stress reactivity (Hypothesis 3).

Methods

Participants

The target sample was 150 participants; however, data collection was ended early due to the COVID-19 pandemic. The sample consisted of undergraduates and community adults (N = 80). Undergraduate students were recruited from psychology courses and were compensated with course credit. Community adults were recruited from flyers and a university research email notification system and were compensated with $50. Participants who met criteria for moderate to high suicide risk (n = 2) or psychotic symptoms (n = 1) were withdrawn immediately and given appropriate referral information. An additional three participants withdrew prior to the second laboratory session. Seventy-four participants completed both study sessions.

The mean age of the sample was 23.99 years (SD = 7.21), ranging from 18 to 53 years (73% female). The ethnicity composition was as follows: White (n = 42; 55%), Asian (n = 18; 23%), Black/African American (n = 9; 12%), Hispanic/Latino (n = 4; 5%), Other (n = 4; 5%). Fifty-seven participants (74%) screened high for OCD symptoms prior to enrollment, and 20 participants (26% screened low). Twenty participants (41%) met criteria for OCD, and 29 participants (59%) were identified as healthy controls (i.e., met criteria for no disorders). Sixty participants (75%) participated in data collection in-person prior to the onset of the COVID-19 pandemic, and 20 participants (25%) participated in data collection virtually following the pandemic onset (see Procedure).

Measures

Diagnostic Status

The *MINI International Neuropsychiatric Interview* (MINI; Sheehan et al., 1998) is a well-validated and widely used semi-structured diagnostic interview that assesses for 17 DSM disorders. The MINI was used to determine diagnostic status (i.e., OCD, subclinical, or healthy control and comorbidity).

Circadian Timing

The *Morningness-Eveningness Questionnaire* (MEQ; Horne and Ostberg, 1976) is a 19-item self-report measure of chronotype and is thought to reflect the individual's circadian rhythms. Items are rated on a Likert scale ranging from 1-6 with answer options varying by item content. Higher scores reflect morningness, and lower scores reflect eveningness. The MEQ demonstrated good internal consistency ($\alpha = 0.90$).

Mid-sleep is the gold-standard subjective indicator of chronotype. Recent evidence suggests that a weekly average mid-sleep more closely approximates intrinsic circadian phase (Kantermann & Burgess, 2017) than mid-sleep on free days (Roenneberg et al., 2007); therefore, mean mid-sleep for the week will be utilized. Variables for calculating mid-sleep were collected via the CSD as described in Study 1.

The *Diagnostic Interview for Sleep Patterns and Disorders* (DISPD; Merikangas et al., 2014) is a semi-structured diagnostic interview that assesses general sleep patterns and 8 DSM sleep disorders. Only the sleep patterns and delayed phase sleep syndrome modules were utilized in the present study to determine delayed sleep-wake phase disorder (DSWPD) diagnostic status.

Sleep disturbance

The ISI (Bastien et al., 2001), CSD (Carney et al., 2012), and actigraphy as described in Study 1 were used to indicate past 2 week sleep disturbance, daily subjective sleep disturbance,

and daily objective sleep disturbance, respectively. The ISI demonstrated adequate internal consistency ($\alpha = 0.84$) in Study 2.

Inhibition

The Stop Signal task (G. D. Logan, 1994) as described in Study 1 was used to measure inhibition.

Stress

The DISE (Almeida et al., 2002) as described in Study 1 was used to measure daily stressors.

A speech anticipation task (Waugh, Panage, Mendes, & Gotlib, 2010) was used to induce stress in the laboratory in order to measure stress reactivity. The task begins with a 5-minute baseline period during which time participants rest quietly. Following baseline, participants are told that they have 2 minutes to prepare a 5-minute speech (the topic being "Why are you a good friend?") that will be both recorded and evaluated live by a judge. Participants are told that there will be 2 coin flips to determine if and when they give the speech. The first coin flip takes place after the 2-minute preparation period and determines whether the speech is delivered immediately or after a 5-minute waiting period. The second coin flip determines whether the speech is delivered or not. In all cases, the coin flips result in no speech given. A 5-minute recovery period occurs after the second coin flip. Participants are asked to report their subjective stress on a subjective units of distress (SUDS) scale from 0 to 100 at the onset of baseline, after the 2-minute speech preparation period, after the 5-minute waiting period, and after the 5-minute recovery period. Heart rate and respiration were measured continuously using a BioNomadix mobile physiology unit, a respiration band, and three non-invasive Ag-AgCl electrodes placed on the torso. Psychophysiological recording equipment was placed on participants at the beginning of the laboratory session to allow for adaptation prior to the onset of the stress task (~30

minutes). Previous work has found the anticipation of a speech effectively elicits subjective and physiological stress similar to actually delivering a speech (Waugh et al., 2010).

Psychophysiological data was analyzed using Acqknowledge 5.0. Data were visually inspected for overall quality, artifacts, and missing R-peaks. Psychophysiological data from 14 participants was missing due to equipment failure, and data from 9 participants was excluded due to overall poor quality and/or minimal signal detection, leaving 30 participants with analyzable psychophysiological data. Psychophysiological data were cleaned and processed according to guidance provided by Biopac. First, a high pass filter was applied. Second, artifacts were removed, and R-peaks that were too small to be detected were multiplied by a constant to amplify them to a detectable level. Third, the Heart Rate Variability procedure in Acqknowledge was used to calculate mean high frequency power for each of the 4 segments of the speech anticipation task. The natural log of the mean high frequency power was then used to indicate HRV.

OCD symptoms

The *Yale-Brown Obsessive Compulsive Scale* (YBOCS; Goodman et al., 1989) is a semi-structured diagnostic interview that measures OCD symptom severity. Higher scores indicate increased OCD symptom severity.

The OCIR (Foa et al., 2002) as described in Study 1 was used to recruit individuals with elevated OCD symptoms. Participants also completed the OCIR in session 2 of Study 2, at which time the measure demonstrated adequate internal consistency ($\alpha = .88$). The daily OCD symptom scale as described in Study 1 was used to indicate daily OCD symptom.

Procedure

Prior to enrollment in the study, participants were screened for OCD symptoms with the OCIR. Those scoring an 21 or higher, indicating clinically significant OCD symptoms (Foa et al., 2002), were recruited for the elevated OCD symptom group. Data collection occurred over 9 consecutive days.

Prior to COVID-19 pandemic

On day 1, participants attended a laboratory session that included informed consent and administration of the MINI, DISPD, and YBOCS. Following the interviews, participants completed the MEQ and ISI and then received an actigraph, CSD, and instructions for the week of daily sleep and OCD symptom monitoring. On days 2 through 8, sleep was monitored continuously with actigraphy, and participants completed the CSD upon awakening each morning. OCD symptoms and daily stress were sampled by surveys sent via email. OCD symptoms were measured in the morning (8:00am), afternoon (2:00pm), and evening (8:00pm). Daily stress was measured once in the evening (8:00pm). Participants were instructed to complete each survey within two hours of receipt. On day 9, participants returned to the laboratory to complete the Stop Signal task, the OCIR, the neutralization task, and the anticipatory stress task.

During COVID-19 pandemic

Following the onset of the COVID-19 pandemic, data collection was halted until June 25, 2020, on which date virtual data collection was initiated. Data was collected virtually on all self-report measures. Measures requiring an in-person encounter (i.e., actigraphy, the Stop Signal task, and the speech anticipation task) were not completed.

On day 1, participants attended a Zoom call that included informed consent and administration of the MINI, DISPD, and YBOCS. The suicide module of the MINI was not

completed virtually. Following the interviews, participants completed the ISI and MEQ and were given instructions for the week of daily sleep and OCD symptom monitoring. On days 2 through 8, participants completed the CSD electronically upon awakening each morning. Measurement of daily OCD symptoms and stress was identical to that completed prior to the pandemic. On day 9, participants attended a second Zoom call to complete the OCIR and the neutralization task.

Data analytic strategy

Data analysis was conducted in SPSS 27 and Mplus 8. Between subjects t-tests and a chi square test were conducted to examine group differences in circadian timing (MEQ, mid-sleep timing, DSWPD status; Hypothesis 1a), sleep disturbance (ISI, subjective and objective total sleep time, and subjective sleep quality; Hypothesis 1b), inhibition (SSRT; Hypothesis 1c), and stress reactivity (DISE, subjective stress response, HRV; Hypothesis 1d). Given that the goal sample size was not achieved, post-hoc power analyses were conducted for non-significant results to examine the effect of inadequate power.

Three 3-level multilevel models were tested to examine the effects of daily subjective and objective sleep duration and sleep timing on next day OCD symptoms. The ecological momentary assessment data was nested as follows: moments (Level 1) nested within days (Level 2) nested within participants (Level 3). Each of the 3 models included 1 sleep predictor (mid-sleep timing, subjective TST, or objective TST). Time (morning, afternoon, and evening) was modeled as a Level 1 predictor of momentary OCD symptoms. Day-level sleep, day-level stressors, and lagged day-level OCD symptoms (i.e., previous day's OCD symptoms), the interaction between day-level sleep and OCD status, and the interaction between day-level sleep and day-level stressors were modeled as Level 2 predictors of day-level OCD symptoms. All Level 2 predictors were person-mean centered, such that deviations from zero represent

deviations from the participant's own mean for a given day. Person-level sleep, person-level stressors, OCD status, participation before/after the onset of the COVID-19 pandemic, the interaction between person-level sleep and OCD status, and the interaction between person-level sleep and person-level stressors as Level 3 predictors of person-level OCD symptoms. The inclusion of inhibition as a Level 3 variable limited the sample to those who participated prior to the pandemic onset and reduced the sample size. Given that inhibition was unrelated to any variable in the models, this variable and its associated hypotheses were dropped to maximize sample size. All Level 3 predictors were grand mean centered, such that deviations from zero represent deviations from the sample mean. All models included a random intercept at Level 2 (varying across days within person) and Level 3 (varying across person) and fixed slopes. The intraclass correlations were 0.04 at Level 2 and 0.85 at Level 3. Full information maximum likelihood estimation was used.

Given that the sample size was smaller than planned due to the COVID-19 pandemic, a post-hoc power analysis was conducted to determine whether there was sufficient power to test the serial mediation model proposed in Hypothesis 3. Results of a Monte Carlo power analysis for indirect effects (https://schoemanna.shinyapps.io/mc_power_med/) for the model testing SSRT and subjective stress reactivity as serial mediators of the relationship between the MEQ and YBOCS (these variables were selected based on the size of their correlations) indicated a sample size of n=74 was vastly underpowered (power < .03) to detect the small observed effects. Hypothesis 3 was therefore modified to test sleep disturbance as a singular mediator of the relationship between circadian timing and OCD symptoms. Results of Monte Carlo power analyses for indirect effects indicated models testing the ISI as a mediator of the relationships between MEQ and DSWPD diagnosis and OCIR were best powered, though still somewhat

underpowered (power=.59 for both models), whereas models testing the ISI as a mediator of the relationships between MEQ and DSWPD diagnosis and YBOCS were slightly less powered (power=.58 and .43, respectively). Therefore, the former two mediation models were tested in Mplus using full-information maximum likelihood estimation. Participation before/after the onset of the COVID-19 pandemic was included as a covariate. The significance of the indirect effects was tested by constructing a bias-corrected bootstrapped confidence interval around the indirect effects.

Results

Descriptive statistics and associations between study variables

Descriptive statistics and associations between study variables are shown in Table 4.

Measure	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.
1. MEQ	--														
2. Mid-sleep	-.70**	--													
3. DSWPD	-.56**	.39**	--												
4. ISI	-.38**	.25*	.44**	--											
5. Obj TST	.16	-.34*	-.07	-.06	--										
6. Subj TST	.11	-.25*	.02	-.21	.78**	--									
7. Sleep quality	.13	-.03	-.17	-.34**	.11	.17	--								
8. SSRT	-.05	-.07	-.08	-.04	.10	.10	-.10	--							
9. DISE	.08	-.08	.14	.25*	.07	.05	-.23*	.12	--						
10. HRV Δ	.22	-.25	-.05	.20	-.05	-.25	-.40*	-.10	.43*	--					
11. SUDS Δ	-.07	-.09	-.09	.08	.04	-.05	.21	.13	.04	-.24	--				
12. Daily OCD	-.25*	.10	.26*	.50**	.39*	.13	.02	.13	.19	-.21	.24	--			
13. YBOCS	-.28*	.20	.35*	.33*	.05	.08	-.06	.23	.18	.17	.10	.47**	--		
14. OCIR	-.36*	.30*	.33*	.36*	.16	.02	.01	.14	.15	-.26	.02	.71**	.67**	--	
15. COVID	.22	-.26*	-.08	-.03	N/A	.28*	-.04	N/A	-.07	N/A	N/A	-.05	-.14	-.18	--
M	48.05	4.50		8.44	388.30	418.30	3.35	264.84	1.33	.14	9.70	6.70	13.38	16.59	
SD	12.18	1.35		5.01	61.41	64.27	.68	78.37	1.12	1.62	22.22	7.75	6.78	11.31	

Range	22-75	1.70-7.55		1-18	210.60-516.00	213.00-575.00	2-5	159.82-727.53	0-5.50	-2.77-5.20	-47-70	0-37.71	0-27	0-51	

Note. MEQ=Morningness-Eveningness Questionnaire; Mid-sleep=mid-sleep timing (decimal format); DSWPD=delayed sleep-wake phase disorder status; ISI=Insomnia Severity Index; Obj TST=objective total sleep time; Subj TST=subjective total sleep time; SSRT=Stop Signal reaction time; DISE=Daily Inventory of Stressful Events; HRV Δ=change in heart rate variability; SUDS Δ= change in subjective units of distress; YBOCS=Yale-Brown Obsessive-Compulsive Inventory; OCIR=Obsessive-Compulsive Inventory-Revised; COVID=participation before/after onset of COVID-19 pandemic.
$^{*}p < .05$ $^{**}p < .01$

Table 4. Descriptive statistics and correlations for study measures (n = 74).

Hypothesis 1a: Individuals with OCD will exhibit later circadian timing compared to healthy controls.

Results of between subject t-tests and a chi square analysis indicated later circadian timing in those with OCD compared to healthy controls. Specifically, those with OCD reported significantly lower morningness (i.e., higher eveningness) (M = 40.60, SD = 9.54) compared to healthy controls (M = 53.66, SD = 13.15), $t(47) = -3.80$, $p < .001$, $d = -1.10$, and significantly later mid-sleep timing (M = 4.93, SD = 1.21) compared to healthy controls (M = 4.02, SD = 1.33), $t(45) = 2.41$, $p < .05$, $d = .71$. There was also a significant relationship between OCD and DSWPD status, $\chi^2(2, n=49)=13.86$, $p<.001$, such that 40% of those with OCD also met criteria for DSWPD, relative to 0% of healthy controls.

Hypothesis 1b: Individuals with OCD will exhibit increased sleep disturbance compared to healthy controls.

Results of between subject t-tests largely did not indicate increased sleep disturbance in those with OCD compared to healthy controls. Specifically, those with OCD did not report significantly different subjective total sleep time (M = 411.44, SD = 71.19) compared to healthy controls (M = 426.34, SD = 61.70), $t(45) = -.77$, $p = .45$, $d = -.23$, objective total sleep time (M = 387.43, SD = 77.06) compared to healthy controls (M = 403.12, SD = 55.42), $t(27) = -.63$, $p = .53$, $d = -.24$, or sleep quality (M = 3.28, SD = .58) compared to healthy controls (M = 3.45, SD = .66), $t(45) = -.93$, $p = .36$, $d = -.27$. Results of post-hoc power analyses indicated inadequate power to detect a significant effect for objective total sleep time (power = .10), subjective total sleep time (power = .12), or sleep quality (power = .15). However, those with OCD did report

significantly higher insomnia symptoms (M = 11.10, SD = 5.03) compared to healthy controls (M = 5.90, SD = 4.22), $t(47) = 3.92$, $p < .001$, $d = 1.14$.

Hypothesis 1c: Individuals with OCD will exhibit decreased inhibition compared to healthy controls.

Results of a between subject t-test did not indicate decreased inhibition in those with OCD compared to healthy controls. Specifically, those with OCD did not exhibit significantly different SSRT (M = 286.16, SD = 129.50) compared to healthy controls (M = 261.06, SD = 43.98), $t(30) = .75$, $p = .46$, $d = .27$. Results of a post-hoc power analysis indicated inadequate power to detect a significant effect of inhibition (power = .11).

Hypothesis 1d: Individuals with OCD will exhibit increased stress compared to healthy controls.

Results of between subject t-tests did not indicate increased stress in those with OCD compared to healthy controls. Specifically, those with OCD did not report significantly different number of daily stressors (M = 1.43, SD = 1.05) compared to healthy controls (M = 1.33, SD = 1.33), $t(46) = .28$, $p = .79$, $d = .08$. Results of post-hoc power analyses indicated inadequate power to detect a significant effect for number of daily stressors (power = .76).

The assumption of sphericity was violated for the 2 (diagnostic status) x 4 (time) repeated measures ANOVA to examine subjective stress reactivity in response to the speech anticipation task; therefore, the Greenhouse-Geisser correction was utilized. There was a significant main effect of time, F (2.16, 64.74) = 17.80, $p < .001$, $\eta^2_p = .37$. Post-hoc tests using Bonferroni correction found that SUDS increased significantly from baseline to after the 2-minute speech preparation period, $p < .001$, and from baseline to after the 5-minute waiting period, $p < .05$, suggesting the onset of the stressor successfully elicited subjective stress. There was not a

significant change in SUDS between the 2-minute speech preparation period and the 5-minute waiting period, $p = 1.0$. There was a significant decrease in SUDS from after the 5-minute waiting period to after the 5-minute recovery period, $p < .001$, and no difference in SUDS between baseline and after the 5-minute recovery period, $p = .10$, suggesting a return to baseline following the offset of the stress task. There was also a significant main effect of diagnostic status, $F(1, 30) = 5.34$, $p < .05$, $\eta^2_p = .15$, indicating that the OCD group reported increased subjective stress overall. However, there was not a significant diagnostic status by time interaction, $F(2.16, 64.74) = .28$, $p = .77$, $\eta^2_p = .009$, indicating that those with OCD and healthy controls did not differ in subjective stress reactivity. Results of post-hoc power analyses indicated inadequate power to detect a significant effect for the diagnostic status x time interaction (power = .05).

Results of a 2 (diagnostic status) x 4 (time) repeated measures ANOVA to examine objective stress reactivity in response to the speech anticipation task did not reveal a significant main effects of time, $F(3, 39) = 1.29$, $p = .29$, $\eta^2_p = .09$, indicating the task did not elicit objective stress. There was also not a significant main effect of diagnostic status, $F(1, 13) = .83$, $p = .38$, $\eta^2_p = .06$, indicating no difference between the OCD group and healthy controls in overall object stress. There was also not a significant interaction between diagnostic status and time, $F(3, 39) = 1.25$, $p = .31$, $\eta^2_p = .09$, indicating that those with OCD and healthy controls did not differ in objective stress reactivity. Results of post-hoc power analyses indicated inadequate power to detect a significant effect for the diagnostic status x time interaction (power = .11).

Hypothesis 2a: Decreased daily sleep duration will predict increased next day OCD symptoms.

All regression coefficients are reported as unstandardized values. There was not a significant conditional main effect of subjective or objective sleep duration on next day OCD symptoms. However, in both models, there was a conditional main effect of daily stressors, such that increased daily stressors were associated with increased daily OCD symptoms (see Tables 5 & 6).

Model 1 Objective Sleep Duration				
Fixed Effects	Predictor	Est	SE	*p*
Level 1 (Moment level)	Time of day	.43	.14	<.01
Level 2 (Day level)	Sleep	.003	.003	.34
	Stress	.40	.17	<.05
	Lagged OCD symptoms	.23	.07	<.01
	Stress x Sleep	.002	.002	.39
	OCD x Sleep	<.001	.005	.98
Level 3 (Person level)	Sleep	.005	.02	.79
	Stress	1.06	1.06	.31
	OCD	7.22	2.02	<.001

	Stress x Sleep	-.02	.02	.31
	OCD x Sleep	.11	.03	<.001
Variance components				
Level 1	Residual variance	9.70	.64	<.001
Level 2	Intercept variance	2.61	.64	<.001
Level 3	Intercept variance	38.06	7.90	<.001

Note. OCD=Obsessive-compulsive disorder.

Table 5. Unstandardized model coefficients for the hypothesized multilevel model predicting OCD symptoms from daily and average objective sleep duration (n = 50).

Model 2 Subjective Sleep Duration				
Fixed Effects	Predictor	Est	SE	*p*
Level 1 (Moment level)	Time of day	.49	.12	<.001
Level 2 (Day level)	Sleep	.001	.002	.55
	Stress	.26	.13	<.05

	Lagged OCD symptoms	.20	.06	<.001
	Stress x Sleep	.003	.001	.05
	OCD x Sleep	-.002	.003	.50
Level 3 (Person level)	Sleep	.01	.02	.45
	Stress	1.04	.80	.19
	OCD	8.17	1.82	<.001
	COVID	-1.69	1.87	.36
	Stress x Sleep	-.01	.02	.46
	OCD x Sleep	.03	.03	.26
Variance components				
Level 1	Residual variance	9.36	.51	<.001
Level 2	Intercept variance	2.16	.49	<.001
Level 3	Intercept variance	4.05	.96	<.001

Note. OCD=Obsessive-compulsive disorder.

Table 6. Unstandardized model coefficients for the hypothesized multilevel model predicting OCD symptoms from daily and average subjective sleep duration (n = 72).

Hypothesis 2b: Later daily sleep timing will predict increased next day OCD symptoms.

There was not a significant conditional main effect of mid-sleep timing on next day OCD symptoms. However, there was a trend-level conditional main effect of daily stressors, such that increased daily stressors were associated with increased daily OCD symptoms (see Table 7).

Model 3 Mid-sleep timing				
Fixed Effects	Predictor	Est	SE	*p*
Level 1 (Moment level)	Time of day	.49	.12	<.001
Level 2 (Day level)	Sleep	.11	.17	.50
	Stress	.26	.13	.05
	Lagged OCD symptoms	.21	.06	<.001
	Stress x Sleep	.08	.45	.65
	OCD x Sleep	-.48	.32	.13
Level 3 (Person level)	Sleep	.39	.70	.58
	Stress	1.85	.76	<.05
	OCD	7.18	1.77	<.001

	COVID	-1.51	1.82	.41
	Stress x Sleep	1.83	.49	<.001
	OCD x Sleep	-2.79	1.44	.05
Variance components				
Level 1	Residual variance	9.33	.51	<.001
Level 2	Residual variance	2.25	.49	<.001
Level 3	Residual variance	37.96	6.57	<.001

Note. OCD=Obsessive-compulsive disorder.

Table 7. Unstandardized model coefficients for the hypothesized multilevel model predicting OCD symptoms from daily and average sleep timing (n = 72).

Hypothesis 2c: The effects of daily sleep duration and timing on next day OCD symptoms will be moderated by OCD status.

At the day-level, OCD status did not moderate the effect of daily sleep duration or timing on next day OCD symptoms (see Tables 5-7). That is, the effect of last night's sleep duration and timing on next day OCD symptoms did not differ between those with and without OCD.

At the person-level, OCD status significantly moderated the effect of average objective sleep duration on OCD symptoms. However, contrary to hypotheses, simple slopes analysis revealed a significant relationship between *increased* average objective sleep duration and

increased OCD symptoms among those with OCD, B = .11, SE = .02, $p < .001$. Average objective sleep duration was unrelated to OCD symptoms among those without OCD, $p > .05$ (see Figure 12). OCD status did not significantly moderate the effect of average subjective sleep duration on OCD symptoms (see Table 6).

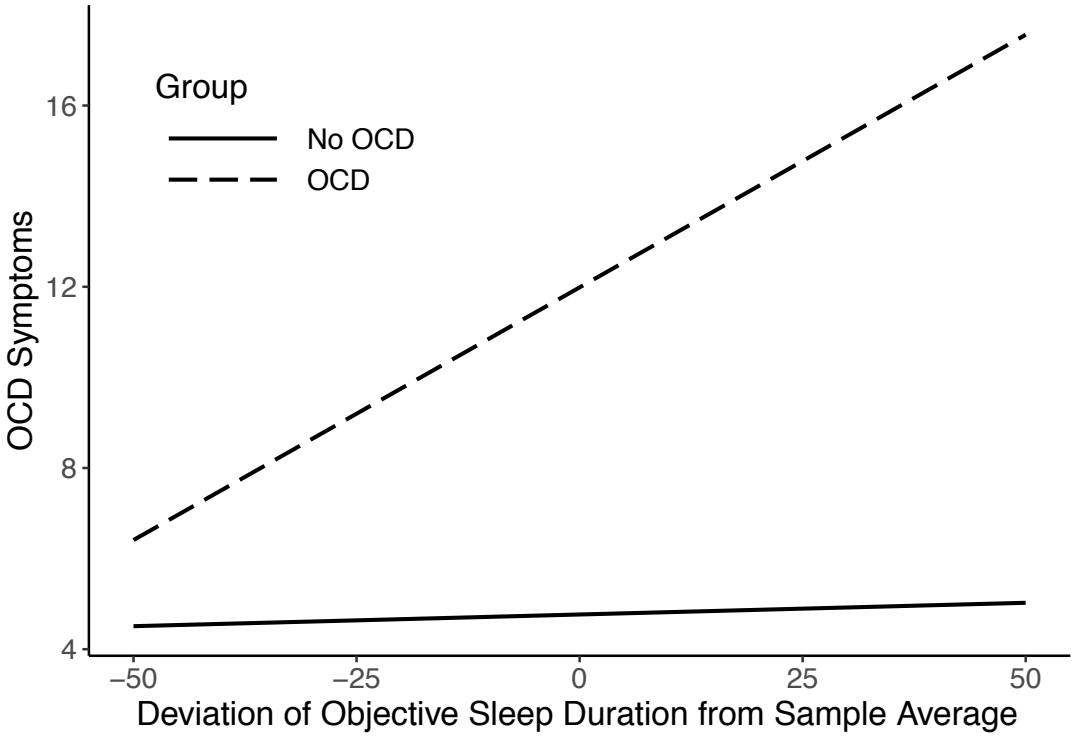

Figure 12. Simple regression slopes of person-level objective sleep duration predicting obsessive-compulsive disorder (OCD) symptoms in those with and without OCD, controlling for participation before/after the onset of the COVID-19 pandemic. Objective sleep duration was grand-mean centered prior to analysis.

At the person-level, there was a trend-level interaction between OCD status and average sleep timing on OCD symptoms (see Table 7). However, contrary to hypotheses, simple slopes analysis revealed a trend-level relationship between *later* average sleep timing and *decreased* OCD symptoms among those with OCD, B = -2.40, SE = 1.22, $p = .05$. Average sleep timing was unrelated to OCD symptoms among those without OCD, $p > .05$ (see Figure 13).

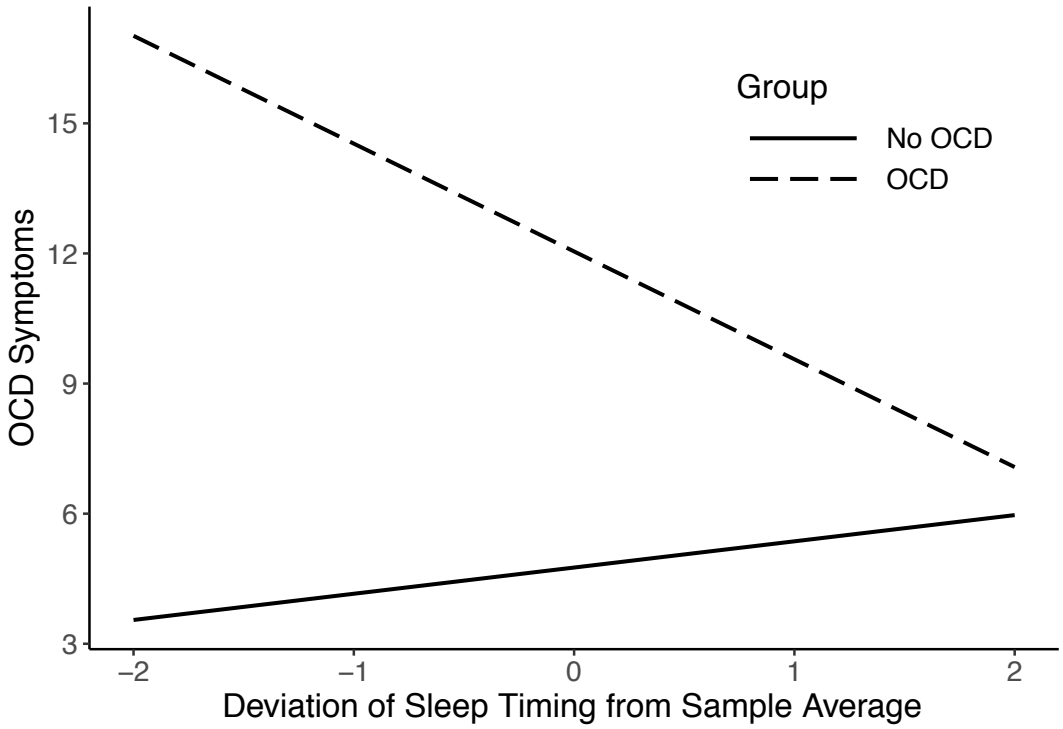

Figure 13. Simple regression slopes of person-level sleep timing predicting obsessive-compulsive disorder (OCD) symptoms in those with and without OCD, controlling for participation before/after the onset of the COVID-19 pandemic. Sleep timing was grand-mean centered prior to analysis.

Hypothesis 2e: The effects of daily sleep duration and timing on next day OCD symptoms will be moderated by daily stressors.

At the day-level, there was a trend-level interaction between subjective sleep duration and stressors to predict OCD symptoms (see Table 6). However, simple slopes analysis did not reveal a significant relationship between subjective sleep duration and OCD symptoms at low, moderate, or high levels of stressors, *p*'s > .05. Daily stressors did not moderate the effect of objective sleep duration or timing on next day OCD symptoms (see Tables 5-7). That is, the effect of last night's objective sleep duration and sleep timing on next day OCD symptoms did not vary by whether the individual experienced more or fewer stressors that day than was typical for them on average.

At the person-level, average daily stressors did not moderate the effect of average sleep duration on OCD symptoms. However, there was a significant interaction between average daily stressors and average sleep timing (see Table 7). Simple slopes analysis revealed a significant relationship between later sleep timing and increased OCD symptoms among those with higher average stressors, B = 2.23, SE = .80, $p < .05$. Sleep timing was unrelated to OCD symptoms among those with moderate and low average stressors, p's > .05 (see Figure 14).

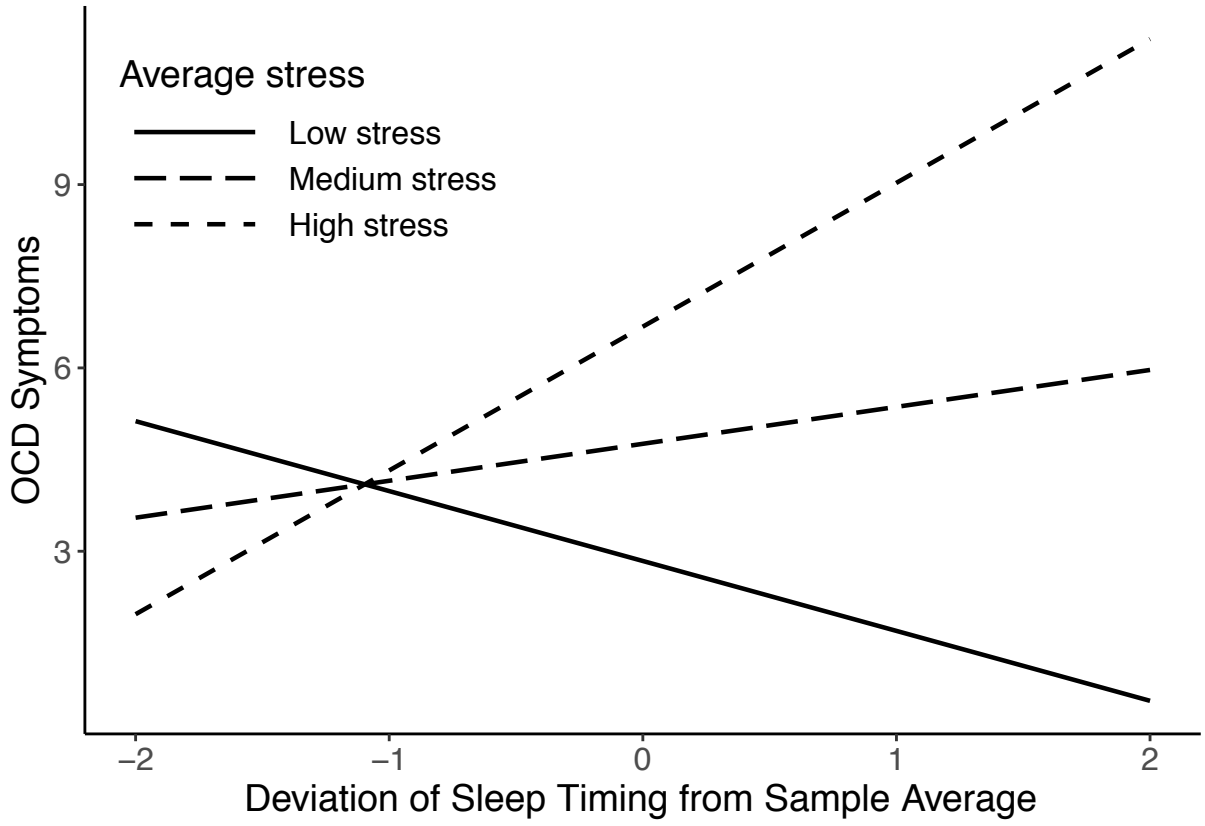

Figure 14. Simple regression slopes of person-level sleep timing predicting OCD symptoms at values of person-level daily stressors, controlling for participation before/after the onset of the COVID-19 pandemic. Sleep timing and daily stressors were grand mean-centered prior to analysis. Low, medium, and high represent the daily stressors sample mean +/- one standard deviation.

Hypothesis 3: The relationship between circadian timing and OCD symptoms will be mediated by sleep disturbance.

All regression coefficients are reported as unstandardized values. Results of model 1 utilizing MEQ as the indicator of circadian timing found that eveningness significantly predicted OCD symptoms through its effects on insomnia symptoms, controlling for participation before/after the onset of the COVID-19 pandemic. Eveningness significantly predicted insomnia symptoms ($a = -.21$, $p < .05$), which in turn significantly predicted OCD symptoms ($b = .60$, $p < .05$). A 95% confidence interval of the indirect effect ($ab = -.10$) based on 10,000 bootstrap samples did not contain zero (-.24 to -.02), indicating a significant mediating effect of insomnia symptoms in the relationship between eveningness and OCD symptoms (see Table 8, Figure 15).

	ISI (M)			**OCIR (Y)**		
Predictor	**B**	**SE**	***p***	**B**	**SE**	***p***
MEQ (X)	-.16	.05	<.001	-.21	.10	<.05
ISI (M)				.60	.26	<.05
COVID (covariate)	.65	1.34	.63	-3.03	2.81	.28
	$R^2 = .15$, $p = .06$			$R^2 = .20$, $p < .01$		

Note. MEQ = Morningness-Eveningness Questionnaire; ISI = Insomnia Severity Index; OCIR = Obsessive-Compulsive Inventory-Revised; COVID = participated before/after the onset of the COVID-19 pandemic.

Table 8. Unstandardized model coefficients for the hypothesized mediation model with MEQ as the indicator of eveningness ($n = 77$).

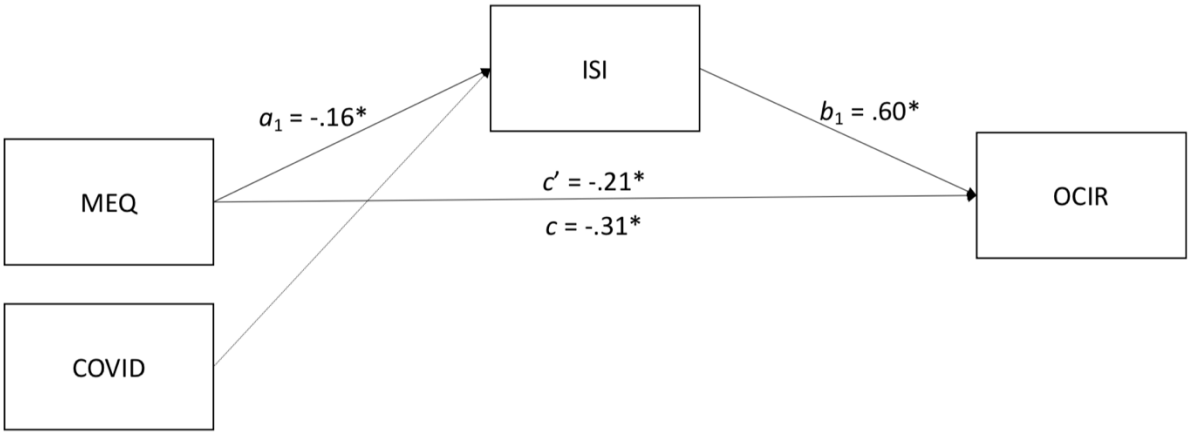

Figure 15. Unstandardized path coefficients for the hypothesized mediation model, in which insomnia symptoms significantly mediate the relationship between later circadian timing (indicated by the Morningness-Eveningness Questionnaire) and OCD symptoms, controlling for participation before/after the onset of the COVID-19 pandemic (n = 77). * p < .05.

Results of model 2 utilizing DSWPD diagnosis as the indicator of circadian timing likewise found that DSWPD significantly predicted OCD symptoms through its effects on insomnia symptoms, controlling for participation before/after the onset of the COVID-19 pandemic. DSWPD significantly predicted insomnia symptoms (a = 6.23, p < .001), which in turn significantly predicted OCD symptoms (b = .62, p < .05). A 95% confidence interval of the indirect effect (ab = 3.89) based on 10,000 bootstrap samples did not contain zero (.99 to 8.53), indicating a significant mediating effect of insomnia symptoms in the relationship between DSWPD and OCD symptoms (see Table 9, Figure 16).

	ISI (M)			OCIR (Y)		
Predictor	**B**	**SE**	***p***	**B**	**SE**	***p***
DSWPD (X)	6.23	1.35	<.001	5.97	23.87	.12
ISI (M)				.62	.23	<.05
COVID (covariate)	.10	1.30	.94	-4.19	2.80	.13

	$R^2 = .19, p < .05$	$R^2 = .19, p < .05$

Note. DSWPD = Delayed sleep-wake phase disorder diagnosis; ISI = Insomnia Severity Index; OCIR = Obsessive-Compulsive Inventory-Revised; COVID = participated before/after the onset of the COVID-19 pandemic.

Table 9. Unstandardized model coefficients for the hypothesized mediation model with DSWPD as the indicator of eveningness (n = 76).

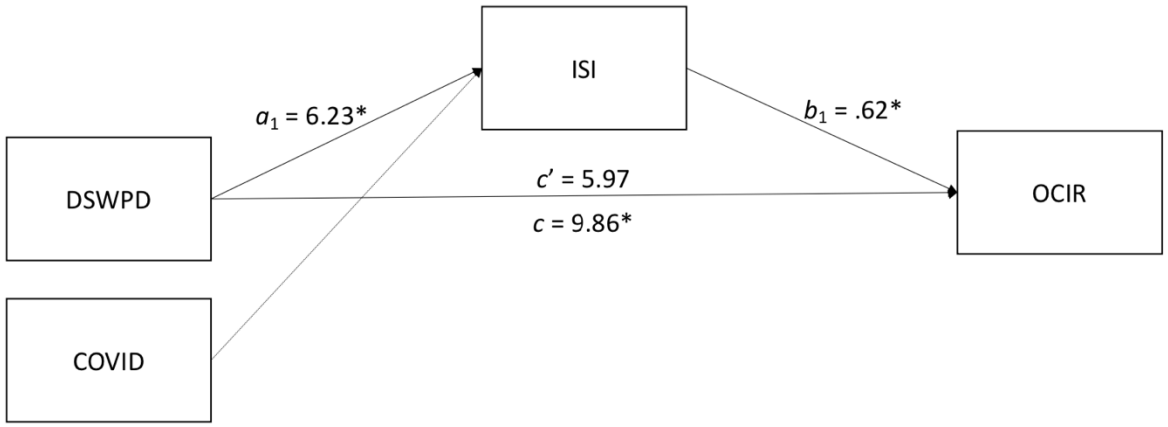

Figure 16. Unstandardized path coefficients for the hypothesized mediation model, in which insomnia symptoms significantly mediate the relationship between later circadian timing (indicated by the delayed sleep-wake phase disorder diagnosis) and OCD symptoms, controlling for participation before/after the onset of the COVID-19 pandemic (n = 76). * $p < .05$.

Study 2 Discussion

Results of Study 2 found support for the hypothesis that those with OCD would exhibit later circadian timing compared to healthy controls. Indeed, later circadian timing in OCD was observed across multiple measures, including morningness-eveningness, mid-sleep timing, and DSWPD status. These findings are consistent with previous research linking indicators of delayed circadian timing to OCD symptoms, including eveningness (Cox, Tuck, et al., 2018), dim light melatonin onset, and DSWPD status (Coles et al., 2020). Though previous work has linked later bedtimes to OCD symptoms (Nota et al., 2020), this is the first study to find later

mid-sleep in those with OCD compared to controls. Mid-sleep is a better indicator of sleep timing, as it reflects the timing of the total sleep period. Further, the large effect sizes found across multiple indicators of circadian timing suggest a robust effect for delayed circadian timing in OCD compared to healthy controls. Likewise, the present finding that 40% of those with OCD also met criteria for DSWPD replicates previous studies finding an almost identical rate of DSWPD in OCD (i.e., 40-42%; M. E. Coles et al., 2020; Turner et al., 2007), again suggesting the robustness of the present findings.

There was partial support for the hypothesis that those with OCD would exhibit increased sleep disturbance compared to healthy controls. Specifically, there was a large significant difference found for insomnia symptoms, such that those with OCD reported increased insomnia symptoms compared to healthy controls. This study is the first to compare insomnia symptom severity between those with OCD and healthy controls, though previous research has found significant associations between insomnia symptoms and OCD symptoms in clinical (Sevilla-Cermeño et al., 2019, 2020) and nonclinical samples (Raines et al., 2015; Timpano et al., 2014). In contrast, there were no significant differences found between those with OCD and healthy controls on objective or subjective sleep duration or sleep quality. Given that there was inadequate power to detect small effects for sleep duration and sleep quality, it is difficult to interpret these discrepant findings. The large effect found for insomnia symptoms may reflect general distress among those with OCD, as the ISI includes items assessing distress and impairment. Such distress may also contribute to retrospective bias that inflates the ISI score, such that those with OCD overestimate sleep disturbance when describing their sleep over the past 2 weeks. Prospective sleep monitoring, as with the CSD and actigraphy, may then yield more accurate results that are not subject to retrospective bias. Interestingly, the extant literature

comparing those with OCD to healthy controls on various measures of sleep disturbance is also mixed. While one study found increased sleep disturbance on the Pittsburgh Sleep Quality Index (PSQI) among those with OCD compared to healthy controls (Donse et al., 2017), another study found group differences in PSQI were better accounted for by comorbid depression (Bobdey et al., 2002). Further, only one study to date has utilized sleep diaries to prospectively monitor subjective sleep and found no differences in subjective sleep duration between those with OCD and healthy controls (Coles et al., 2020). In contrast, results from our recent meta-analysis found a large effect for decreased objective sleep duration in those with OCD compared to healthy controls (Cox & Olatunji, 2020), and this effect was not accounted for by comorbid depression. This finding suggests that subjective distress may not wholly explain the group differences observed on the ISI. Given insufficient power, additional research utilizing multiple measures of sleep is needed to characterize possible sleep disturbance in OCD.

The present study did not find support for the hypothesis that those with OCD would exhibit decreased inhibition compared to healthy controls. Several previous studies have found evidence for decreased inhibition in those with OCD using the Stop Signal Task, and a recent meta-analysis found a moderate effect size for increased SSRT in those with OCD compared to controls (Snyder et al., 2015). Thus, the present null finding is likely due to insufficient power. Still, it is worth noting that an effect for increased SSRT has not been consistently found in OCD (Kalanthroff et al., 2017), and future studies may benefit from incorporating multiple measures of inhibitory control.

The present study did not find support for the hypothesis that those with OCD would experience increased daily stressors and increased subjective and objective stress reactivity compared to healthy controls. Post-hoc power analyses found insufficient power to detect small

effects on these variables. There was particularly low power for the stress reactivity task, which could not be completed following the onset of the COVID-19 pandemic. The extant research on the role of stress in OCD is relatively limited. Though research has linked stressful life events to the onset of OCD (Real et al., 2011; Rosso et al., 2012), no study to date has examined the number of daily stressors in those with OCD compared to healthy controls. In addition to being underpowered, the onset of the COVID-19 pandemic may have further masked any group differences in number of daily stressors between those with OCD and healthy controls. Further, findings regarding stress reactivity are mixed. Though some studies have found heightened cortisol reactivity and subjective stress in response to a stressor among women with postpartum OCD (Lord et al., 2011, 2012), one found a blunted response among children with OCD (Gustafsson et al., 2008), and another study found no differences between adults with OCD and healthy controls on cortisol reactivity or HRV in response to a stressor (Kawano et al., 2013). Notably, these studies also utilized varying stress tasks, including a modified Trier Social Stress Task (TSST), a cold-pressor task, exposure therapy, and electrical shock, respectively, highlighting how different stress tasks can elicit different stress responses. In the present study, the use of an anticipatory stress task may have also contributed to the null findings, as merely anticipating (rather than experiencing) the stressor may have been insufficiently stressful and/or the deception involved in the task may not have been believable. Indeed, although the speech anticipation task did successfully increase subjective stress in the full sample, there was not a significant change in HRV throughout the task, suggesting this task may not be as potent as the gold-standard TSST.

Results from the multilevel models did not find support for a relationship between last night's sleep duration or timing and next day OCD symptoms. These results are inconsistent with

extant research utilizing ecological momentary assessment to examine the relationship between daily sleep and anxiety-related symptoms. Indeed, one of our earlier studies found that decreased objective and subjective sleep duration predicted increased anxiety the following day, controlling for the previous day's anxiety (Cox, Sterba, et al., 2018). Other ecological momentary assessment studies have found similar effects of last night's sleep on next day anxiety (Kalmbach et al., 2017), worry in generalized anxiety disorder (Thielsch et al., 2015), and PTSD symptoms in PTSD (Short et al., 2017). However, these findings are partially consistent with the one study to date that utilized an ecological momentary assessment approach to examine the effects of night's sleep duration and timing on next day OCD symptoms, which likewise found no main effects of subjective sleep duration or bedtimes in a sample of those with OCD and healthy controls (Schubert et al., 2019). Together these findings suggest that OCD symptoms may be less sensitive to daily variability in sleep duration and timing than general anxiety or worry.

However, Schubert et. al. (2019) did find an interaction between bedtimes and OCD status, such that later bedtimes predicted increased OCD symptoms in those with OCD. The present study found no such interaction at the daily level and an opposite and unexpected trend-level interaction at the person level, such that later average mid-sleep was associated with *decreased* average OCD symptoms among those with OCD, but was unrelated to OCD symptoms in those without OCD. Further, Schubert et al. (2019) found no interaction between subjective sleep duration and OCD symptoms. The present study likewise found no interactions for subjective sleep duration but did find a significant and unexpected interaction between objective sleep duration and OCD status at the person level, such that *increased* average objective total sleep time was associated with *increased* average OCD symptoms among those with OCD, but was unrelated to OCD symptoms among those without OCD. Given the high rate

of DSWPD in the OCD group (i.e., 40%), the relationship between later sleep timing and decreased OCD symptoms in the OCD group may indicate better functioning among those who are able to sleep on a schedule consistent with their later circadian timing. In this case, later sleep timing may represent *decreased* circadian misalignment, which is then associated with better functioning. The finding that increased average objective total sleep time was associated with increased average OCD symptoms in the OCD group is in apparent contradiction with our earlier meta-analysis finding decreased objective sleep duration in OCD compared to controls. Measurement issues may partially account for the discrepancies between these findings and the findings of Schubert et al. (2019). The present study utilized a 15-item OCD measure which included a disproportionate number of contamination items (Macatee et al., 2013), whereas Schubert et al. (2019) used simpler visual analogue scales assessing obsessions/compulsions frequency, distress, and control. The latter represents a lower burden measure which may be more suitable for capturing momentary OCD symptoms. Further, although participation before/after the COVID-19 pandemic was included as a covariate, the high number of contamination items in the daily OCD symptom measure may have captured adaptive responses to the pandemic and masked potential associations between our predictors and non-pandemic OCD symptoms.

In contrast, there was evidence for a significant main effect of daily stressors, such that increased number of daily stressors was associated with increased daily OCD symptoms. A significant effect at the person level was also found in the sleep timing model, indicating that increased average number of stressors over the week was associated with increased average OCD symptoms over the week. Though few studies have examined the role of daily stress in OCD, one study likewise found an association between increased number of daily stressors and

increased daily OCD symptoms in an unselected sample (Macatee et al., 2013). Together these findings suggest that daily OCD symptoms may be exacerbated by experiencing naturalistic daily life stressors. Further, week-average sleep timing significantly interacted with week-average stressors to predict week-average OCD symptoms, such that the highest average OCD symptoms were reported by those who reported later average sleep timing and more stressors over the duration of the week. This finding suggests that the effect of sleep timing may depend on context. For example, those experiencing a particularly stressful week may attempt to compensate by shifting their sleep period later, which may then result in increased OCD symptoms.

The hypothesis that sleep disturbance would mediate the relationship between later circadian timing and OCD symptoms was supported by two mediation models using eveningness and DSWPD status as the indicators of circadian timing and insomnia symptoms as the indicator of sleep disturbance, controlling for participation before/after the onset of the COVID-19 pandemic. Both eveningness and DSWPD significantly predicted increased insomnia symptoms. Eveningness has consistently been associated with sleep disturbance, including insomnia symptoms (Merikanto et al., 2012), increased daily variability in sleep (Bei et al., 2016), and general sleep disturbance (Suh et al., 2017). Likewise, insomnia symptoms are one of the diagnostic criteria for DSWPD (American Psychiatric Association, 2013), and previous studies have found high rates of insomnia in DSWPD (Sivertsen et al., 2013), as well as increased sleep onset latency (Micic et al., 2016) and variability in sleep duration and timing (Burgess et al., 2017). Later circadian timing may interfere with sleep through several mechanisms. Insomnia symptoms may develop among those with later circadian timing who are attempting to initiate sleep at an earlier time that is inconsistent with their internal circadian phase. Those with later

circadian timing may also attempt to fit their sleep timing to environmental demands during the week (e.g., the need be at work by 8:00am) and then sleep on a schedule that is more consistent with their internal circadian phase on the weekends. Such variability in sleep timing may then contribute to insomnia symptoms by interfering with consistent circadian entrainment (e.g., morning light exposure is received at variable times) and/or contributing to variability in homeostatic sleep pressure on subsequent nights.

Insomnia symptoms also significantly predicted increased OCD symptoms, which is consistent with previous research implicating sleep disturbance in OCD (Cox, Jessup, et al., 2018; Nota et al., 2015). Extant research has also linked insomnia symptoms to increased OCD symptoms in unselected samples (Raines et al., 2015; Timpano et al., 2014), including evidence for a predictive effect of insomnia symptoms on increased OCD symptoms over time (Cox, Cole, et al., 2018; Cox, Tuck, et al., 2018). This study is the first to show an association between insomnia symptoms and OCD symptoms in a sample that includes individuals with OCD, indicating that previous findings in unselected samples also extend to clinical samples. Insomnia is associated with a wide range of daytime consequences that may contribute to increased OCD symptoms, including depression and general anxiety symptoms (Hellberg et al., 2019), emotion dyresgulation (Palagini et al., 2017), and impaired cognitive function, including working memory, episodic memory, and problem solving (Wardle-Pinkston et al., 2019).

In both models, the effects of eveningness and DSWPD on increased OCD symptoms were significantly mediated by insomnia symptoms. Our previous work found a similar mediating effect between eveningness and OCD symptoms over 6 months in a sample of unselected adults (Cox, Tuck, et al., 2018), and the present finding extends this to a clinical sample. Further, though previous research has linked DSWPD to psychopathology broadly (Reid

et al., 2012) and OCD specifically (Coles et al., 2020), this study offers the first is evidence for the mediating role of insomnia in this relationship. These mediation models suggest that later circadian timing may contribute to increased OCD symptoms through its effect on sleep. For example, those with later circadian timing may experience insomnia symptoms or poor sleep quality when attempting to sleep on a schedule that is misaligned with their circadian phase. These sleep disturbances may then confer vulnerability for increased OCD symptoms. This interpretation is supported by prior research showing that sleep disturbance mediates the effect of eveningness on mental health outcomes, including depression and anxiety symptoms (Dickinson et al., 2018; Merikanto & Partonen, 2021; Zhou et al., 2021). These findings integrate the developing literatures linking delayed circadian rhythms and sleep disturbance to OCD.

Though the ecological momentary assessment findings did not indicate a proximal effect of daily sleep duration and timing on daily OCD symptoms, there was robust evidence for delayed circadian timing and increased insomnia symptoms in OCD, as well as evidence for a mediating role of insomnia symptoms in the relationship between later circadian timing and increased OCD symptoms. These findings have important clinical implications for the assessment and treatment of OCD. First, sleep and circadian timing should be assessed in OCD patients. Indeed, the finding that 40% of the OCD group met criteria for DSWPD suggests that DSWPD is an important yet overlooked OCD comorbidity. These findings suggest a significant piece of the clinical presentation is missing if these processes are not evaluated in OCD patients, as recent studies suggest sleep disturbance predicts worse treatment outcome in both children and adults with OCD (Donse et al., 2017; Ivarsson & Skarphedinsson, 2019). Further, targeting sleep and circadian rhythms may improve OCD treatment efficacy. Indeed, one recent study found that inpatient OCD treatment facilities that programs with a set “lights out” time have a

higher rate of treatment response (Coles & Stewart, 2019). Another recent study examining the efficacy of a sleep and circadian intervention in evening type adolescents found that reduced eveningness mediated the impact of the treatment on multiple aspects of overall health, including emotional health (Dong et al., 2019). No study to date has examined the impact of sleep interventions on OCD symptoms. However, previous meta-analyses indicate that CBTI is associated general anxiety (Belleville et al., 2011) and PTSD symptom reduction (Ho et al., 2016), suggesting that targeting insomnia symptoms in OCD treatment may have similar effects.

The present study largely found evidence for roles of later circadian timing and insomnia symptoms in OCD, whereas there was no evidence for an effect of last night's sleep duration and timing on next day OCD symptoms. However, these findings should be considered within the context of the study limitations. First and most notably, the onset of the COVID-19 pandemic prohibited achieving the desired sample size and resulted in approximately 1/3 of the sample participating virtually. Several hypotheses of interest were limited by lack of power, particularly regarding inhibition and stress reactivity. Further, the low number of healthy controls recruited prior to the pandemic precluded the ability to consider pre/post pandemic onset in the group comparison analyses. Although dimensional analyses included pre/post pandemic onset as a covariate, it is possible that the unprecedented nature of a global pandemic impacted these results over and above what could be accounted for by this covariate. Second, though multiple indicators of circadian timing were utilized, we did not include an objective measure of circadian phase, such as dim light melatonin onset, which may better capture physiological circadian rhythms. Third, a large number of participants were excluded from the HRV analyses due to equipment failure or low quality recordings, which further contributed to the problem of low power. Fourth, the sample was disproportionately female, making the degree to which these

findings apply to males unclear. Fifth, the lack of an experimental manipulation precludes the ability to make a causal inference regarding the direction of the relationships between later circadian timing, insomnia symptoms, and OCD. Despite these limitations, this study offers additional support for later circadian timing and increased insomnia symptoms in those with OCD and provides the first evidence for a mediating role of insomnia symptoms in the relationship between later circadian timing and OCD symptom severity.

Chapter IV

Conclusions and Future Directions

Results of Study 1 suggest that decreased inhibition is associated with increased OCD symptoms and intrusive cognition following sleep loss, particularly among those with lower sleep efficiency prior to sleep restriction. However, there was no evidence for decreased inhibition and increased OCD symptoms following sleep restriction, nor evidence for a role of stressors in OCD symptoms following sleep restriction. Study 2 found later circadian timing and increased insomnia symptoms in those with OCD compared to healthy controls, as well as a mediating effect of insomnia symptoms in the relationship between later circadian timing and increased OCD symptoms in the full sample. In contrast to Study 1, Study 2 also found that later sleep timing was associated with increased daily OCD symptoms among those who experienced more daily stressors over 1 week. Taken together, these findings suggest that later circadian timing and sleep disturbance may contribute to increased OCD symptoms and are associated with OCD status and symptom severity. These studies offer support for the pathways in the proposed model linking delayed circadian rhythms to OCD through the effect of sleep disturbance (see Figure 17). These studies also offer modest support for the roles of inhibition and stress as potential mechanisms linking sleep and circadian disruption to OCD, though it remains unclear whether the possible effects of inhibition and stress occur in a pathway downstream of delayed circadian rhythms and sleep disturbance, as suggested in the proposed model (see Figure 17). Additional research is needed to further test the potential mediating roles of inhibition and stress in the pathway from delayed circadian timing to sleep disturbance to OCD symptoms.

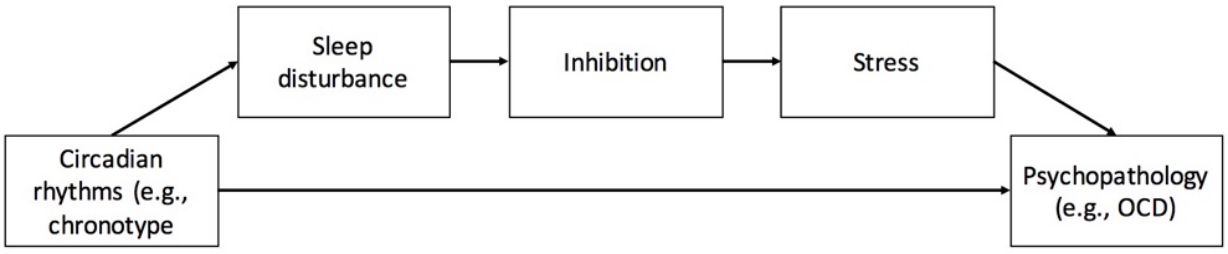

Figure 17. Proposed model linking circadian rhythms to OCD through the intervening effects of sleep disturbance, inhibition, and stress.

The results of these studies raise several interesting questions for future research. First, evidence for links between sleep and anxiety-related outcomes suggests that the neural mechanisms of sleep may offer insight into the neural mechanisms of anxiety disorders. Indeed, the locus coeruleus, a key neural region in the regulation of wake and NREM sleep, is also known to project to regions associated with anxiety and fear, including the amygdala, hypothalamus, and prefrontal cortex (Sullivan et al., 1999). More recently, orexin, which is involved in signaling arousal and suppressing REM sleep, has been implicated in promoting fear learning and impairing extinction (Flores et al., 2014; Sears et al., 2013). Together these findings suggest the utility of exploring the roles of known neural mechanisms of sleep in anxiety disorders, including OCD.

These findings also raise interesting questions about circadian misalignment; that is, desynchrony in the timing of sleep vs the timing of circadian phase. Circadian misalignment may account for the associations between later circadian timing and OCD observed in Study 2. Likewise, if circadian misalignment underpins the effect of later circadian timing, this may explain the unexpected finding that later sleep timing was associated with decreased OCD symptoms among the OCD group. That is, later daily sleep timing may reduce misalignment by

increasing the match between sleep timing and circadian phase. Future research sampling sleep timing and dim light melatonin onset is needed to clarify the role of circadian misalignment in OCD.

Another interesting area for future research involves the role of entrainment cues in OCD. Entrainment cues are stimuli in the external environment that facilitate synchronization of circadian phase with the 24-hour light/dark cycle and include light exposure, exercise, social contact, and eating (Mistlberger & Skene, 2005). Exposure to entrainment cues varies by chronotype, and previous findings indicate more irregular social rhythms (Martin et al., 2012) and decreased light exposure (Martin et al., 2012; Van der Maren et al., 2018) in evening chronotypes. Future research sampling entrainment cues in those with OCD would offer a more thorough characterization of the role of circadian rhythms in OCD and could identify additional circadian-related targets for intervention.

These findings also suggest the utility of examining OCD symptoms during phases of life characterized by sleep and circadian rhythm disruption. One such phase is adolescence, during which time circadian rhythms and sleep/wake timing shift later (Crowley et al., 2007; R. W. Logan & McClung, 2019), creating a mismatch between desired sleep timing and external demands (e.g., school start times). Adolescence may then represent a vulnerable period for the impacts of sleep and circadian rhythm disruption on OCD. Indeed, a recent study found that the average of OCD symptom onset is 17 (Albert et al., 2015). We have noted that previous research found chronotype is unrelated to OCD symptoms in adolescents, but relations between indicators of delayed circadian rhythms and OCD symptoms emerge beginning in college-aged samples (Cox & Olatunji, 2019a). Circadian rhythms begin a gradual phase advance in early adulthood that continues across the lifespan (R. W. Logan & McClung, 2019). Together these findings raise

the possibility that those who do not exhibit a circadian advance following adolescence may be at risk for the onset of OCD. Longitudinal studies tracking circadian rhythms, sleep/wake schedules, and OCD symptoms across the transition from adolescence to early adulthood are needed to explore this possibility.

Another potential critical period for the relationships between sleep and circadian rhythm disruption and OCD is pregnancy and postpartum. Sleep disturbance in the perinatal period has been well-documented (Bei et al., 2015), and the developing literature on postpartum OCD suggests pregnancy/postpartum is associated with both the onset and worsening of OCD symptoms (Speisman et al., 2011). Further, a small but growing literature links insomnia and sleep disturbance to anxiety in the perinatal period (Gueron-Sela et al., 2020; Okun et al., 2018; Swanson et al., 2011). Indeed, recent studies have found that insomnia during pregnancy predicts postpartum anxiety (Osnes et al., 2019, 2020) and OCD symptoms (Osnes et al., 2020), and one study found that later sleep timing relative to their circadian phase in the third trimester predicts increased postpartum OCD symptoms (Obeysekare et al., 2020). Additional research is needed to characterize the links between sleep and circadian rhythm disturbance and OCD symptoms in the perinatal period, as this may represent a time of particular vulnerability for the onset or exacerbation of OCD symptoms in women.

Relatedly, the present findings raise exciting possibilities about the use of sleep and circadian interventions in OCD treatment. Indeed, CBTI has been shown to decrease anxiety symptoms (Belleville et al., 2011; de Bruin et al., 2018), including intrusive cognition such as worry and rumination (Kalmbach et al., 2019). However, no study to date has examined the efficacy of CBTI for OCD symptoms. Findings from Study 2 also suggest that targeting delayed circadian rhythms may be beneficial for treating OCD. Indeed, one recent study found that

consistent entrainment cues were associated with better treatment outcomes in an inpatient OCD treatment program (Coles & Stewart, 2019), and recent pilot studies have shown preliminary evidence for the efficacy of light therapy in treating PTSD and Tourette's disorder (Ricketts et al., 2021; Zalta et al., 2019), which share clinical features with OCD. Thus, chronotherapeutic approaches, including reducing circadian misalignment and stabilizing exposure to entrainment cues, may have clinical utility in OCD treatment. Additional research is needed to further characterize the role of sleep and circadian rhythms in OCD and determine whether targeting sleep disturbance and later circadian timing may hold clinical utility for treating OCD.

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