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Structural and Functional Correlates of the Sleep-Suicidal Ideation Association

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ABSTRACT

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Each year, about 800,000 individuals die by suicide globally, affecting millions more. Mitigating suicide risks by targeting modifiable factors such as the sleep disturbances of insomnia and nightmares, which are prevalent and linked to suicidality is important. This study investigated the structural and functional brain differences related to sleep disturbances and suicidality, with the anterior cingulate (caudal and rostral), insula, middle frontal gyrus, posterior cingulate, thalamus, amygdala, and orbitofrontal cortex as seed regions.

Participants had no history of suicidal ideation (NSI; n=43) or suicidal ideation within the past two weeks (SI; n=25). Measures for analyses included the Insomnia Severity Index (ISI), Disturbing Dream and Nightmare Severity Index (DDNSI), and Frequency of Suicidal Ideation Inventory (FSII). The relationships between group (control vs suicidal ideation), structural measurements (cortical surface area, cortical thickness, gray matter volume), insomnia and nightmares across the eight regions in each hemisphere were examined. Functional connectivity-change differences were measured across wake and sleep with the eight regions as seeds.

The SI group had smaller cortical surface area and gray matter volumes in the left insula ($t = 2.58$, $p = 0.012$; $t = 2.44$, $p = 0.017$); however, not after adjusting for multiple comparisons. ISI and FSII total scores correlated with each other and the surface area and gray matter volume of the left insula. In a mediation model, ISI total score was significantly related to insula surface area and FSII total score ($p = 0.023$; $p = 0.027$), but the insula surface area was not significantly

associated with FSII total score ($p = 0.075$). The indirect effect of ISI on FSII through the left insula surface area was not significant ($p = 0.161$). The SI group had smaller changes from wake to sleep than the NSI group in the functional connectivity of the right thalamus to the left and right superior/middle temporal regions.

Other neurological mechanisms could be at play as only the cortical surface area and gray matter volume in the left insula had implied differences between groups and the structural differences did not mediate the relationship between insomnia and suicidality. Smaller functional connectivity-changes differences across wake and sleep for SI compared to NSI, potentially indicate deficits in auditory inhibition.

Keywords: suicidal ideation, insomnia, mediation, structural MRI, resting state fMRI, insula, temporal

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Suicidality, which ranges from thinking about suicide to planning or attempting suicide, affects millions of individuals world-wide (Pitman et al., 2014). Every year, around 800,000 people die by suicide around the world (Naghavi, 2019). Millions more are impacted (Pitman et al., 2014). Every year, between 6-14% of the general population express suicidal ideation during a 12-month period (Akram et al., 2020; Mortier et al., 2018). According to the Centers for Disease Control and Prevention, in 2021, around 12.3 million adults in America seriously thought about suicide, 3.5 million planned an attempt, and 1.7 million attempted (Substance Abuse and Mental Health Administration, 2023). Known risk factors for suicidality include mental disorders, previous suicide attempts, childhood maltreatment, and substance abuse (Franklin et al., 2017). Despite the awareness regarding risk factors of suicidality, the challenge researchers face is identifying and understanding modifiable risk factors of suicidality.

Based on several prevailing theories for suicidality (De Beurs et al., 2019; Mann et al., 1999; O'Connor & Kirtley, 2018; Van Orden et al., 2010), the most consistent risk factors for suicide are related to mental and physical health, past suicide attempts, family conflict and early life adversity, interpersonal needs, unemployment, and sensitivity to emotional pain. While these are the top risk factors, many of them are not modifiable. A few modifiable risk factors that are often overlooked are sleep disturbances (Pigeon et al., 2012; Trauer et al., 2015; Yücel et al., 2020). Sleep disturbances are related to all the major risk factors for suicidality including, but not limited to, mental disorders (Baglioni et al., 2016), previous suicide attempts (Batterham et al., 2021; Simmons et al., 2021), family conflict (Bernert et al., 2007; Gregory et al., 2006), childhood trauma (Simon & Admon, 2023; Yu et al., 2022), social isolation (Hom et al., 2017), unemployment (Blanchflower & Bryson, 2021), and emotional functioning (Van Someren, 2021;

Vanek et al., 2020). Sleep disturbances, such as insomnia or nightmares, are related to many psychiatric and medical conditions (Pruiksma et al., 2021; Sivertsen et al., 2014) which in turn are associated with suicidality. This review addresses the basics of suicidality and sleep disturbances, how they are related, and presents a theoretical context to frame the mechanism through which suicidality and sleep disturbances relate to each other.

Suicidality Theories

Jollant et al.'s (2011) neurocognitive model of suicidal behavior provides a framework for understanding the complex interplay of psychological and neurobiological factors contributing to suicidal tendencies. Central to this model is the recognition of the suicidal process involving stages, beginning with triggers of negative emotions and culminating in suicidal ideation and potentially, a suicidal act. In the initial triggering and prolonged states, individuals prone to later suicide attempts may exhibit difficulties in accurately assigning value to external events along with regulating emotional and cognitive responses.

Neurobiological studies have identified specific patterns of brain activity associated with these early stages of the suicidal process. Research by Jollant et al. (2008) indicates heightened responses to angry versus happy faces in the ventrolateral prefrontal cortex (PFC) among individuals vulnerable to suicide, suggesting a dysregulated emotional response to negative stimuli. Additionally, decreased activation in this area for risky versus safe choices, as observed in studies by Jollant et al. (2010), further underscore deficits in decision-making processes among this population.

Furthermore, individuals experiencing the initial triggering and prolonged states may also exhibit impairments in emotional and cognitive regulation. Areas such as the mediodorsal and

anterior cingulate cortex are implicated in previous research, potentially linked functionally to psychological pain or hopelessness (van Heeringen et al., 2010). The medial prefrontal cortex has been associated with negative moral feelings about oneself (Takahashi et al., 2004), while rumination and self-referencing, characteristic of these states, involve the medial prefrontal cortex, anterior cingulate gyrus, and precuneus (Nejad et al., 2013; Ochsner & Gross, 2005). Additionally, increased rumination has been linked to heightened activity in the amygdala and ventrolateral prefrontal cortex during reappraisal of situations (Ray et al., 2005), highlighting the intricate interplay between emotional regulation and cognitive processing. Moreover, the dorsolateral prefrontal cortex plays a crucial role in cognitive control mechanisms (Kouneiher et al., 2009), further contributing to our understanding of the neural correlates underlying the early stages of the suicidal process.

The Interpersonal Theory of Suicide posits that constructs of social disconnectedness such as thwarted belonging and perceived burdensomeness plus a hopelessness about changing those states contribute to an individual's progression from passive to active suicidality (Bernert et al., 2005; Van Orden et al., 2010). The findings from multiple studies shed light on the neural mechanisms underlying thwarted belongingness represented by social exclusion and loneliness, and its impact on emotional and cognitive processes. Eisenberger et al. (2003) demonstrated that during social exclusion, the anterior cingulate cortex (ACC) exhibits increased activity, positively correlated with self-reported distress. Concurrently, the right ventral prefrontal cortex is also active during exclusion but negatively correlated with distress, suggesting a regulatory role. Kim & Suh (2023) further explored the relationship between social connectedness and brain activity, highlighting the involvement of the medial prefrontal cortex in loneliness. Lonely individuals exhibit greater functional connectivity within the default mode network (DMN),

potentially reflecting increased mentalizing and self-reflection. Olie et al. (2017) corroborated these findings, identifying key brain regions involved in social exclusion and loneliness, including the dorsolateral prefrontal cortex, medial prefrontal cortex, anterior cingulate cortex, insula, and temporoparietal junction. Mwilambwe-Tshilobo and Spreng (2021) emphasized the role of the default network in social exclusion, with activation observed in various brain regions implicated in self-cognition and emotional processing. Finally, Wong (2022) conducted a meta-analysis on loneliness and emotion processing, revealing a proposed theory of upregulation of cognitive control networks in response to loneliness, which may subsequently impact affective regulation.

Collectively, these findings underscore the intricate neural processes underlying social exclusion and loneliness, highlighting the involvement of brain regions associated with emotional regulation, self-reflection, cognitive control, and social cognition.

Suicidal Ideation

According to the National Institute of Mental Health, suicidal ideation references thoughts about, considerations or plans of suicide (National Institute of Mental Health, 2024). These suicidal thoughts may come as individuals feel a sense of entrapment with their thoughts or defeated and humiliated when it comes to social circumstances (O'Connor & Kirtley, 2018). Individuals might also experience a lack of belonging or a perceived burdensomeness on others (Van Orden et al., 2010).

Neuropsychological studies as related up above implicate various structures and functions in suicidality. In a recent review of structural and functional brain correlates with suicidal ideation, Vieira and colleagues (Vieira et al., 2023) identified regional differences for individuals

specifically with suicidal thoughts. Based on studies reporting structural differences for those with and without suicidal ideation, 60% reported alterations in frontal regions and 40% reported parietal lobe variabilities. Functional connectivity alterations were reported most with frontal (75%), temporal (56%), and limbic (50%) regions. Vieira et al. (2023) also reported that alterations in the prefrontal cortex, temporal regions and amygdala could be related to emotional processing for suicide ideators while the orbitofrontal cortex and anterior cingulate cortex were related to decision-making for suicide attempters. Among the key areas highlighted in previous neuroimaging findings are the anterior cingulate cortex, insula, middle frontal gyrus, posterior cingulate cortex, thalamus, amygdala, and prefrontal cortex (Aquino et al., 2024).

The regions have been related to risky decision making (anterior cingulate, amygdala; Brand et al., 2007; Fishbein et al., 2005; Jung et al., 2018), cognitive control (anterior cingulate, medial prefrontal cortex; Jiang, 2024), and additional executive functions (middle frontal gyrus, posterior cingulate, thalamus; Drummond et al., 2013; Leech et al., 2011; Pergola et al., 2013). Additionally, most have a part to play in emotion regulation processes (thalamus, medial prefrontal cortex; Winecoff et al., 2013; Zhou et al., 2021), including negative emotion persistence (anterior cingulate; Seo et al., 2018), nonconscious emotional processing (anterior cingulate; Killgore & Yurgelun-Todd, 2004), emotion encoding (medial prefrontal cortex; Winecoff et al., 2013), and exaggeration of experienced emotions (amygdala; Frank et al., 2014). Finally, a portion of these regions process self-awareness of internal body signals (insula; Hübner et al., 2022) and external noxious signals (anterior cingulate, medial prefrontal cortex, insula; Gamal-Eltrabily et al., 2021).

Increased functional connectivity of the anterior cingulate cortex may play a role in negative emotion persistence or inflexibility (Seo et al., 2018; Son et al., 2018) as the anterior

cingulate cortex is an area responsible for emotional processing and integration of emotional and cognitive experiences (Phillips et al., 2003; Reimann et al., 2023). Previous studies report gray matter volume (He et al., 2022) and cortical thickness decreases (Wagner et al., 2012) in the anterior cingulate cortex for individuals with suicidality. There is also evidence in individuals with suicidality of decreased functional connectivity from the anterior cingulate cortex to orbitofrontal (Du et al., 2017) along with decreased connectivity within the dorsal anterior cingulate during extinction learning (Seo et al., 2018). Other studies indicate that for individuals with suicidality, functional connectivity increased between the anterior cingulate cortex to the superior frontal gyrus (Shi et al., 2020), within the dorsal anterior cingulate cortex during early extinction recall (Seo et al., 2018), and in the right anterior cingulate in emotionally valanced tasks (Pang et al., 2018).

The insula, a crucial hub in the brain's salience network, is heavily involved in interoception, the central nervous system's processing of bodily signals (Haruki & Ogawa, 2021; Uddin, 2015). Moreover, disruptions in insular activity are linked to interference with slow-wave sleep generation, as suggested by Chen (2014), highlighting its involvement in sleep regulation. From structural research, there are reports of insular gray matter volume (Hwang et al., 2010) and cortical thickness decreases (Harenski et al., 2020; Kim et al., 2021; Taylor et al., 2015). Functional connectivity literature supports increases with the amygdala (Kang et al., 2017) and with itself during learning tasks (Li et al., 2020) but decreased functional connectivity with the right superior frontal gyrus (Gosnell et al., 2019), the anterior insula during social inclusion (Cáceda et al., 2020). Suicide risk is also correlated with the superior insula during a cyberball social task (Olié et al., 2017).

The middle frontal gyrus, implicated in higher-order executive functions such as working memory, has garnered attention in studies on insomnia. Drummond et al. (2013) highlights the challenges individuals with insomnia face in engaging task-appropriate brain regions and suppressing activation of task-irrelevant regions during working memory tasks, shedding light on the neural underpinnings of sleep disturbances and cognitive deficits. Specifically, for individuals with suicidality, there are reports of gray matter volume (Segreti et al., 2019; Wang et al., 2020) and cortical thickness decreases (Campos et al., 2021; Taylor et al., 2015) with functional connectivity decreases between the left middle frontal gyrus and left superior parietal gryus (Cao et al., 2021).

Similarly, the posterior cingulate cortex, another DMN node, is integral to self-processing and self-awareness, as delineated by Brewer et al. (2013). Its involvement in directing attention, as noted by Leech et al. (2011), and heightened processing activity, as observed by Kay et al. (2017), further emphasize its multifaceted role in cognitive functioning. For individuals with suicidality compared to those without, there are both gray matter volume increases (Hwang et al., 2010) and decreases (Harenski et al., 2020; He et al., 2022). In the functional neuroimaging literature for individuals with suicidality, the left posterior cingulate cortex has greater functional connectivity to the left inferior frontal gyrus (Li et al., 2022) and left cerebellum/cingulate (Chase et al., 2017; Schreiner et al., 2019) and decreased functional connectivity in subnetworks associated with suicidal ideation (Chen et al., 2021; Kim et al., 2017; Reis et al., 2022).

The thalamus, known for its role in cortical activation and synchrony, is implicated in sleep consolidation (Gent et al., 2018). Studies by Zhou et al. (2021) underscore its significance in encoding salience stimuli and emotional regulation. Previous research describes gray matter

volume (Campos et al., 2021; Segreti et al., 2019) and cortical thickness decreases (Kim et al., 2021; Segreti et al., 2019) for individuals with suicidality along with less functional connectivity in whole-brain analyses (Kang et al., 2017) and negative correlations with the severity of suicidal ideation (Kang et al., 2017).

The amygdala is involved in processing primary emotions, including positively and negatively valanced feelings (Reimann & Bechara, 2010). Fear conditioning is one area of emotion regulation that the amygdala is recruited (Dolan, 2002; Hashizume et al., 2024). It also helps with decision making by providing information to the prefrontal cortex about needs or previous danger (Marek et al., 2013). There is additional evidence supporting amygdala involvement in memory consolidation of emotional memories (Bocchio et al., 2017; Paré et al., 2002). For those with suicidality, there are gray matter volume increases (Monkul et al., 2007) and decreases (Harenski et al., 2020) and shape volume differences (Kang et al., 2020). Also, individuals with suicidality show greater functional connectivity between the amygdala and precuneus/cuneus (Kong et al., 2018), superior frontal and middle gyri, left middle temporal gyrus (Li et al., 2022), paracentral lobule, and precuneus (Wang et al., 2020). Other research indicates greater functional connectivity in the amygdala decreased in connectivity to the inferior parietal lobule, precentral gyrus, postcentral gyrus, right angular gyrus, and middle temporal gyrus (Li et al., 2022).

The prefrontal cortex is heavily implicated in suicidality research (Schmaal et al., 2020) as various portions of it involve emotion processing and executive functioning. The lateral ventral prefrontal cortex region is involved during response inhibition, especially in emotional contexts (Dixon et al., 2017; Mitchell, 2011). Other portions of the prefrontal cortex such as the medial prefrontal cortex are involved in emotion and reward processing (Dixon et al., 2017; Levy &

Glimcher, 2012) and self-reflection (Murray et al., 2012). For those with suicidality, there are gray matter volume decreases in the ventrolateral prefrontal cortex (Ding et al., 2015), dorsomedial prefrontal cortex (Hwang et al., 2010), dorsal prefrontal cortex (Harenski et al., 2020), and right dorsolateral prefrontal cortex (Jollant et al., 2018). Cortical thickness is also smaller in the ventrolateral prefrontal cortex (Wagner et al., 2012), and, in general, the prefrontal cortex is positively correlated with suicidality severity (Kang et al., 2022). Within the prefrontal cortex for individuals with suicidality, there is increased BOLD response specifically within the dorsolateral region for regulating responses (Chen et al., 2018) and emotion face-word tasks (Malhi et al., 2019) and increased functional connectivity with the ventromedial prefrontal cortex for suicidal individuals with increased impulsivity (Brown et al., 2020).

Together, these findings above underscore the elaborate functional connectivity and diverse roles of specific brain regions in supporting various cognitive and emotional processes. Altered structure and functioning in these regions or processes, potentially influenced by sleep disturbances, could be part of the underlying mechanism of suicidality and suicide risk.

Sleep Theories

Several theories and models have been suggested to describe the etiology of insomnia and nightmares, but only a few of them will be addressed here. Proposed by Spielman et al. in 1987, the then 3P Model, now 4P Model delineates predisposing, precipitating, perpetuating, and Pavlovian conditioning factors that each contribute to insomnia disorder (Spielman et al., 1987). Predisposing factors can be genetic or personality characteristics while precipitating and perpetuating factors are stressful life events or poor habitual strategies used to cope with sleep loss ie naps. Pavlovian conditioning is in reference to circumstances such as creating the bedroom or bed as a conditioned stimulus one associates with wake instead of sleep.

Branching off this model is the popular hyperarousal model of insomnia where the arousal component of insomnia is underscored by predisposing and perpetuating factors (Perlis, 2015). This heightened arousal in multiple systems (cognitive, emotional, physiological) occurs during the nighttime and day, and could be the result of a malfunction in the switch between sleep-wake activation and deactivation (Dressle & Riemann, 2023). It is proposed that hyperarousal can be a state (Dressle & Riemann, 2023), potentially caused by interrupted inhibitory processes due to altered activity in executive control regions of the brain (Altena et al., 2008; Drummond et al., 2013; Kay & Buysse, 2017). There is reason to believe that hyperarousal may not be the only process at play in insomnia though. Kay and Buysse proposed an alternative model that, considering evidence from neuroimaging studies, indicates there may be more going on. The heuristic sleep-wake model and associated theory will be addressed later on under the local sleep theory section.

Gieselmann et al. (2019) proposed a model for nightmares that built on previous models, concluding that factors such as trait affect distress from traumatic experiences, childhood adversity, and trait susceptibility, along with maladaptive cognitive factors and physiological factors contribute to impaired fear extinction and hyperarousal. These underlying conditions set the stage for nightmares to occur initially and then, long after the original stressor has faded, dreams that are similar in nature may activate an expected dream script, looping over and over (Spoormaker, 2008).

Impaired fear extinction is theorized to involve an overactive amygdala with dysfunctional frontal regulatory pathways, specifically the medial prefrontal cortex (Germain et al., 2008; Nielsen, 2017; Nielsen & Levin, 2007) while hyperarousal was observed in individuals with disrupted REM sleep (Feige et al., 2008). The anterior cingulate cortex, ventral medial

prefrontal cortex, and amygdala have previously been implicated during REM sleep (Bush et al., 2000; Desseilles et al., 2006; Maquet et al., 2005; Schwartz & Maquet, 2002). Frontal lobe areas may be responsible for downregulating activity within the amygdala, reducing conditioned fear (Nielsen & Levin, 2007). Dysregulation of this pathway which includes the anterior cingulate cortex could be evidence for increased distress from nightmares (Shen et al., 2016)

Sleep Disturbances and Suicidality

Insomnia & Suicidal Ideation

Insomnia disorder is characterized by an impairing and distressing difficulty in going to sleep or go back to sleep in the night (American Psychiatric Association, 2013). Worldwide, insomnia disorder affects over 10% of individuals (Chung et al., 2015), and contributes to over 100 billion US dollars in health care costs yearly (Taddei-Allen, 2020). Up to 42% of the general population experience at least one symptom of insomnia at a given point in time (Walsh et al., 2011). Not only is insomnia prevalent, but the chronic nature of the disorder contributes to increased financial and health burden on society and the individual (Leger & Bayon, 2010; Reynolds & Ebben, 2017).

Insomnia is related to suicidal ideation, but across the years, the findings have been mixed on how they are related when other suicide risk factors like PTSD, anxiety, hopelessness, drug abuse, alcohol abuse, and in particular, depression, are controlled for. Several studies demonstrate relationships between insomnia and suicidal ideation that do not remain significant after controlling for various factors (Choi et al., 2015; Don Richardson et al., 2014; Nadorff et al., 2014; Nadorff et al., 2011; Sjostrom et al., 2007). However, majority of the literature supports a relationship between insomnia and suicidality with covariates included. In a recent

meta-analysis for the relationship between sleep disturbances and suicidal thoughts, insomnia and nightmares were weak overall risk factors but were the strongest sleep disturbance risk factors of suicidal ideation (Harris et al., 2020). In a sample of undergraduate students, insomnia symptom duration along with nightmare duration were significantly related to suicidal ideation and behavior while controlling for anxiety symptoms, depressive symptoms, and posttraumatic symptoms (Nadorff et al., 2014). When accounting for other top suicide risk factors like depression, hopelessness, anxiety, and PTSD, self-reported insomnia symptoms were associated with suicidal ideation (Ribeiro et al., 2012) and unique predictors of suicide attempts (Ribeiro et al., 2012). Several other studies report that insomnia is a predictor of suicidal ideation (McCall et al., 2010; Owusu et al., 2020; Pigeon et al., 2014; Wojnar et al., 2009). One reports that for a group of adults older than 50 years, those with insomnia symptoms, especially moderate to severe, had greater odds of suicidal thoughts or behavior (Owusu et al., 2020). In another, veterans who had trouble falling asleep or staying asleep within the past month were 1.2 times more likely to experience moderate to severe suicidal ideation compared to those who did not experience sleeping difficulties (Bishop et al., 2013).

Several researchers have tested models to see if insomnia and suicidal ideation are mediated by related variables such as depression (Allan et al., 2017; Bozzay et al., 2016; Kato, 2014; McCall et al., 2013; Nadorff, Nazem et al., 2013). Several studies found that insomnia was indirectly related to suicidal ideation through depression symptoms (Allan et al., 2017; Kato, 2014; Nadorff et al., 2014) while other models provided evidence of mediation through socio-cognitive factors that were related to sleep deficits (Bozzay et al., 2016) and dysfunctional beliefs and attitudes about sleep (McCall et al., 2013).

Neuropsychological findings suggest that insomnia is associated with deficits in executive functioning (Medrano-Martinez & Ramos-Platon, 2016), affect processing (Sheline et al., 2009), and self-referential processing (Lemyre et al., 2019). Insomnia is associated with executive functioning deficits in information updating (Aasvik et al., 2018; Fortier-Brochu & Morin, 2014; Wardle-Pinkston et al., 2019), mental shifting (Fortier-Brochu & Morin, 2014; Liu et al., 2014; Wardle-Pinkston et al., 2019), and response inhibition (Miyake et al., 2000; Zhao et al., 2018).

In addition to executive functioning, insomnia is associated with dysregulated affect processing in mental disorders (Baglioni et al., 2011; L. Li et al., 2016; Medrano-Martinez & Ramos-Platon, 2016; O'Brien et al., 2011; Pigeon et al., 2017; Ten Have et al., 2016; Tsuno et al., 2005). In healthy individuals, insomnia has been linked to deficits in emotional processing (Koranyi et al., 2018; Kyle et al., 2014; Schmidt et al., 2011; Watling et al., 2017). Insomnia is also associated with deficits in self-referential processing (Kay et al., 2016), and more particularly, rumination (Carney et al., 2013; Galbiati et al., 2018; Lancee et al., 2017; Lemyre et al., 2019) and dysfunctional beliefs about sleep (Akram et al., 2015; Fairholme et al., 2012).

The neuropsychological difficulties that individuals with insomnia experience appear in areas of executive functional and emotional processing that also appear to be difficult for individuals with suicidality. These deficits correlate with localized regions specializing in those functions. (Nardo et al., 2015). For example, suicidality and insomnia overlap with abnormalities or dysfunctions of the middle frontal gyrus (Aquino et al., 2024; Dobbertin et al., 2023), posterior cingulate cortex (Aquino et al., 2024; Vieira et al., 2023), and thalamus (Aquino et al., 2024; Schmaal et al., 2020) For individuals with insomnia and suicidality, the regions with the

greatest overlap include the anterior cingulate cortex, insula, middle frontal gyrus, posterior cingulate cortex and thalamus.

Within the anterior cingulate cortex, the structural findings are mixed with those experiencing insomnia symptoms having both smaller (Grau-Rivera et al., 2020; G. Li et al., 2018) and larger gray matter volumes (Li et al., 2021; Tahmasian et al., 2018) along with smaller (Suh et al., 2016) and larger cortical thicknesses (Desseilles et al., 2008; Yu et al., 2020; Zhao et al., 2015). The decreases in gray matter volume and cortical thickness are similar to those with suicidal ideation (He et al., 2022; Wagner et al., 2012). In individuals with insomnia, functional connectivity is greater between the anterior cingulate cortex and middle frontal gyrus (Luo et al., 2022) and the left executive control network (Wei et al., 2020) as well with itself during extinction recall and fear conditioning (Seo et al., 2018), and during relieving of self-conscious emotional experiences (Wassing et al., 2019). Functional connectivity also shows decreases in variability with the left executive control network (Wei et al., 2020) and during rest (Marques et al., 2017). Individuals with suicidality have smaller functional connectivity between the anterior cingulate cortex and middle frontal gyrus (Shi et al., 2020) in contrast to the greater functional connectivity with the middle frontal region that is apparent in insomnia.

Like individuals with suicidality, those with insomnia demonstrate smaller gray matter volumes in the insula (C. Li et al., 2018) however those with insomnia have greater cortical thickness (Desseilles et al., 2008; Yu et al., 2020) and shape decreases and changes (Afshani et al., 2023; C. Li et al., 2018). Functional connectivity in the insula was greater with the right anterior cingulate cortex (Wang et al., 2017), with itself during early fear extinction (Seo et al., 2018), and during stage N2 sleep (Y. Li et al., 2022) but decreased in connectivity during fear

conditioning (Seo et al., 2018), wake (Y. Li et al., 2022), and in variability with the left executive control network (Wei et al., 2020).

In the middle frontal gyrus, individuals with insomnia have smaller (Li et al., 2021; Wu et al., 2020) and larger gray matter volumes (Gao et al., 2023), along with cortical thickness decreases (Falgàs et al., 2021) and increases (Yu et al., 2020). Functional connectivity decreased in the left middle frontal gyrus during an executive working memory task (Drummond et al., 2013) and also decreased during a spatial working memory task (Y. Li et al., 2016). These findings are similar to those found in the middle frontal gyrus for individuals with suicidality.

The posterior cingulate cortex for those with insomnia, in similarity to individuals with suicidality, has evidence for smaller (Grau-Rivera et al., 2020; G. Li et al., 2018) and larger gray matter volume (Li et al., 2021; Yu et al., 2020), but there is additional evidence of smaller (Falgàs et al., 2021; Suh et al., 2016) and larger cortical thickness (Zhao et al., 2015). Functional connectivity in this region was smaller in some instances (Marques et al., 2017; Pang et al., 2017) but greater during a response inhibition task (Orff, 2010). Regional glucose metabolism also increased in this area during sleep (Kay et al., 2016).

For the thalamus of individuals with insomnia compared to controls, there were smaller (Grau-Rivera et al., 2020; Xie et al., 2022) and larger gray matter volumes (Desseilles et al., 2008) with shape decreases (Emamian et al., 2021; Li et al., 2019 2019), while those with suicidality only showed smaller gray matter volumes (Campos et al., 2021; Segreti et al., 2019). Functional connectivity was greater between the thalamus and superior parietal and medial superior frontal gyri (Kim et al., 2021), sensory regions, in the left thalamus during an attention task (Perrier et al., 2023), and in the right thalamus, functional connectivity increased with the left MFG (Huang et al., 2022). There was decreased functional connectivity with the anterior

cingulate cortex, orbitofrontal, caudate, putamen, hippocampus (Li et al., 2019) and with itself during a working memory task (Drummond et al., 2013). In contrast, those with suicidality only showed functional connectivity decreases with the thalamus (Kang et al., 2017).

In these regions of emotional processing and executive function, there are some similarities between individuals with insomnia and those with suicidality. Exploring these overlapping regions may provide more insight into how suicidality and insomnia come together within a structural and functional context. This study may be the first to examine neuroimaging findings in those with suicidal ideation across sleep/wake states in relation to sleep disturbances, particularly insomnia. Previous studies have looked at neuroimaging of suicidality (Bani-Fatemi et al., 2018) or insomnia (Wu et al., 2020) during wake but not simultaneously across sleep and wake.

Nightmares and Suicidality.

Nightmares, according to the DSM-5, tend to be extremely dysphoric, remembered, and result in significant distress (American Psychiatric Association, 2013). In the general population, the prevalence of nightmares occurring once a week or more is between 1-7% (Bjorvatn et al., 2010; Janson et al., 1995; Levin, 1994; Li et al., 2010; Schredl, 2010). Frequent nightmares, at least once a week, occur in 5% of the public (Li et al., 2010). Only around 12% of individuals with nightmares seek help (Schredl et al., 2016). Individuals with nightmares may experience deficits in cognitive labeling of emotion (Carr et al., 2016), increased emotional reactivity (Carr & Nielsen, 2017), difficulty in executive tasks requiring suppression of previous emotion (Simor et al., 2012), and worry (Rek et al., 2017).

Many studies involving nightmares conjunctively looked at other sleep disturbances, including insomnia, in relation to suicidal ideation and behavior with mixed results (Bernert et al., 2005; Don Richardson et al., 2014; Golding et al., 2015; McCall et al., 2013; Nadorff et al., 2011, 2013). In several cases, the symptoms or duration of nightmares and insomnia were associated with suicidal ideation and/or behavior, but after controlling for various covariates, nightmare symptoms alone remained significantly associated (Bernert et al., 2005; Golding et al., 2015; Nadorff et al., 2014; Nadorff et al., 2011). A further study indicated that neither insomnia nor nightmares were good predictors of suicidal ideation (Don Richardson et al., 2014) in contrast to a finding from the previous year that both nightmare and insomnia duration were associated with suicide risk (Nadorff, Fiske, et al., 2013). The mixed evidence of the relationship between nightmares and suicidal ideation and behavior makes it difficult to determine mechanisms behind the relationship. Complicating matters further are other variable studied in relation to nightmares and suicidal ideation and behavior such as perceived interpersonal burdensomeness (Suh et al., 2016), defeat, entrapment, and hopelessness (Littlewood et al., 2016) along with cognition and emotion regulation (Andrews & Hanna, 2020; Kang et al., 2020).

For example, a pair of researchers reviewed 12 articles on the nightmare-suicidal thoughts and behaviors association and concluded that cognitive appraisal and affect/emotion regulation played significant roles in the relationship between nightmares and suicidal ideation (Andrews & Hanna, 2020). Another study provided evidence that for those with difficulties in emotion regulation compared with those without emotion regulation difficulty, there was a stronger positive association between nightmare frequency and suicide attempts (Kang et al., 2020). The relationship between nightmares and suicidality could specifically be related to emotional processing since individuals with nightmares experience deficits in regions associated

with cognitive appraisals and emotion regulation (Andrews & Hanna, 2020). These deficits could be in localized regions specializing in those functions, overlapping with suicidality literature regions. The regions of overlap include the anterior cingulate cortex, insula, amygdala and prefrontal cortex.

Within the anterior cingulate, for individuals with nightmares, they have smaller gray matter volumes (Nardo et al., 2015), like those with suicidality. Few studies have looked at the functional connectivity of brain regions but there is evidence of increased regional homogeneity of the left anterior cingulate (Shen et al., 2016), negative correlations between nightmare distress and regional cerebral blood flow (Marquis et al., 2019) and decreased regional cerebral blood flow with nightmare distress (Nardo et al., 2015). There is a study describing functional connectivity increases in the anterior cingulate cortex during threat conditions, not in the context of nightmares but potentially relating to similar circumstances (Sambuco et al., 2020). In the context of emotions, these mixed results are like the mixed functional results in individuals with suicidality.

The insula of those with nightmares compared to those without has smaller gray matter volume (Nardo et al., 2015), comparative to the smaller gray matter in those with suicidality (Hwang et al., 2010). Again, very few studies have examined functional connectivity in the context of nightmares. The insula did have greater functional connectivity with itself in threat conditions without nightmares and also as pain increased (Sambuco et al., 2020) and one study indicated increased regional cerebral blood flow (Nardo et al., 2015) for individuals with nightmares. While the functional studies in the insula for individuals with nightmares are few, it is still a region that overlaps in nightmares and suicidality.

Individuals with nightmares have smaller gray matter volumes in the amygdala than those without (Nardo et al., 2015) and functional connectivity with the medial prefrontal cortex during fear extinction (Gieselmann et al., 2020) but no alterations in regional homogeneity (Shen et al., 2016). The amygdala is also implicated in dreaming (De Gennaro et al., 2011). Between individuals with nightmares and those with suicidality, the amygdala is involved in emotion-based experiences (Gieselmann et al., 2020).

For those experiencing nightmares, the prefrontal cortex, and specifically the medial portion of it shows decreased functional connectivity during wake (Carr et al., 2016), and negative correlations between nightmare distress and regional cerebral blood flow (Carr et al., 2016). The cortical thickness and functional results in individuals with nightmares contrast with those in suicidality (Brown et al., 2020; Chen et al., 2018; Malhi et al., 2019; Wagner et al., 2012), but the region is implicated in both.

While the structural and functional results in individuals with nightmares may at times contrast with those experiencing suicidality, the regions of interest continue to overlap. There may be complex mechanisms relating nightmares to suicidality that can be explored.

Local Sleep Theory: Local Sleep Deprivation Hypothesis

The local sleep theory posits that waking and sleep states are influenced by localized processes and that manipulations of local brain activity during wake or sleep can alter these processes (Krueger et al., 2019). For example, a group of individuals completing reaction time tasks before sleep showed increased glucose metabolism in their left dorsal premotor cortices and the pre-supplementary motor areas during rapid eye-movement (REM) sleep, indicating that manipulating waking localized blood flow altered their localized sleep (Laureys et al., 2001;

Maquet, 2000). As an outgrowth from this theory, the local sleep hypothesis proposes that individuals with sleep disturbances have increased processing during sleep which deprives local regions of sleep, resulting in less information processing in those specific areas during wakefulness (Kay & Buysse, 2017).

Given in a model described by Kay and colleagues in several previous papers (Dzierzewski et al., 2010; Kay & Buysse, 2017), sleep-wake states are determined by three factors: sleep drive, wake drive, and conscious awareness. Regions of interest are described in association with each of the three factors. Sleep drive, or the processes engaged in promoting sleep, involves the hypothalamus and thalamus as well as circadian rhythm processes (Borbély et al., 2016). Wake drive, or the processes engaged in promoting arousal, is influenced by nuclei in the brainstem, midbrain, and basal forebrain. Conscious awareness, or the processes engaged in promoting awareness of self and environment, is associated with activation in the insula (Koubeissi et al., 2014), claustrum (Koubeissi et al., 2014), anterior and posterior cingulate cortices (Bush et al., 2000), the precuneus (Cavanna & Trimble, 2006), and left prefrontal cortex (Del Cul et al., 2009) in addition to functional connectivity across the default mode and executive control networks more broadly (Boveroux et al., 2010; Vanhaudenhuyse et al., 2010).

Each factor helps regulate the sleep or wake state an individual is in at any point in time. The factors operate on a continuum where the global state depends on where an individual falls in their sleep drive, wake drive, and conscious awareness. For example, an individual with healthy sleep will likely have a high sleep drive, low wake drive, and low conscious awareness that is consistent with NREM sleep. For context, healthy wake fluctuates between high wake drive, low sleep drive, and high conscious awareness (active wake) and a state where wake drive is reduced but sleep drive remains high (quiet wake). Healthy REM sleep differs from NREM in

that wake drive is higher than NREM, but sleep drive stays high and conscious awareness remains low. In addition to applying to healthy individuals, this model can be applied to a variety of psychiatric conditions or disorders including sleep disturbances like insomnia and nightmares.

Suicidality, Sleep Disturbances and Local Sleep Theory.

The local sleep deprivation hypothesis would suggest that individuals with sleep disturbances like insomnia and nightmares have alterations in sleep-wake regulation (sleep drive, wake drive, conscious awareness) processes that then confer risk for regionalized alterations in brain regions tasked with modulating and integrating emotional regulation and decision-making information. The regional alterations in emotion and decision-making then confer risk for suicidality. Alternatively, individuals with suicidality could already have difficulty with emotion regulation and decision-making that is then perpetuated by insomnia and nightmare alterations in sleep-wake regulation in localized brain regions which continues the downward cycle forward.

Insomnia and Local Sleep Theory. According to the local sleep theory, the main symptoms of insomnia can result from combinations of high sleep drive, low wake drive, and high conscious awareness during the time one would like to sleep (Dzierzewski et al., 2010; Kay & Buysse, 2017). Very few studies have characterized the functional connectivity of the brain during sleep; however, a few have provided evidence of alterations in sleep-wake regulation processes. One study, comparing sleep-wake differences in individuals with insomnia compared to healthy controls, found that those with insomnia experienced smaller differences in relative regional glucose metabolism from sleep to wake in areas involved in conscious awareness (Kay et al., 2016). The smaller differences from sleep to wake could reflect higher conscious awareness in individuals with insomnia during sleep than healthy controls. Also, if cognitive processes from daytime decision-making and emotion processing are still occurring in regions

like the OFC, IFG, and dACC during sleep, information processing and functional connectivity could be adding to the conscious awareness factor.

Additionally, several limbic brain regions presented lower relative regional glucose metabolism during NREM sleep for those with insomnia compared to controls (Kay et al., 2016). The lower relative regional glucose metabolism could be reflective of higher sleep drive during NREM sleep.

Nightmares and Local Sleep Theory. According to the local sleep theory, the main symptoms of nightmares can result from combinations of high sleep drive, high wake drive, and potentially increasing conscious awareness during sleep. In one sample of individuals, the sleep architecture of those with nightmares does not seem to differ from healthy controls even though those with nightmares describe poorer sleep quality (Paul et al., 2015). In another sample, however, differences in sleep architecture between those with and without nightmares were found (Simor et al., 2012). Those with nightmares had increased wakefulness and nocturnal awakenings, a reduction in slow wave sleep and longer durations of REM. Both studies suggest that the heightened sleep and wake drives could be competing during sleep with one drive or the other winning out to either keep sleep architecture continuous or to contribute to awakenings. A follow-up study to the previous indicated that individuals with nightmares compared to healthy controls had increased alpha waves (wake-like) during transitions from NREM to REM, but stable levels following REM (Simor et al., 2014). Again, this could indicate that individuals with nightmares experience an increase in wake drive simultaneous with sleep drive during the night. In areas such as the anterior cingulate cortex, insula, thalamus, amygdala, and prefrontal cortex and especially those involved in emotion regulation (Nardo et al., 2015; Nielsen & Levin, 2007),

activation could be occurring in response to vivid and frightening dreams, potentially increasing conscious awareness or pressure to wake.

Conclusion

Changes in the three factors of sleep (sleep drive, wake drive, and conscious awareness) are implicated in sleep disturbance conditions like insomnia and nightmares. Alterations in brain structure and functional connectivity in cortical and limbic regions (anterior cingulate cortex, insula, middle frontal gyrus, posterior cingulate cortex, thalamus, amygdala, and prefrontal cortex) for individuals with suicidality could be indications that sleep-wake regulation processes are conferring increased risks. For individuals with greater insomnia severity, sleep-wake regulation processes of conscious awareness could be heightened due to information processing occurring still and therefore altered in individuals with suicidal ideation. For individuals with greater nightmare severity, sleep-wake regulation processes of wake drive and conscious awareness could be heightened also altering brain activity in individuals with suicidal ideation. Understanding how regional dynamics of suicidality and sleep disturbances intersect could provide additional evidence to support targeting sleep disturbance as a line of prevention for suicidal ideation.

This project aimed to examine differences in cortical structure and functional connectivity between sleep-wake states in individuals with and without suicidality, across a subset of regions that overlap between sleep disturbances and suicidality conditions. Structural and functional magnetic resonance imaging were used to measure cortical/subcortical structure and functional connectivity.

Aim 1) To examine structural differences between individuals with and without suicidal thoughts, across a subset of regions that overlap between suicidality and sleep disturbance conditions related to areas associated with executive functioning and emotional processing.

Hypothesis 1a: We hypothesized that there would be structural differences in the anterior cingulate cortex, insula, middle frontal gyrus, posterior cingulate cortex, thalamus, amygdala and medial pre-frontal cortex across both hemispheres for those with and without suicidal ideation.

Hypothesis 1b: We hypothesized that the structural differences in the anterior cingulate cortex and insula would be related to insomnia and nightmare severity. The structural differences in the middle frontal gyrus, posterior cingulate and thalamus would be related to insomnia severity, and the structural differences in the amygdala and medial pre-frontal cortex would be related to nightmare severity.

Hypothesis 1c: Contingent on the results of Hypothesis 2, we hypothesized that the relationship between insomnia severity and suicidal ideation frequency would be mediated by regions with structural differences (anterior cingulate cortex, insula, middle frontal gyrus, posterior cingulate and thalamus) and that the relationship between nightmare severity and suicidal ideation frequency would be mediated by regions with structural differences (anterior cingulate cortex, insula, amygdala, and medial pre-frontal cortex)

Aim 2) To examine functional-change differences in magnitude across wake and perceived sleep between individuals with and without suicidal thoughts across a subset of regions that overlap in suicidality and sleep disturbance conditions

Hypothesis 2: We hypothesized that across wake and perceived sleep, there would be smaller functional connectivity differences between bilateral regions of the anterior cingulate cortex,

insula, middle frontal gyrus, posterior cingulate cortex, thalamus, amygdala and medial pre-frontal cortex and the rest of the brain for those with suicidality when compared to those without.

Method

Participants

Data for this study was collected from 68 individuals up to a two-hour radius of Provo (from Logan, UT down to Fillmore, UT). With up to 34 individuals in each group, a two-mean power analysis in Stata 17.0 reported that a 0.7 standard deviation difference in means was detectable at 80% power (See Figure 1). A sensitivity analysis for MANOVA following data collection in G*Power 3.1.9.7 indicated that with an alpha of 0.05, power of 0.80, a total sample size of 68, with two groups and eight response variables, a 0.25 Cohen's f^2 was detectable (Faul et al., 2007).

Based on a correlation power analysis, the minimum detectable effect size for a sample of 68 with 80% power was 0.33. Exploratory analyses were performed on a subset of the participants and with 23 participants, there was power to detect a 1.2 functional connectivity-change difference between two means at 80% power, a correlational effect size of 0.56 at 80% power, and a 0.67 effect size for a 2x2 ANOVA analysis. To provide additional power for future studies, this study will feed into other protocols.

Participants (N = 68) were recruited into two groups: those with no history of suicidal ideation (NSI; n = 43) and individuals with suicidal ideation within the previous two weeks (SI; n = 25). In the total sample, the median age was 22 (IQR[21, 24]), 69% had completed some college, 62% identified as female, 85% were white, 13% endorsed a Hispanic or Latino origin, and 57% were employed part-time. The NSI group's median age was 22 (IQR[21, 24]), 70% had

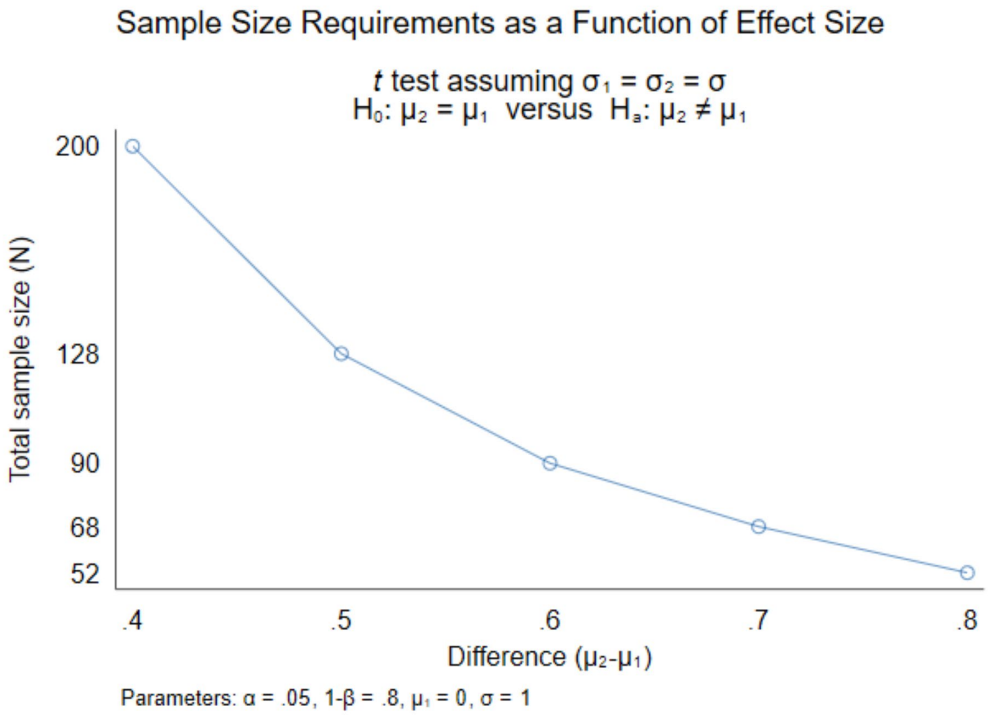
completed some college, 58% identified as female, 88% were white, 9% endorsed a Hispanic or Latino origin, and 56%were employed part-time. The SI group's median age was 21 (IQR[21, 24]), 68% had completed some college, 68% identified as female, 80% were white, 20% endorsed a Hispanic or Latino origin, and 60% were employed part-time. See Table 1 for additional demographic information.

Inclusion/Exclusion Criteria

Participants in this study included those with current suicidal ideation and those without any history of suicidality. Participants were right-handed (Edinburgh Handedness Inventory>0 (Oldfield, 1971); men and women ages 18-65. Exclusion criteria included the following:

Figure 1.

Power Analysis for Two Means



Note. This figure evaluates the detectable effects sizes of mean differences in structural measurements based on various sample sizes

Participants were excluded if they had (1) sleep disorders other than insomnia or nightmares as determined by The Structured Clinical Interview for DSM-5 Sleep Disorder (Taylor et al., 2018) including sleep apnea, hypersomnia, restless leg syndrome, sleep phase disorders, narcolepsy or shift work due to their known associations with distinct brain abnormalities; (2) history of severe psychiatric disorders based on self-report or The Structured Clinical Interview for DSM-5 (First et al., 2015) (e.g., OCD, ADHD, substance abuse, depression with psychosis, PTSD, learning disability); (3) MRI contraindications (e.g. permanent retainer, braces ferromagnetic material in the body, fear of closed spaces etc.); (4) self-reported recreational drug use in the past month; (5)

Table 1.

Comparison of Sample Characteristics between Participants with No Suicidal Ideation and Suicidal Ideation

Characteristic	Total sample (N = 68)	NSI (n = 43)	SI (n = 25)	*df*	$t/z/\chi^2$	*p-value*
Age, years	22[21,24]	22[21,24]	21[21,24]		$z = 0.00$	1.000
Education				4	$\chi^2 = 1.71$	0.788
High School	4(6%)	3(7%)	1(4%)			
Some College	47(69%)	30(70%)	17(68%)			
Associate degree	7(10%)	5(12%)	2(8%)			
Master's degree	3(4%)	2(5%)	1(4%)			
Doctorate degree	0(0%)	0(0%)	0(0%)			
Female, *n*	42(62%)	25(58%)	17(68%)	1	$\chi^2 = 0.65$	0.420
Race, *n*				3	$\chi^2 = 3.61$	0.307
Asian	2(3%)	2(5%)	0(0%)			
White	58(85%)	38(88%)	20(80%)			
Undisclosed	5(7%)	2(5%)	3(12%)			
Multiracial	3(4%)	1(2%)	2(8%)			
Hispanic/Latino, *n*	9(13%)	4(9%)	5(20%)	1	$\chi^2 = 1.57$	0.209
Employed, *n*				2	$\chi^2 = 0.31$	0.855
Not Employed	19(28%)	13(30%)	6(24%)			
Part-time	39(57%)	24(56%)	15(60%)			
Full-time	10(15%)	6(14%)	4(16%)			

Characteristic	Total sample ($N = 68$)	NSI ($n = 43$)	SI ($n = 25$)	*df*	$t/z/\chi^2$	*p-value*
Sleep Measures						
ISI screening, total score	17[11,20]	13[10,19]	19[17.20]	-	$z = 3.06$	0.002**
ISI pre-MRI, total score	12.5[10,18]	11[9,13]	18[15,19]	-	$z = 4.16$	<0.001***
HSI, total score	21[15,25]	17[14,23]	24[21,26]	-	$z = 3.93$	<0.001***
PROMIS-SD, total score	58[45,75]	49[43,66]	68[59,82]	-	$z = 3.96$	<0.001***
DDNSI, total score	0[0,6.5]	0[0,4]	6[0,9]	-	$z = 2.42$	0.016*
WASO, average min	6.9[4,17]	5.3[2, 14]	10[6,18]	-	$z = 1.96$	0.050
SOL, average min	31.3[21,49]	30.8[21, 46]	31.8[21,53]	-	$z = 0.09$	0.929
Suicidality Measures						
SBQ, total score	5[3,9]	4[3,5]	10[8,12]	-	$z = 5.55$	<0.001***
FSII, total score	8[5,14]	5[5,8]	17[10,20]	-	$z = 6.18$	<0.001***
IAT- Suicide/Death	-0.47[-0.77, -0.15]	-0.55(0.34)	-0.24(0.47)	66	$t = 3.16$	0.002**
Mood Measures						
PROMIS-ED-A, total score	20(6)	16.9(5.2)	24.1(4.8)	65	$t = 5.66$	<0.001***
PHQ-9 screening, total score	8[3,13]	4[1,9]	14[11,17]	-	$z = 5.31$	<0.001***
PHQ-9 pre-MRI, total score	8[2,14]	4[11,17]	14[11,17]	-	$z = 5.15$	<0.001***

Note. M(SD), Median[Inter-quartile Range]; NSI = No suicidal ideation, SI = Suicidal Ideation; ISI = Insomnia Severity Index, HSI = Hypersomnia Severity Index, PROMIS-SD = Patient-Reported Outcomes Measurement Information System - Sleep Disturbance, DDNSI = Disturbing Dream and Nightmare Severity Index, WASO = Wake after sleep onset, SOL = Sleep onset latency, SBQ = Suicidal Behavior Questionnaire, FSII = Frequency of Suicidal Ideation Inventory, IAT- Suicide/Death = Implicit Association Task for Suicide/Death, PROMIS-ED-A = Patient-Reported Outcomes Measurement Information System Emotional Distress – Anxiety, PHQ-9 = Patient Health Questionnaire.

* $p<0.05$, ** $p<0.01$, ***p<0.001

excessive alcohol use in the past month, more than 8 (women) or 15 (men) drinks per week due to its association with brain abnormalities (Sullivan & Pfefferbaum, 2019); (6) changes to their medications within the last month; and (7) previous suicide attempts as suicidal ideation was the aspect of interest.

Procedures

Participants were recruited through social media (Facebook, Instagram, KSL) and flyers both on-campus at Brigham Young University as well as throughout the surrounding communities. Individuals were screened through an online Qualtrics questionnaire prior to scheduling an intake assessment. As part of the screening questionnaire, individuals answered questions about their demographics, health, sleep, and suicidality to help determine eligibility. Demographic information collected included age (range 18-65), education (High School/GED, some college, associate degree, bachelor's degree, master's degree, doctoral degree, other), sex (male or female), race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Undisclosed, Multiracial), ethnicity (Not Hispanic/Latino or Hispanic/Latino), and employment status (not employed, part-time, full-time). Participants were recruited into two groups – NSI and SI. Individuals were considered for the suicidality group if they endorsed experiencing suicidality within the past two weeks and were considered for the no suicidal ideation group if they did not endorse any suicidal ideation or self-harm. During the intake assessment, participants provided written informed consent prior to completion of any study procedures. Enrolled participants completed a structured clinical interview that confirmed the group status with questions about past and current suicidality, and answered questionnaires on health, sleep, and psychological functioning. Prior to the conclusion of the intake, all individuals with any endorsement of active suicidality were provided with a

coping card (See Figure in Appendix) containing information about a crisis response plan and support based on Joiner's suicide risk assessment (Joiner Jr et al., 1999).

Following the intake, participants completed sleep diaries with included information about suicidal ideation frequency, severity, and duration. Participants' responses on the suicidal aspects of the daily diaries were reviewed daily. The daily diaries occurred concurrently with actigraphy (Actiwatch Spectrum Plus) and were followed by an overnight ambulatory polysomnography sleep study in the participants' home on the final night of sleep monitoring. During the polysomnographic wire-up procedures, participants completed surveys and suicidality-related task. Participants were left alone with the ambulatory equipment for the night during recording.

The morning after the overnight sleep study, participants brought the equipment to the BYU MRI facility. They completed a series of scans and several questionnaires of sleep and mood. The ensuing evening, participants returned to the MRI facility one hour before their habitual sleep time for a 100-min evening electroencephalogram-fMRI sleep scan that included additional scans (resting state and task based) and final questions about their sleep, mood, and self-reported suicidality following the sleep period. Participants were compensated for their participation. The study was reviewed and approved by The Human Institutional Review Board at Brigham Young University. Only procedures and questionnaires relevant to the study will be examined and listed for the purposes of this dissertation. Each sleep, suicidality, and mood measure helped set the stage and describe the overall mental health, sleep health, and suicidality characteristics of the recruited sample.

Measures

Sleep Measures

The Insomnia Severity Index (ISI) is a validated scale that uses 7 items to assess insomnia over the last month (Bastien et al., 2001; Morin, 1993). The ISI total score was used to characterize participants' levels of sleep disturbance, specifically insomnia, in relation to structural and functional connectivity differences in local regions of interest. Scores on the ISI range from 0-28 with higher scores indicative of more severe insomnia. The internal consistency of the ISI was Cronbach $\alpha = 0.90$ in a community sample and $\alpha = 0.91$ in a clinical sample. A cutoff score of 10 can identify clinical insomnia in community samples (Morin et al., 2011). The ISI was administered in the screening survey and prior to the evening MRI. The ISI score acquired prior to the evening MRI was used to determine insomnia severity as individuals' extreme scores on the screening often regress to the mean on the second ISI questionnaire.

The Hypersomnia Severity Index (HSI) is a scale that uses six items to assess severity of hypersomnolence by asking questions about sleeping too much, difficulty awakening, feeling sleepy, and how much the symptoms interfere with everyday life. (Fernandez-Mendoza et al., 2021; Kaplan et al., 2019). The HSI total score was used first to identify whether individuals had hypersomnia in conjunction with insomnia and whether the insomnia symptoms were greater for exclusion purposes. Secondly, the HSI added more information characterizing participants' sleep. Higher scores indicated greater severity of hypersomnia. The internal consistency of the HIS is $\alpha = 0.79$ and has correlations less than and equal to 0.2 with unrelated measures like sleep effort, and reactivity indicating good divergent validity (Fernandez-Mendoza et al., 2021).

The Patient-Reported Outcomes Measurement Information System Sleep Disturbance (PROMIS-SD) is an item bank consisting of 27 items that assess sleep disturbance and sleep quality (Buysse et al., 2010; Cella et al., 2010). The PROMIS-SD is useful for measuring the

severity of sleep-wake difficulties along a continuum rather than assessing symptoms of specific sleep disorders (Yu et al., 2011). As such, the PROMIS-SD total score was used to characterize the participants' general sleep disturbance rather than focusing on any one sleep disorder. Higher scores indicated greater levels of sleep disturbance.

The Disturbing Dream and Nightmare Severity Index (DDNSI) is a 5-item measure of disturbing dream and nightmare frequency along with severity (Krakow et al., 2002; Krakow & Zadra, 2006). Individuals are asked about the frequency of nightmares, how often they result in awakenings, and the severity/intensity of the nightmares. The DDNSI has been validated in student samples (Allen et al., 2021). The DDNSI total score characterized participants' levels of sleep disturbance, specifically nightmare severity, in relation to the structural differences between groups and functional connectivity-change differences of local regions of interest.

Sleep Onset Latency (SOL) and Wake after Sleep Onset (WASO) from sleep diaries. Participants completed daily sleep/wake diaries for 9-21 days in their home setting after the intake. The Morning Sleep Diary provides a self-report record of several sleep dimensions including time in bed, time until sleep onset, amount of time spent awake during the night, and wake up time in addition to several other questions (Monk et al., 1994). For the purposes of this study, SOL was obtained using answers to the question "How long did it take you to fall asleep from the time you got into bed?" in minutes. WASO was obtained using answers to the questions "Last night after I finally fell asleep, I woke up __ times. Altogether, these awakenings lasted __ minutes". Sleep onset latency and wake after sleep onset in minutes were used to characterize participants' levels of sleep disturbance as they are standard measurements acquired and reported in majority of sleep studies (Trauer et al., 2015). Sleep diaries are a validated tool for assessing subjective sleep experience (Espie et al., 2001).

Suicide Measures

The Suicidal Behaviors Questionnaire-Revised (SBQ-R) has four items asking about lifetime suicide ideation/attempt, the frequency of suicidal ideation over the last year, the threat of suicide attempt, and the likelihood of suicidal behavior in the future. Total scores range from 3-18 with higher scores indicating greater suicidality. With 93% sensitivity and 95% specificity, a cut-off score of seven or greater indicates a risk of suicide (Osman et al., 2001). The SBQ-R total score was used to characterize the risk of suicide for the individuals in the sample.

The Frequency of Suicidal Ideation Inventory (FSII) is a five-item scale asking about the frequency of suicidal ideation over the past year (Chang & Chang, 2016). Individuals indicated on a 5-point Likert-type scale, from 1 (*never*) to 5 (*always*), how often they experienced suicidal thoughts over the past year. Higher scores indicated greater suicidal ideation frequency. The internal consistency of the FSII was tested in US, Turkey, Hungary, and China with $\alpha = 0.91$, 0.85, 0.93, and 0.85, respectively (Chang & Chang, 2016). The FSII has significant correlations of 0.88 and 0.85 with the Adult Suicidal Ideation Questionnaire (Reynolds & Ebben, 2017; Reynolds, 1991) and the Suicidal Behaviors Questionnaire-Revised (Osman et al., 2001). It was used both to describe the sample's suicidal ideation and as an outcome variable when characterizing the relationship between insomnia, structural differences and suicidal ideation.

The Death and Suicide Implicit Association Task (Death/Suicide – IAT) is a version of the Implicit Association Test (Greenwald et al., 1998) to provide an implicit cognitive measure of the association between death/suicide and self (Nock et al., 2010). The Death/Suicide-IAT reaction time was administered via Millisecond's Inquisit Web software and used as a measure of suicidality risk to characterize participants' suicidality from a behavioral point of view. It measures the time it takes individuals to classify pairings of self/death and others/life, and vice

versa. Then it compares the reaction time for the death/self-blocks to the life/self blocks. The specifics of the Death/Suicide IAT are explained in a previous paper (Nock et al., 2010). Positive scores support a stronger association between 'Me-Death' and 'Not Me-Life' than for opposite pairings while negative scores support a stronger association between 'Me-Life' and 'Not Me-Death' than for opposite pairings.

Mood Measures

The Patient-Reported Outcomes Measurement Information System – Emotional Distress – Anxiety (PROMIS-ED-A) is an 8-item short form scale that measures anxiety symptoms (Yu et al., 2011). The item bank asks about anxiety symptoms in the past seven days on how often they occur from "Never" to "Always". In other adult samples, there is evidence to support accuracy in capturing clinical criteria for generalized anxiety disorder (Batterham et al., 2019). The PROMIS-ED-A was used to characterize an aspect of the sample's mental health for descriptive purposes. Previous suicidality studies describe the importance of screening for mood disorders as descriptors of individuals' mental health (J. Li et al., 2022). Higher scores on the PROMIS-ED-A indicate greater anxiety.

The Patient Health Questionnaire-9 (PHQ-9) is a 9-item scale that measures depression in individuals (Kroenke et al., 2001). The PHQ-9 was used for screening as well as for characterization of depression in the participants as depression is an important characteristic to identify in individuals with suicidality (J. Li et al., 2022). For screening, item 9 "thoughts that you would be better off dead, or thoughts of hurting yourself in some way" at any point in the past 2 weeks characterized the suicidal ideation group. The PHQ-9 total score administered before the MRI scan was used to characterize depression. It has been validated against diagnostic

interviews to identify major depression at a cut-off score of 10 (Levis et al., 2019). Higher scores indicated greater depression severity.

Neuroimaging Measures and Protocol

Neuroimaging Protocol – Morning

Participants arrived at 8:00 am following an overnight ambulatory polysomnography sleep study. They completed a urine drug test, an MRI safety form, and questionnaires, of which only the ISI and PHQ-9 are included in this protocol. Following the initial protocol, several types of scans were acquired. Participants were scanned using a Siemens 3T Magnetom Vida scanner at the Brigham Young University MRI Research Facility with a 20-channel head coil. High-resolution T1-weighted structural images were collected using the magnetization-prepared rapid acquisition with gradient echo sequence (MPRAGE) and had the following scanner parameters: TR = 2300 ms, TE = 2.41 ms, FoV = 240x240, voxel size = 0.8x0.8x0.8 mm^3, matrix size = 300x300x208, Flip Angle = 8 degrees, slice thickness = 0.8 mm, slices = 208.

Resting-state fMRI images (rs-fMRI) lasting around 10.5 minutes for the morning were acquired using multiband echo planar imaging (EPI) with the following scanner parameters: multiband acceleration factor = 4, TR = 2770 ms , TE = 44 ms, FoV = 208x181, voxel size = 1.9x1.9.x2.0 mm^3 , matrix size = 109x95x72, number of measurements = 220, slice thickness = 2, slices = 72 interleaved, flip angle = 40^o. Participants were instructed to stay awake, still, and keep their gaze on a cross that was visible on a screen in the MRI. The ten-minute scan was used for subsequent pilot analyses as the wake scan.

Neuroimaging Protocol – Evening

The evening of the morning MRI, participants were instructed to return to the MRI facility about an hour prior to their habitual sleep onset time to receive an evening fMRI scan. Upon arrival participants were wired up with an fMRI compatible polysomnographic recordings system. The cap was a 64-channel Quik-Cap Neo Net. According to Wahab and colleagues (2022), there were no differences in identifying effective connectivity in the default mode network between 10- and 15-minute scans. A ten-minute sleep period was identified based on the first ten minutes after self-reported sleep onset, recorded in the awareness questionnaire following the evening scan. Sleep data from 23 participants was used in the exploratory functional analyses.

The two evening rs-fMRI scans were around 45 minutes each and were acquired using multiband EPI with the following scanner parameters: multiband acceleration factor = 4, TR = 2770 ms , TE = 44 ms, FoV = 208x181, voxel size = 1.9x1.9.2.0 mm^3, matrix size = 109x95x72, number of measurements = 969, slice thickness = 2, slices = 72 interleaved, flip angle = 40^o. The evening resting state MRI scans for the initial 45 participants were unusable due to a mismatch between the scanning parameters and head coil which was adapted prior to admitting the final 23 participants. Of the 68 participants, 23 completed the procedures with usable evening MRI scans.

Statistical Analysis

Demographics

Analyses were conducted in StataSE 18 64-bit. Assumptions of normality were checked for each variable using the Shapiro-Wilk test for normality, and variables with normal distributions were reported as mean (standard deviation) while variables with non-normal distributions was reported as median [interquartile range]. Missingness was checked to see if it

was < 5%. Demographic, sleep disturbance, suicidality, and mood measures were compared across groups with Student *t* if normally distributed*, Mann-Whitney U* if non-normally distributed*,* or Fisher's exact chi-square test for categorical data (Table 1).

Structural Analyses

Preprocessing. The structural T1 scans of each participant were visually checked for image quality and converted into NIfTI format using dcm2niix (X. Li et al., 2016). Each T1 image was processed using the recon-all command in FreeSurfer (Dale et al., 1999; Fischl, Sereno, & Dale, 1999). With recon-all, the T1-weighted images underwent skull stripping (Ségonne et al., 2004), intensity normalization (Sled et al., 1998), volumetric labeling and white matter segmentation (Fischl et al., 2002; Fischl, Salat et al., 2004), surface atlas registration (Fischl, Sereno, Tootell et al., 1999), surface extraction and gyral labeling (Desikan et al., 2006; Fischl, van der Kouwe et al., 2004). Following processing, each participant was manually checked, edited, and re-run for pial and white matter errors using autorecon-pial, autorecon2-wm and autorecon3.

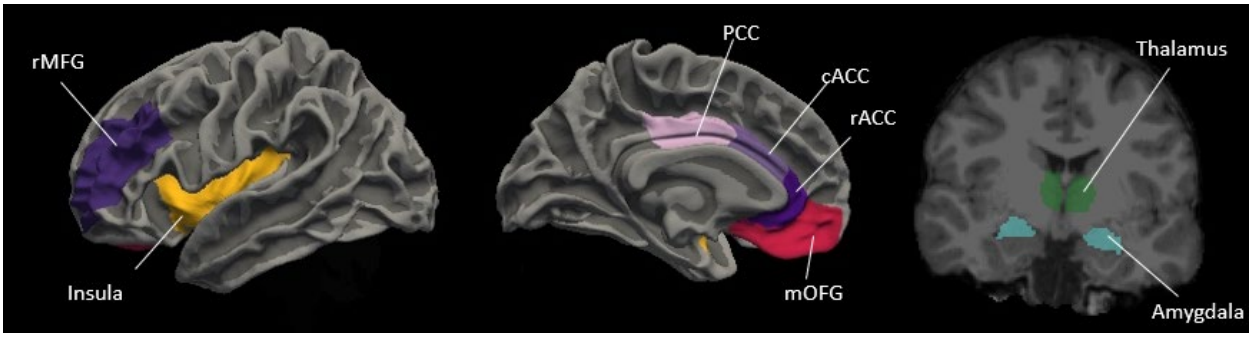
Eight regions of interest defined by FreeSurfer parcellation and segmentation schemes (Desikan et al., 2006; Fischl, Salat et al., 2004) were used in subsequent analyses: caudal anterior cingulate, rostral anterior cingulate, insula, rostral middle frontal gyrus, posterior cingulate, thalamus, amygdala and medial orbitofrontal cortex. Surface area, cortical thickness, and gray matter volume values were extracted for the caudal and rostral anterior cingulate, insula, rostral middle frontal gyrus, posterior cingulate and medial orbitofrontal cortex while only gray matter volume values were extracted for the thalamus and amygdala (See Figure 2).

Structural Surface Area, Cortical Thickness, and Gray Matter Volume Analyses.

According to a previous genetics paper, gray matter volume and surface area in regional

Figure 2

Structural Regions of Interest



Note. The brain images on the left and middle depict the regions-of-interest (ROIs) with extracted values for surface area, cortical thickness, and gray matter volume. The image on the right depicts the ROIs with extracted values for gray matter volume alone. rMFG = rostral middle frontal gyrus, PCC = posterior cingulate cortex, cACC = caudal anterior cingulate cortex, rACC = rostral anterior cingulate cortex, mOFG = medial orbitofrontal gyrus.

areas are highly related while cortical thickness and surface area are not. The researchers suggested that surface area and cortical thickness have different genetic origins (Winkler et al., 2010). There is evidence from schizophrenia literature suggesting that discrepancies in gray matter volume and cortical thickness measurements could reflect distinct cellular mechanisms and therefore are of use in the same analysis (Kong et al., 2015); however, these discrepancies have not been examined in the suicide or sleep disturbance literatures. Smaller cortical thickness in particular seems to be related to shortened sleep at night (Stolicyn et al., 2024). Surface area measurements could reflect the region's computational capacity and resource allocation while cortical thickness measurements might reflect efficiency in knowledge-based tasks (Tadayon et al., 2020). Researchers propose that cortical thickness and surface area measurements capture distinct properties (Sanabria-Diaz et al., 2010; Yang et al., 2016). There are several other studies

indicating that surface area, cortical thickness, and gray matter contribute uniquely to our understanding of the networks of various conditions (Joshi et al., 2011; Yang et al., 2016); therefore, all three will be included in subsequent analyses.

Using Stata SE 18 64-bit, six Multivariate Analysis of Variance (MANOVA) were proposed with group status (SI/NSI) as the between-subjects effect. The first pair of MANOVAs were set up to compare the surface area of the left and right rostral and caudal anterior cingulate, insula, middle frontal gryus, posterior cingulate, and rostral middle frontal gyrus. The second pair of MANOVAs were set up to compare those same regions on cortical thickness. The final pair of MANOVAs were set up to compare the gray matter volume of the thalamus and amygdala in addition to the previous six regions mentioned.

The following assumptions for multivariate normality were checked and adjusted for: multivariate outliers, normality, linear relationships by group, homogeneity of variances and covariances, and multicollinearity. None of the variables had univariate outliers extending beyond the median +/- twice the interquartile range. Based on Hadi's method for multivariate outlier detection (Gould & Hadi, 1993; Hadi, 1992), a single participant (P016) was identified as an outlier for the left hemisphere surface area and gray matter volume measurements. For those areas, the participant was removed to check for the rest of the assumptions. Multivariate normality was checked with Mardia's measure of multivariate skewness and kurtosis along with Doornik-Hansen's omnibus test and Henze-Zirkler's consistent test. The left hemisphere surface area and left hemisphere gray matter volumes regions did not meet the assumptions for multivariate normality. Based on scatterplots and Pearson correlations of each combination of measurement and hemisphere, all the structural measurements were linearly related. Homogeneity of variances and covariances were tested using Box's M test (Box, 1949). The left

hemisphere surface area did not meet this assumption, but the remainder did. There was no multicollinearity for any of the tests.

Since the left hemisphere surface area and gray matter volume regions did not pass multivariate normality and the left hemisphere surface area did not meet the assumption of homogeneity of variances and covariances, Student *t* analyses were used to test for group differences. Each of the six regions for surface area (rostral and caudal anterior cingulate, insula, middle frontal gyrus, posterior cingulate, medial orbitofrontal gyrus) and 8 regions for gray matter volume (rostral and caudal anterior cingulate, insula, middle frontal gyrus, posterior cingulate, thalamus, amygdala, medial orbitofrontal gyrus) were compared by group. MANOVAs were utilized for the other four areas (right surface area, left/right cortical thickness, right gray matter volume). The False Discovery Rate (FDR) was applied to address Type 1 error rates due to multiple comparisons and the adjusted p-values were reported following each relevant statistic (Benjamini et al., 2001).

Following the MANOVA and Student *t* tests, Pearson's bivariate correlations were conducted between significant regions, insomnia severity and nightmare severity based on the pre-MRI ISI and DDNSI total scores, and the frequency of suicidal ideation (FSII, total score) to identify whether these relationships were significant. Finally, contingent on the significant correlations, structural equation modeling in Stata 18 SE 64-bit was used to perform uncontrolled mediation analyses to understand the role structural brain differences played in the relationship between sleep disturbances (insomnia severity and nightmare severity) and suicidal ideation frequency, and were FDR-adjusted as well.

Seed-Based rs-FC Analyses

To explore our model that sleep and suicidality are related, functional connectivity of individuals with and without suicidal ideation were compared across wake and perceived sleep states. Seed-to-voxel whole-brain analyses using a 2x2 mixed ANOVA with *z*-transformed correlation values were used to identify if there was abnormal functional connectivity for the interaction between group (suicidal ideation vs. control) and condition (wake vs. sleep) in each seed region (anterior cingulate cortex, bilateral insula, bilateral middle frontal gyrus, posterior cingulate cortex, bilateral thalamus, bilateral amygdala, and bilateral fronto-orbital cortex).

Results included in this manuscript come from analyses performed using CONN (Whitfield-Gabrieli & Nieto-Castanon, 2012) RRID:SCR_009550 release 22.a (Nieto-Castanon, 2022) and SPM (Penny, 2011) RRID:SCR_007037 release 12.7771.

Preprocessing. Functional and anatomical data were preprocessed using a flexible preprocessing pipeline (Nieto-Castanon, 2020c) including realignment with correction of susceptibility distortion interactions, outlier detection, direct segmentation and MNI-space normalization, and smoothing. Functional data were realigned using SPM realign & unwarp procedure (Andersson et al., 2001), where all scans were coregistered to a reference image (first scan of the first session) using a least squares approach and a 6 parameter (rigid body) transformation (Friston et al., 1995), and resampled using b-spline interpolation to correct for motion and magnetic susceptibility interactions. Potential outlier scans were identified using ART (Whitfield-Gabrieli, 2011) as acquisitions with framewise displacement above 0.5 mm or global BOLD signal changes above 3 standard deviations (Calhoun et al., 2017; Nieto-Castanon, submitted) segmented into grey matter, white matter, and CSF tissue classes, and resampled to 2 mm isotropic voxels following a direct normalization procedure (Nieto-Castanon, submitted; Power et al., 2014) using SPM unified segmentation and normalization algorithm (Ashburner,

2007; Ashburner & Friston, 2005) with the default IXI-549 tissue probability map template. Last, functional data were smoothed using spatial convolution with a Gaussian kernel of 8 mm full width half maximum (FWHM).

Denoising. In addition, functional data were denoised using a standard denoising pipeline (Nieto-Castanon, 2020b) including the regression of potential confounding effects characterized by white matter timeseries (10 CompCor noise components), CSF timeseries (5 CompCor noise components), motion parameters and their first order derivatives (12 factors) (Friston et al., 1996), outlier scans (below 161 factors) (Power et al., 2014), session and task effects and their first order derivatives (6 factors), and linear trends (2 factors) within each functional run, followed by high-pass frequency filtering of the BOLD timeseries (Hallquist et al., 2013) above 0.01 Hz. CompCor (Behzadi et al., 2007; Chai et al., 2012) noise components within white matter and CSF were estimated by computing the average BOLD signal as well as the largest principal components orthogonal to the BOLD average, motion parameters, and outlier scans within each subject's eroded segmentation masks. From the number of noise terms included in this denoising strategy, the effective degrees of freedom of the BOLD signal after denoising were estimated to range from 227.6 to 519.5 (average 445.1) across all subjects (Nieto-Castanon, submitted).

First-Level Analysis. Seed-based connectivity maps (SBC) were estimated characterizing the patterns of functional connectivity with 12 ROIs (anterior cingulate cortex, bilateral insula, bilateral middle frontal gyrus, posterior cingulate cortex, bilateral thalamus, bilateral amygdala, and bilateral fronto-orbital cortex). Functional connectivity strength was represented by Fisher-transformed bivariate correlation coefficients from a weighted general linear model (weighted-GLM (Nieto-Castanon, 2020d)), defined separately for each pair of seed

and target areas, modeling the association between their BOLD signal timeseries. Individual scans were weighted by a boxcar signal characterizing each individual task or experimental condition convolved with an SPM canonical hemodynamic response function and rectified.

Group-Level Analyses. These were performed using a General Linear Model (GLM) (Nieto-Castanon, 2020d). For each individual voxel a separate GLM was estimated, with first-level connectivity measures at this voxel as dependent variables (one independent sample per subject and one measurement per task or experimental condition, if applicable), and groups or other subject-level identifiers as independent variables. In this study, the independent variable group consisted of those with suicidal ideation and those without. Voxel-level hypotheses were evaluated using multivariate parametric statistics with random-effects across subjects and sample covariance estimation across multiple measurements. Inferences were performed at the level of individual clusters (groups of contiguous voxels). Cluster-level inferences were based on nonparametric statistics from randomization/permutation analyses (Bullmore et al., 1999; Nieto-Castanon, 2020a), with 1000 residual-randomization iterations. Results were thresholded using a combination of a cluster-forming $p < 0.01$ voxel-level threshold, and a familywise corrected p-FDR < 0.05 cluster-mass threshold (Chumbley et al., 2010).

In summary, changes in functional connectivity across wake and sleep were compared by group for significant clusters in a 2x2 mixed ANOVA design. Effect sizes for each combination of group and condition were plotted.

Results

Demographics

Twelve individuals were excluded, of which ten were based on exclusion criteria: narcolepsy (n=2), shift work (n=1), braces (n=1), previous suicide attempts (n=4), no current

suicidal ideation (n=2). The final two participants excluded withdrew from the study: one before the overnight polysomnography and another for discomfort in the dark during the evening MRI scan. All demographic variables were checked for normality and appropriate tests were conducted (See Table 1). All the variables had <5% missingness. The number of missing observations by variable were: pre-MRI ISI (2), PROMIS-SD(3), SBQ(1), FSII(1), PROMIS-ED-A (1), PHQ-9 (1). Missing observations were dropped in their respective analyses. The groups did not differ on age (z = 0.00, p = 1.00), education (χ^2 = 1.71, p = 0.788), sex (χ^2 = 0.65, p = 0.42), race (χ^2 = 3.61, p = 0.307), ethnicity (z = 1.57, p = 0.209), employment status (χ^2 = 0.31, p = 0.855), average WASO (z = 1.959, p = 0.05), or average SOL (z = 0.09, p = 0.929). The SI group scored higher on the ISI screening (z = 3.06, p = 0.002) and ISI pre-MRI (z = 4.16, p <0.001), HSI (z = 3.93, p<0.001), PROMIS-SD (z = 3.96, p<.0.001), DDNSI (z = 2.42, p = 0.016), SBQ (z = 5.55, p <0.001), FSII (z = 6.18, p<0.001), IAT-Suicide/Death (t(66) = 3.16, p=0.002), PROMIS-ED-A (z = 5.66, p<0.001), PHQ-9 screening (z = 5.31, p<0.001), and PHQ-9 pre-MRI (z = 5.15, p<0.001).

Structural Analyses

MANOVAs by Hemisphere

Surface area measurements for the left hemisphere did not meet the assumption of multivariate normality (Mardia mSkewness χ^2 (56)=87.608, p=0.004; Mardia mKurtosis χ^2 (1) =1.75, p<0.19; Henze-Zirkler χ^2 (1)=0.054, p=0.816; Doornik-Hansen χ^2 (12) = 21.72, p=0.04), so Mann-Whitney U tests were used on the non-normal data. In the right hemisphere, the SI and NSI groups did not significantly differ in cortical surface area within the anterior cingulate, insula, middle frontal gyrus, posterior cingulate, and medial orbitofrontal gyrus [F(6,60)=1.58, p = 0.169, FDR-adjusted p = 0.382, η_p^2= 0.14].

Cortical thickness measurements for the left and right hemispheres did not differ by group in any of the regions [$F(6,60) = 0.42$, $p=0.866$, FDR-adjusted $p = 0.764$, $\eta_p^2= 0.04$; $F(6,60) = 1.05$, $p=0.401$, FDR-adjusted $p = 0.512$, $\eta_p^2= 0.10$ respectively].

Volume measurements for the left hemisphere did not meet the assumptions of multivariate normality (Mardia mSkewness χ^2 (120)=202.03, $p<0.001$; Mardia mKurtosis χ^2 (1) = 2.89, $p=0.089$; Henze-Zirkler χ^2 (1)=8.23, $p=0.004$; Doornik-Hansen χ^2 (16) = 54.94, $p<0.001$). In the right hemisphere, there were no significant volume differences between the SI and NSI groups in any regions (anterior cingulate, insula, middle frontal gyrus, posterior cingulate, thalamus, amygdala, or medial orbitofrontal gyrus) [$F(9,57) = 1.91$, $p = 0.069$, FDR-adjusted $p = 0.382$, $\eta_p^2= 0.23$].

Student's t

There were no significant differences in left hemisphere cortical surface area between groups for the caudal anterior cingulate ($t(66) = 0.70$, $p = 0.484$, FDR-adjusted $p = 0.544$, Cohen's $d = 0.18$), rostral anterior cingulate ($t(66) = 0.960$, $p = 0.341$, FDR-adjusted $p = 0.375$, Cohen's $d = 0.24$), rostral middle frontal gyrus ($t(66) = 0.361$, $p = 0.719$, FDR-adjusted $p = 0.654$, Cohen's $d = 0.09$), posterior cingulate ($t(66) = 1.92$, $p = 0.059$, FDR-adjusted $p = 0.181$, Cohen's $d = 0.48$), and medial orbitofrontal cortex ($t(66) = 1.15$, $p = 0.254$, FDR-adjusted $p = 0.292$, Cohen's $d = 0.29$). However, there was a significant difference between groups in the surface area of the insula ($t(66) = 2.588$, $p = 0.012$, FDR-adjusted $p = 0.139$, Cohen's $d = 0.65$) with the SI group demonstrating smaller surface area. After adjusting for multiple comparisons, it did not remain significant.

There were no significant differences in left hemisphere gray matter volume between groups for the caudal anterior cingulate ($t(66) = 0.25$, p = 0.800, FDR-adjusted p = 0.654, Cohen's d = 0.06), rostral anterior cingulate ($t(66) = 1.20$, p = 0.233, FDR-adjusted p = 0.292, Cohen's d = 0.303), rostral middle frontal gyrus ($t(66) = 0.27$, p = 0.784, FDR-adjusted p = 0.654, Cohen's d = 0.07), posterior cingulate cortex ($t(66) = 1.89$, p = 0.064, FDR-adjusted p = 0.181, Cohen's d = 0.47), thalamus ($t(66) = 1.91$, p = 0.061, FDR-adjusted p = 0.181, Cohen's d = 0.48), amygdala ($t(66) = 1.78$, p = 0.08, FDR-adjusted p = 0.189, Cohen's d = 0.45), and medial orbitofrontal cortex ($t(66) = 1.36$, p = 0.179, FDR-adjusted p = 0.257, Cohen's d = 0.34). However, there was a significant difference between groups in the volume of the insula ($t(66) = 2.44$, p = 0.017, FDR-adjusted p = 0.139, Cohen's d = 0.61), with the SI group having smaller gray matter volume than the NSI group. Again, the significance did not remain after addressing multiple comparisons.

Correlations and Mediation Analysis

Bivariate correlations were reported in Table 2. The correlations between the ISI total score and the left insula surface area and gray matter volume were significantly, negatively associated (r = -0.28, p = 0.021 ; r = -0.27, p = 0.031, respectively). ISI total score was significantly, positively associated with FSII total score (r = 0.35, p = 0.005). The left insula surface area and gray matter volume were significantly, negatively associated with FSII total score (see Table 2). Bivariate correlations between the DDNSI, the left insula surface area and gray matter volume were not significant *(*r = -0.19, p = 0.127; r = -0.173, p = 0.162, respectively*)* while the correlation between the DDNSI and FSII was significant (r = 0.26, p = 0.03).

Results for the structural equation models of aim 1 analysis are found in Figure 3. Mediation of the association between insomnia severity and suicidal ideation frequency by the

Table 2

Correlations between Left Insula Cortical Surface Area, Gray Matter Volume, Insomnia, Nightmare, and Suicidality Severity

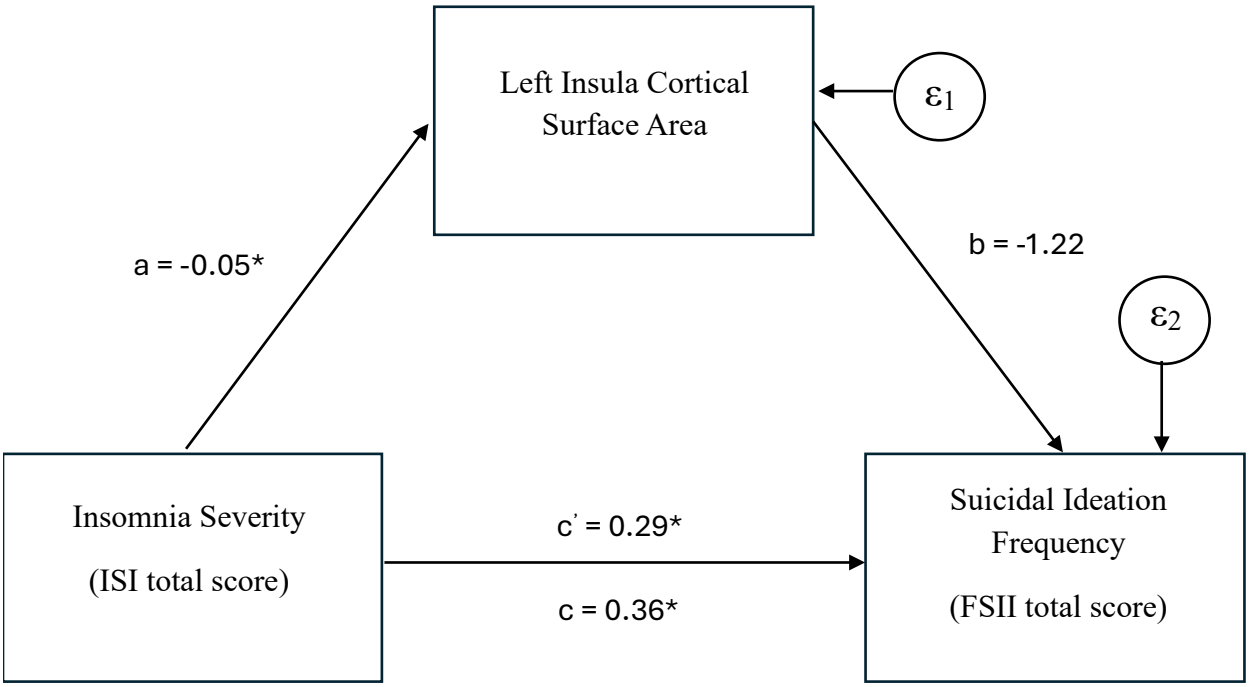
Variable	ISI total score	DDNSI total score	FSII total score	L Insula Surface Area	L Insula Volume
ISI total score	-				
DDNSI total score	0.33*	-			
FSII total score	0.35*	0.26*	-		
L insula surface area	-0.28*	-0.18	-0.28*	-	
L insula volume	-0.27*	-0.17	-0.26*	0.87*	-

Note. *p<0.05. L = left. ISI = Insomnia Severity Index, DDNSI = Disturbing Dream and Nightmare Severity, FSII = Frequency of Suicidal Ideation

left insula cortical surface area was done using structural equation modeling with maximum likelihood estimation with missing values. Cortical surface area and gray matter volume are mathematically related to each other and as surface area had stronger relationships with ISI and FSII total scores, the mediation analysis was tested only using surface area. The left insula cortical surface area was centered and standardized to help with model fit. Chi-squared fit statistics were not reported as the model was just identified. The baseline vs saturated model was χ^2 (3, N = 68) = 15.323, p = 0.002. Unstandardized beta values were reported.

Figure 3.

Mediation Model for Left Insula Cortical Surface Area in the Insomnia Severity-Suicidal Ideation Association



Note: ISI: Insomnia Severity Index, FSII: Frequency of Suicidal Ideation Inventory. Path a is the direct relationship between ISI total score and left insula cortical surface area. Path b is the direct relationship between left insula cortical surface area and FSII total score. Path c is the total effect of the relationship between ISI and FSII total score and path c' is the direct path of ISI total score to FSII total score. $p<0.05$*

Regarding the direct effects, insomnia severity was significantly associated with left insula surface area (β = -0.05, p = 0.023) and suicidal ideation frequency (β = 0.290, p =0.027), but the left insula surface area was not significantly associated with suicidal ideation frequency (β = -1.22, p = 0.075). The total effect between insomnia severity and suicidal ideation frequency was significant (β = 0.36, p =0.006); however, the indirect effect of insomnia severity on suicidal

ideation frequency through the left insula surface area was not significant ($\beta = 0.06$, $p = 0.161$). While insomnia severity is significantly related to suicidal ideation frequency, structural changes in the left insular cortical surface area do not appear to mediate their relationship.

Exploratory Functional Analyses

Using a cluster threshold of p<0.05, cluster-mass p-FDR corrected, voxel threshold p<0.01 p-uncorrected, there were no GroupxCondition differences in functional connectivity between the anterior cingulate cortex, bilateral insula, bilateral middle frontal gyrus, posterior cingulate cortex, left thalamus, bilateral amygdala, bilateral frontal orbital cortex, and bilateral insula with the rest of the brain [F(2,20)<5.85]. However, there was a significant GroupxCondition difference in functional connectivity in the right thalamus. The change in functional connectivity between the right thalamus and left superior/middle temporal lobe from wake to sleep was different for the NSI group compared to the SI group t(21)=6.09, p-FDR(false-discovery rate)<0.001 (see Table 3). The change in functional connectivity between the right thalamus and right superior/middle temporal lobe from wake to sleep was also different for the NSI group compared to the SI group t(21)=5.37, p-FDR<0.001 (see Table 3). In both

Table 3.

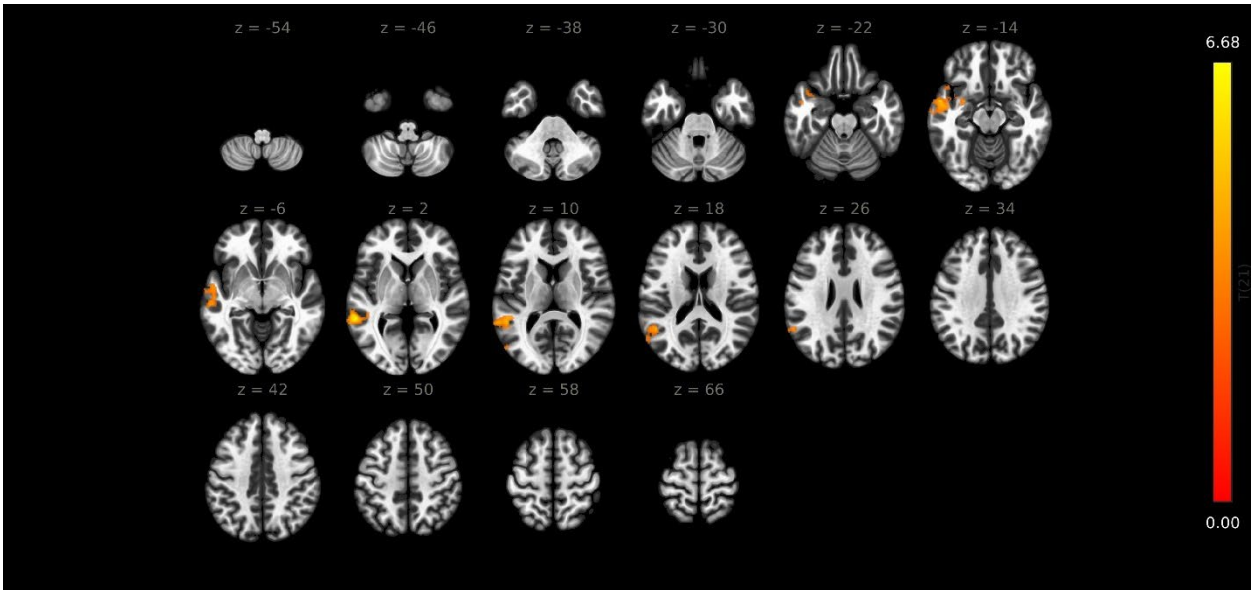
Functional Connectivity between Right Thalamus and Temporal Regions

Region	Subregion	(x, y, z)	Cluster Size (voxels)	size p-FWE	Mass Size	mass p-FDR
Left Superior/Middle Temporal Region		-58 -40 +02	1599	0.039	19868	0.04
	Middle Temporal Gyrus, posterior division left	-60, -28, -4	211			
	Angular Gyrus left	-54, -54, +18	174			
	Superior Temporal Gyrus, anterior division left	-54, -4, -10	150			
	Supramarginal Gyrus, posterior division left	-58, -48, +12	141			
	Temporal Pole Left	-42, +10, -18				
	Middle Temporal Gyrus, temporooccipital part left	-58, -48, +6	111			
	Middle Temporal Gyrus, anterior division left	-58, -48, -14	109			
	Superior Temporal Gyrus, posterior division left	-60, -30, +2	103			
	Lateral Occipital Cortex, superior division left	-56, -64, +16	42			
	Lateral Occipital Cortex, inferior division left	-52, -72, +10	37			
	Planum Polare left	-46, +0, -14	29			
	Insular Cortex left	-38, +6, -16	16			
	Amygdala	-30, +0, -16	16			
	Frontal Orbital Cortex left	-42, +18, -16	6			
	Unlabled	-52, -24, -2	324			
Right Superior/Middle Temporal Region		+48, -14, -16	1008	0.046	13174	0.04
	Middle Temporal Gyrus, posterior division right	+56, -12, -16	204			
	Temporal Pole Right	+54, +10, -18	172			
	Superior Temporal Gyrus, anterior division right	+54, +0, -14	139			
	Middle Temporal Gyrus, anterior division right	+58, -2, -20	113			
	Planum Polare Right	+50, +0, -10	59			
	Superior Temporal Gyrus, posterior division right	+54, -14, -8	29			
	Inferior Temporal Gyrus, posterior division right	+54, -14, -26	6			
	Unlabeled	+50, -8, -14	286			

Note. Results were thresholded using a combination of a cluster-forming $p < 0.01$ voxel-level threshold, and a familywise corrected p-FDR < 0.05 cluster-mass threshold

Figure 4.

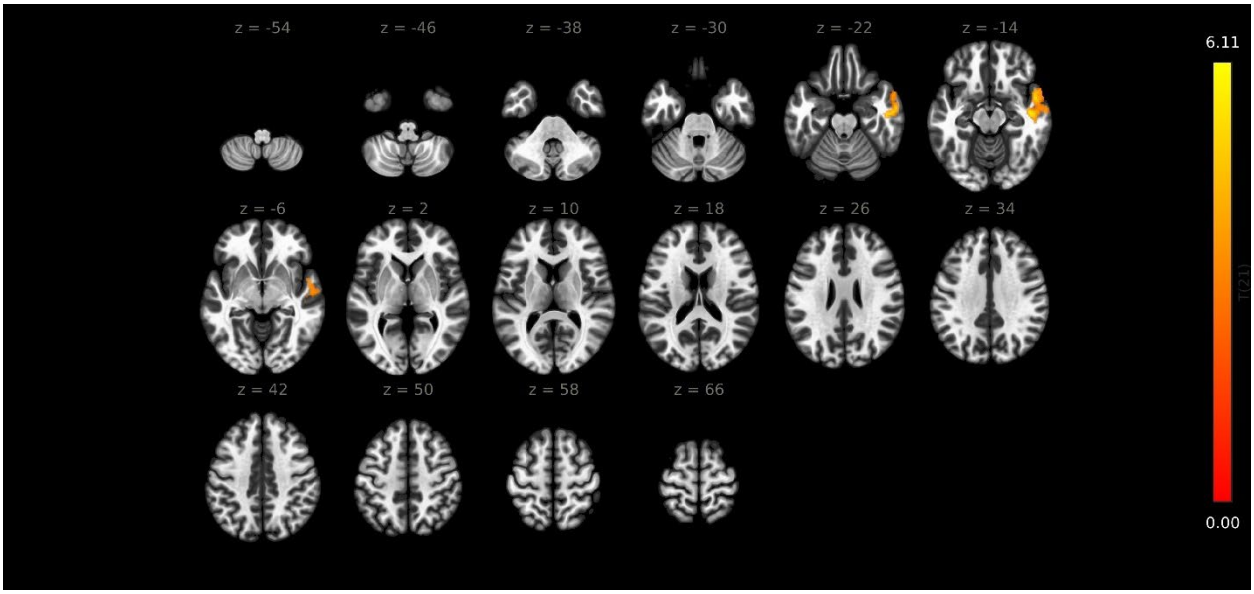
Functional Connectivity-Change Differences etween Right Thalamus and Left Superior/Middle Temporal Regions for Individuals with and without Suicidal Ideation



Sagittal view of regions with significant group differences in functional connectivity across wake and sleep. Color code; yellow/orange, regions for which the control group exhibited greater functional connectivity differences from wake to sleep than the suicidal group. Significant regions were thresholded using a combination of a cluster-forming $p < 0.01$ voxel-level threshold, and a familywise corrected p-FDR < 0.05 cluster-mass threshold

Figure 5.

Functional Connectivity-Change Differences etween Right Thalamus and Right Superior/Middle Temporal Regions for Individuals with and without Suicidal Ideation



Sagittal view of regions with significant group differences in functional connectivity across wake and sleep. Color code; yellow/orange, regions for which the control group exhibited greater functional connectivity differences from wake to sleep than the suicidal group. Significant regions were thresholded using a combination of a cluster-forming $p < 0.01$ voxel-level threshold, and a familywise corrected p-FDR < 0.05 cluster-mass threshold

regions, the NSI group showed greater functional connectivity changes between wake and sleep than the SI group (see Figures 4-7).

Discussion

The first aim was to compare cortical structure differences between individuals with and without suicidal ideation in seven executive functioning and emotional processing regions that overlap between suicidality and sleep disturbance conditions. We hypothesized that there would be structural differences in the anterior cingulate cortex, insula, middle frontal gyrus, posterior cingulate cortex, thalamus, amygdala and medial pre-frontal cortex across both hemispheres for those with and without suicidal ideation. We found that there were cortical surface area and gray matter volume differences in the left insula but not once accounting for multiple comparisons.

Figure 6.

Effect Size for Functional Connectivity between Right Thalamus and Left Temporal Region for Individuals Across Wake and Sleep, with and without Suicidal Ideation

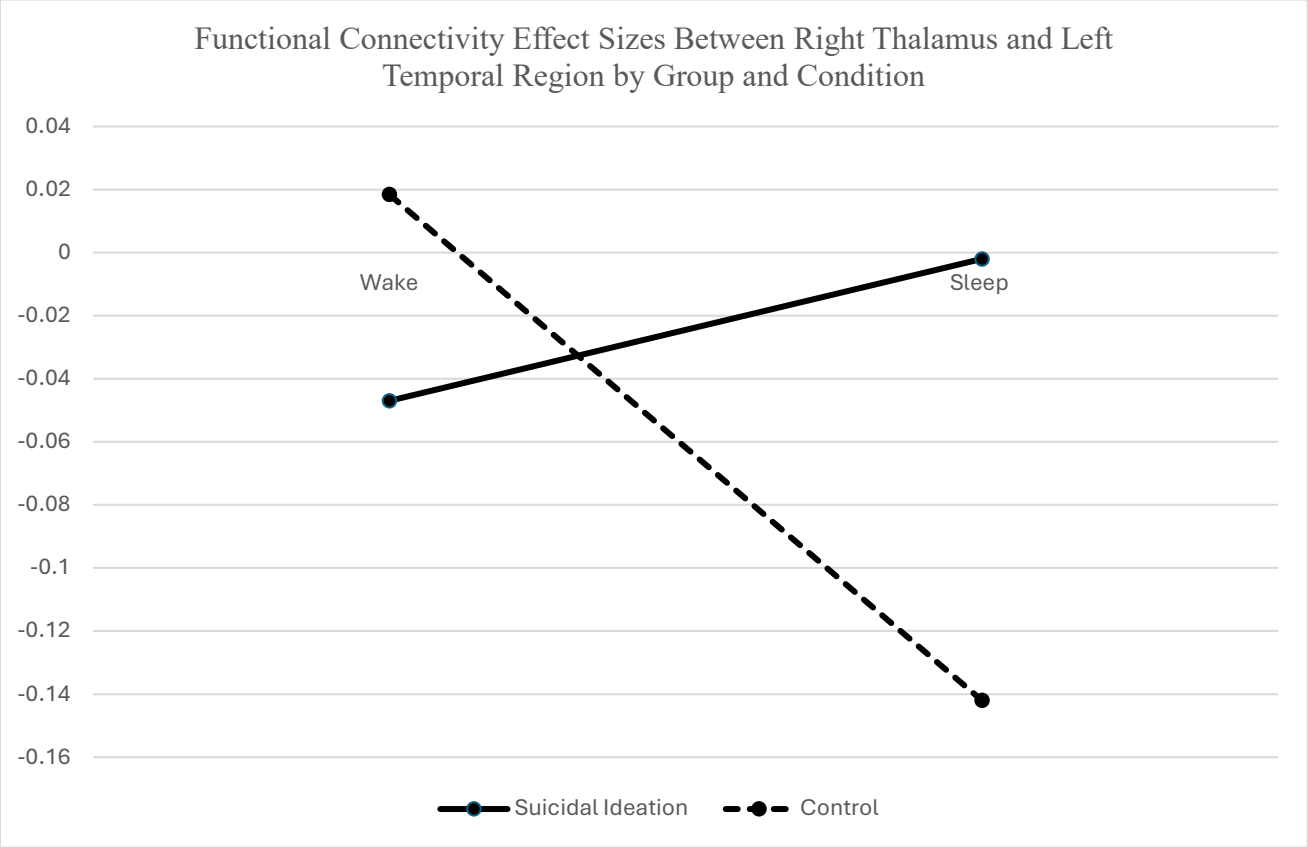
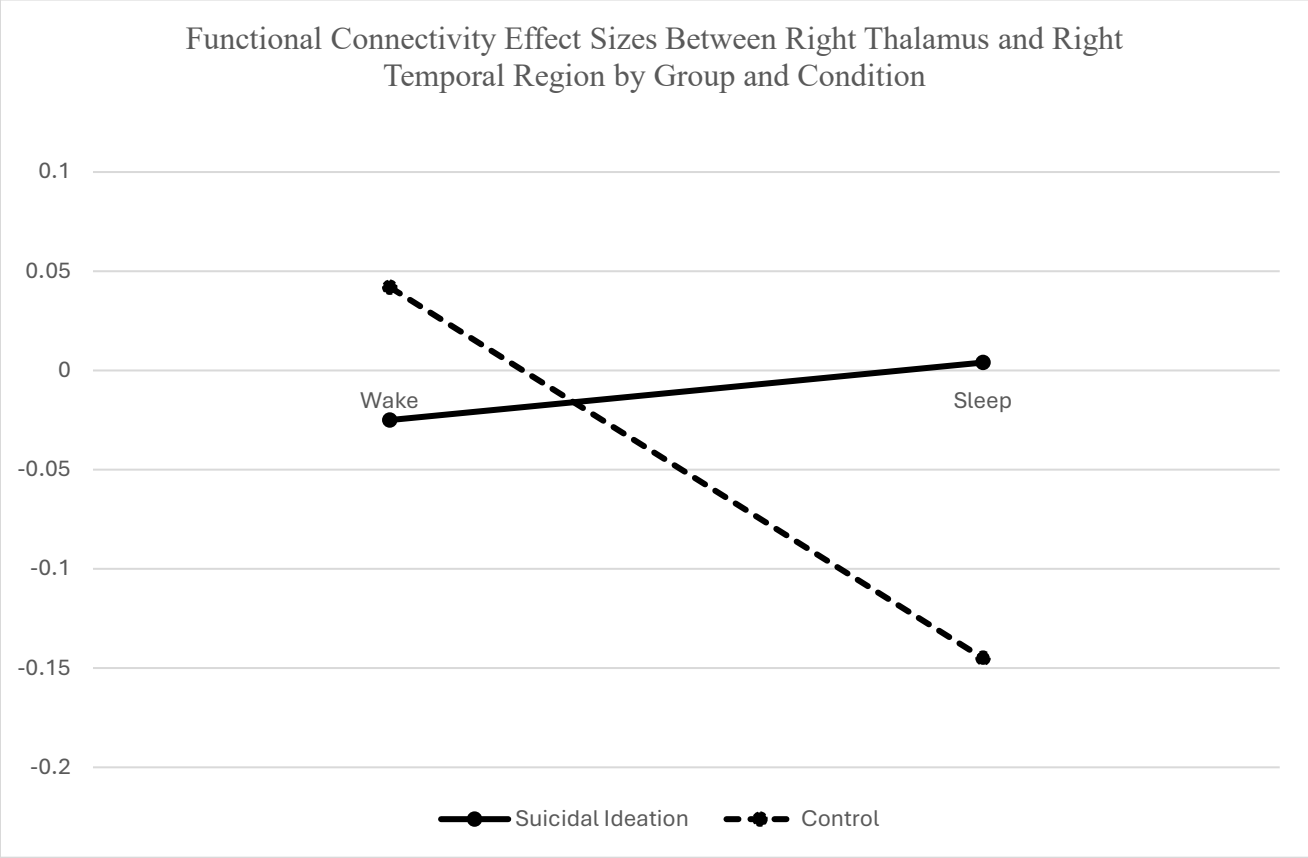


Figure 7.

Effect Size for Functional Connectivity between Right Thalamus and Right Temporal Region for Individuals Across Wake and Sleep, with and without Suicidal Ideation



Our findings partially supported our hypothesis, but only as it pertained to the surface area and volume in the left insula. We also hypothesized that any regions with structural differences between groups would be significantly related to insomnia severity and nightmare severity. More specifically, we hypothesized that the anterior cingulate and insula differences would be related to both insomnia and nightmare severity while differences in the middle frontal gyrus, posterior cingulate and thalamus would be related to insomnia severity and differences in the amygdala and medial prefrontal cortex would be related to nightmare severity. We found that insomnia

severity was significantly related to structural differences in the left insula surface area and gray matter volume which was consistent with our hypothesis. Again, this was prior to multiple comparisons, as the difference was not significant after adjustment. Nightmare severity, however, was not significantly related to insular surface area and gray matter volume. For nightmare severity, our hypothesis was not supported.

Contingent upon the previous hypothesis, we hypothesized that structural differences, in this case, the left insula cortical surface area, would mediate the relationship between insomnia severity and suicidal ideation frequency. There was a direct relationship between insomnia severity and suicidal ideation frequency, but because the relationship between insula surface area and suicidal ideation frequency was not significant, there was not a mediating effect. Our hypothesis was not supported that regions with structural alterations would mediate the insomnia-suicidality relationship.

Our second aim was to explore functional differences across wake and perceived sleep periods in those with and without suicidal ideation, specifically in regions of executive functioning and emotional processing associated with sleep disturbances and suicidal ideation. We hypothesized that those with suicidal ideation would have smaller functional connectivity differences across wake and sleep than those without suicidal ideation in the anterior cingulate cortex, insula, middle frontal gyrus, posterior cingulate cortex, thalamus, amygdala and medial pre-frontal cortex. We found that for all regions except the right thalamus, there were no functional connectivity differences across group and condition. In the right thalamus, there were significant differences between those with and without suicidal ideation across wake and sleep, particularly in the bilateral superior/middle temporal gyrus regions. The control group had larger functional connectivity change-differences between sleep and wake. Our hypothesis that there

would be functional connectivity-change differences across condition by group was partially supported as there were only differences in the right thalamus region.

Previous studies found gray matter volume (Hwang et al., 2010) and cortical thickness differences in the insula (Harenski et al., 2020; Kim et al., 2021; Taylor et al., 2015) with those experiencing suicidal ideation having smaller gray matter volume and cortical thickness compared to those without suicidal ideation. These findings are partially consistent with the results of our study indicating that gray matter volume and cortical surface area were smaller for those with suicidal ideation than without while cortical thickness was not different across groups; however, they did not explore surface area.

The insula has been identified as a region involved with processing self-awareness of internal body signals (Uddin, 2015; Wei et al., 2016) along with external noxious signals (Gamal-Eltrabily et al., 2021) and slow-wave sleep generation (Chen et al., 2014). The smaller gray matter volume and cortical surface area in individuals with suicidal ideation could suggest that these areas are underutilized, potentially resulting in blunted assessments of internal body signals and external noxious signals. There is evidence that individuals who have attempted suicide have blunted interoceptive responses related to reduced functional connectivity in insular regions (DeVille et al., 2020), but individuals with insomnia experience increased interoception (Wei et al., 2016). The insula is a region also implicated in social exclusion and loneliness (Consoloni et al., 2018). The potential upregulation in cognitive control networks as a response to loneliness (Wong et al., 2022), could, over time, contribute to changes in structural features. For individuals experiencing suicidal ideation, they could be having thoughts of social exclusion and loneliness, triggering cognitive control networks to increase in regulation, calling on more resources to process socio-affective experiences.

At the same time, our results indicated that the structural differences in the insula did not mediate the insomnia severity-suicidal ideation relationship even though insomnia and suicidal ideation were both associated with structural differences. Within the mediation model, structural alterations in the insula were not significantly related to suicidal ideation. In a study examining the viability of using structural alterations in individuals with major depressive disorder clinically, Winter and colleagues found that structural differences between those with and without major depressive disorder were small. The groups were relatively similar and group classification accuracy was between 54-56% (Winter et al., 2022). In a similar way, our groups may not have been different enough to capture the effects of small alterations in structure measurements. While the individuals with suicidal ideation had significantly more suicidal thoughts than the individuals without, they only reported moderate amounts of suicidal thoughts within the past year. The suicidal ideation could have been mild enough in frequency and duration that any structural differences would also be mild. It is also possible that individuals with suicidality manifest it in different ways, with some experiencing structural differences while others do not.

In reference to aim 2, the thalamus has previously been identified as a region with abnormalities in the suicidality and insomnia literature (Aquino et al., 2024; Schmaal et al., 2020). It is often primarily identified as a relay station for sensory information (Guillery & Sherman, 2002) but is also associated with executive functioning and emotion regulation processing (Pergola et al., 2013; Rikhye et al., 2018; Zhou et al., 2021). Additionally, the thalamus is highlighted in encoding salience stimuli (Zhou et al., 2021) and assisting with sleep consolidation and promotion (Borbély et al., 2016; Gent et al., 2018; Szabó et al., 2022). Previous functional studies found decreases in the thalamus compared to the whole brain for

those with suicidal ideation. The severity of suicidal ideation was also negatively correlated with functional connectivity within the thalamus (Kang et al., 2017). For individuals with insomnia, functional connectivity changes occur between the thalamus and various regions (Huang et al., 2022; Kim et al., 2021; Li et al., 2019; Perrier et al., 2023).

Within the context of the hyperarousal theory of insomnia, individuals experience an increase in various cognitive and physiological systems which may increase their sensitivity to sensory stimulation. Killgore and colleagues studied the effects of difficulty sleeping on functional connectivity between sensory processing regions (Killgore et al., 2013). They found increased functional connectivity between primary auditory cortices and supplementary motor cortices associated with sleep initiation difficulty. They proposed that greater functional connectivity between sensory and motor regions could perpetuate environmental sensory processing, thus contributing to increased sleep latency. This is consistent with the functional connectivity change differences identified in the sample of individuals with and without suicidality. The control group showed greater changes across wake and sleep in the functional connectivity between the thalamus and temporal regions. During wake, control participants were potentially experiencing auditory processing from the noise of the scanner which decreased dramatically as they fell asleep. In opposition to that, the individuals with suicidality did not experience as much auditory processing during wake but increased during sleep. The suicidality group experienced fewer changes in auditory processing, but the increased auditory processing during sleep could be perpetuating difficulty in maintaining sleep due to an inability to block out auditory signals.

While few studies have indicated more than a passing connection between the thalamus and temporal regions for individuals with suicidal ideation (Meda et al., 2024), a meta-analysis

on individuals with suicidal ideation and behaviors identified increased functional connectivity in the bilateral superior temporal gyrus, bilateral middle occipital gyrus, and left middle temporal gyrus. Even more clear was the robust finding of the bilateral superior temporal gyrus having consistent functional connectivity differences for individuals with suicidality (Chen et al., 2022). Similarly, Vieira (2023) reported that temporal regions are related to emotional processing for individuals with suicidal ideation. In general, the superior temporal gyrus is functionally implicated in auditory processing (Yi et al., 2019), working memory (Park et al., 2011) along with emotion regulation (Chen et al., 2021; Deen et al., 2015), mentalizing processes (Tholen et al., 2020) and the sense of power and hope (Yang et al., 2022). Alterations in the thalamus-temporal processing, in addition to increasing sensitivity to sound, could be impacting emotion regulation or individuals' sense of hope.

As individuals experience suicidal thoughts, they may have heightened arousal and anxiety which disrupts sleep (Bernert et al., 2014) and potentially exemplifies insomnia symptoms. Within the context of the local sleep theory (Krueger et al., 1999), insomnia symptoms may influence the wake-sleep dynamic to where the thalamus and superior/middle temporal regions have local sleep deprivation, resulting in fewer changes across wake and sleep. As the thalamus has a role in filtering signals that come through during sleep (Halassa et al., 2014), individuals with suicidality may have alterations of thalamic filtering with potentially increasing insomnia symptoms. Fewer changes from wake to sleep in regions associated with auditory and emotional processing and sleep promotion could perpetuate the cycle as typical auditory senses augment and emotional processes functions less effectively, creating a higher suicide risk, and worsen insomnia symptoms.

There were several limitations for the current study. The small sample size was powered to only find large effects. It would have been ideal to recruit more participants; however, due to limitations in the timeframe of the dissertation, a maximum of 68 participants was feasible for the proposed project. A power analysis prior to the study identified a range of detectable effect sizes that were possible with the sample size that was feasible according to the constraints. In the case of the exploratory functional connectivity analyses, our sample size was small, but the nonparametric method of analysis was ideal for smaller sample sizes. Another limitation was the use of perceived sleep versus EEG recorded sleep. There have not been studies examining accuracy differences between perceived sleep and physiologically recorded sleep within an MRI scanner, but studies on sleep and misperception suggest that individuals, especially those with insomnia, may need longer period of uninterrupted sleep to perceive sleep onset (Hermans et al., 2020). This could have affected the results as the sleep perception window may have been different than the actual sleep window. Additionally, we did not specifically obtain information about neurologic disorders including traumatic brain injuries or multiple sclerosis to exclude. Neurological conditions could have potentially impacted structural or functional differences in the results. Finally, the data is cross-sectional and the relationships between these variables could go the opposite direction with insomnia being related to suicidal ideation and then functional connectivity differences. There is evidence supporting the bidirectional relationship between insomnia and suicidality (Bernert et al., 2014; Pigeon et al., 2012) and longitudinal studies or experimental designs are needed to further test the directionality of the relationships between sleep disturbances, suicidality, and functional connectivity.

Methodologically, using EEG to identify sleep periods during functional MRI scans could provide additional information on functional connectivity patterns as well as provide insight into

the functional connectivity during perceived sleep vs physiologically derived sleep. Future studies with larger samples could be employed to better characterize the relationships between suicidality and functional connectivity, identifying targets in reducing suicide risk. Testing whether the implementation of a treatment such as cognitive behavioral therapy for insomnia (CBT-I) could alter functional connectivity changes from wake to sleep, and in the process, reduce risk for suicidality would extend this research further into practical applications.

As it is, there is evidence that for individuals experiencing pain, using single-pulse transcranial magnetic stimulation (TMS) in the superior temporal gyrus reduces bias in later recollection of pain (Houde et al., 2020). For individuals with insomnia or suicidality, there may be misperceptions in pain experiences (physical or emotional), and the use of TMS in the temporal region might help with that misperception and reduce the severity of insomnia or suicidality symptoms. There is also preliminary evidence that, in general, TSM could be a viable treatment option for individuals experiencing suicidality (Bozzay et al., 2020; Terpstra et al., 2023), even in conjunction with CBT-I.

This study aimed to compare cortical structure differences in specific brain regions between individuals with and without suicidal ideation, hypothesizing structural differences in areas that included the insula and thalamus. Results showed differences in the left insula's cortical surface area and gray matter volume that were associated with insomnia severity and not nightmare severity. Structural differences in the insula did not mediate the relationship between insomnia severity and suicidal ideation frequency but indicated that insomnia has a direct relationship with suicidal ideation frequency. Functionally, only the right thalamus showed significant connectivity differences between those with and without suicidal, influenced by insomnia severity. Consistent with previous studies indicating smaller gray matter volumes in the

insula for suicidal individuals, this study found smaller volumes and surface area, suggesting a potential over-utilization of these areas due to increased self-awareness and external signal processing demands. Additionally, the thalamus showed significant functional connectivity-change differences linked to sleep disturbances, impacting sensory/emotional processing and potentially perpetuating insomnia and suicidal ideation. Limitations include a small sample size and reliance on perceived sleep data. Future research should explore EEG-based sleep measures and interventions like cognitive behavioral therapy for insomnia (CBT-I) and transcranial magnetic stimulation (TMS) as potential treatments for suicidality and related sleep disturbances.

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Appendix

Coping Card

1) Call someone

2) Complete three emotional regulation activities (Joiner Jr et al., 1999)

3) Do steps 1 & 2 again

4) Emergency #: Suicide Hotline (1800273TALK)

6) Call 911, or take/go to ER

Insomnia

Insomnia Severity Index

The Insomnia Severity Index has seven questions. The seven answers are added up to get a total score. When you have your total score, look at the 'Guidelines for Scoring/Interpretation' below to see where your sleep difficulty fits.

For each question, please CIRCLE the number that best describes your answer.

Please rate the CURRENT (i.e. LAST 2 WEEKS) SEVERITY of your insomnia problem(s).

Insomnia Problem	None	Mild	Moderate	Severe	Very Severe
1. Difficulty falling asleep	0	1	2	3	4
2. Difficulty staying asleep	0	1	2	3	4
3. Problems waking up too early	0	1	2	3	4

4. How SATISFIED/DISSATISFIED are you with your CURRENT sleep pattern?

Very Satisfied	Satisfied	Moderately Satisfied	Dissatisfied	Very Dissatisfied
0	1	2	3	4

5. How NOTICEABLE to others do you think your sleep problem is in terms of impairing the quality of your life?

Not at all Noticeable	A Little	Somewhat	Much	Very Much Noticeable
0	1	2	3	4

6. How WORRIED/DISTRESSED are you about your current sleep problem?

Not at all Worried	A Little	Somewhat	Much	Very Much Worried
0	1	2	3	4

7. To what extent do you consider your sleep problem to INTERFERE with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc.) CURRENTLY?

Not at all Interfering	A Little	Somewhat	Much	Very Much Interfering
0	1	2	3	4

Hypersomnia

1. For these next few questions, please consider your SLEEP IN THE PAST MONTH. To what extent do you think that you:

	Not at All	A Little	Somewhat	A Lot	Very Much
Sleep too much at night?	0	1	2	3	4
Have difficulty waking up in the morning or from naps?	0	1	2	3	4
Sleep during the day?	0	1	2	3	4
Feel sleepy during the daytime?	0	1	2	3	4

2. How SATISFIED/dissatisfied are you with your current sleep pattern?

Very satisfied		Moderately satisfied		Very dissatisfied
0	1	2	3	4

3. To what extent do you consider your sleep problem to INTERFERE with your daily functioning (e.g., daytime fatigue, ability to function at work/daily chores, concentration, memory, mood, etc.)?

Not at all	A little	Somewhat	Much	Very much
0	1	2	3	4

4. How NOTICEABLE to others do you think your sleeping problem is in terms of impairing the quality of your life?

Not at all Noticeable	Barely	Somewhat	Much	Very much Noticeable
0	1	2	3	4

5. How WORRIED/DISTRESSED are you about your current sleep problem?

Not at all	A little	Somewhat	Much	Very much
0	1	2	3	4

6. Do you ever have "sleep attacks," defined as unintended sleep in inappropriate situations?

Not at all		Sometimes		All the time
0	1	2	3	4

Sleep Disturbance

In the past 7 days...

		Not at all	A little bit	Somewhat	Quite a bit	Very much
Sleep105	My sleep was restful.	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
Sleep106	My sleep was light.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep107	My sleep was deep.	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
Sleep108	My sleep was restless.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep115	I was satisfied with my sleep.	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
Sleep116	My sleep was refreshing.	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
Sleep125	I felt lousy when I woke up.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep20	I had a problem with my sleep.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep44	I had difficulty falling asleep.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep65	I felt physically tense at bedtime.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

In the past 7 days…

		Not at all	A little bit	Somewhat	Quite a bit	Very much
Sleep67	I worried about not being able to fall asleep.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep68	I felt worried at bedtime.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep69	I had trouble stopping my thoughts at bedtime.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep70	I felt sad at bedtime.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep71	I had trouble getting into a comfortable position to sleep.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep72	I tried hard to get to sleep.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep78	Stress disturbed my sleep.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep86	I tossed and turned at night.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep93	I was afraid I would not get back to sleep after waking up.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

In the past 7 days…

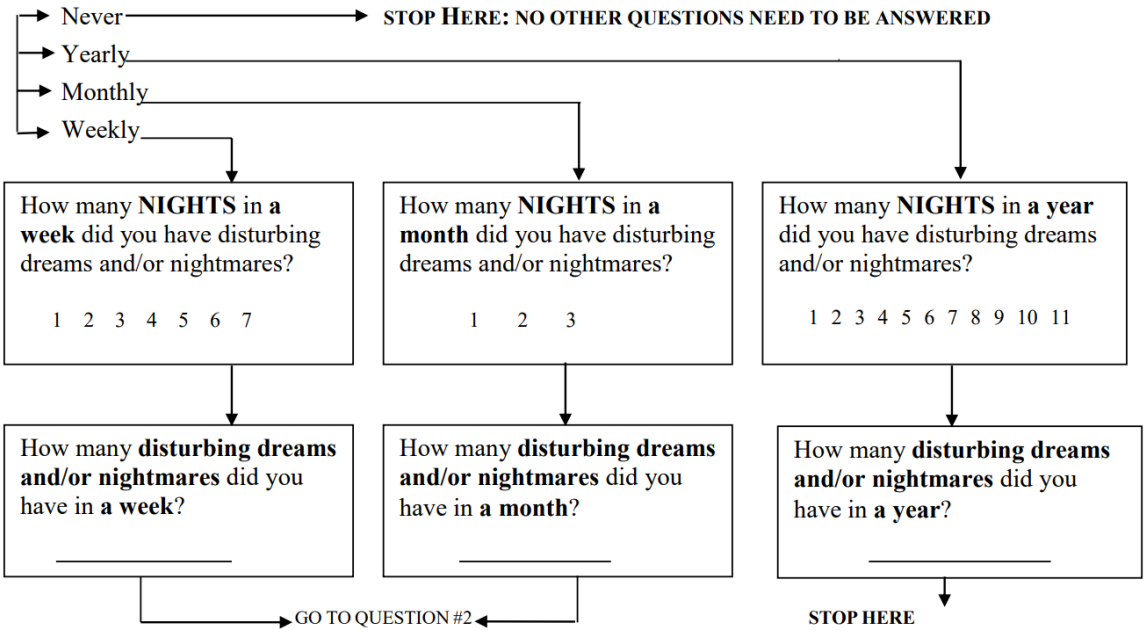
		Never	Rarely	Sometimes	Often	Always
Sleep110	I got enough sleep.	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
Sleep42	It was easy for me to fall asleep.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
Sleep45	I laid in bed for hours waiting to fall asleep.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep50	I woke up too early and could not fall back asleep.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep87	I had trouble staying asleep.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep90	I had trouble sleeping.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Sleep92	I woke up and had trouble falling back to sleep.	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

	In the past 7 days…	Very poor	Poor	Fair	Good	Very good
Sleep109	My sleep quality was…	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

Nightmare Frequency, Severity, and Distress

Disturbing Dream and Nightmare Severity Index

1. How often do you have disturbing dreams and/or nightmares: (Circle one, then follow the arrow)



2. Please estimate the NUMBER of months or years you have had disturbing dreams and/or nightmares:

_____months _____years

3. On average, do your nightmares wake you up? (Circle answer)

Never/Rarely Occasionally Sometimes Frequently Always

4. How would you rate the SEVERITY of your disturbing dreams and/or nightmare problem? (Circle answer)

No Problem | Minimal Problem | Mild Problem | Moderate Problem | Severe Problem | Very Severe Problem | Extremely Severe Problem

5. How would you rate the INTENSITY of your disturbing dreams and/or nightmares? (Circle answer)

Not Intense | Minimal Intensity | Mild Intensity | Moderate Intensity | Severe Intensity | Very Severe Intensity | Extremely Severe Intensity

Scoring: Add nights/per week (0 to 7) + nightmares/week* +Q3 (0 to 4 scale) +Q4 (0 to 6 scale) + Q5 (0 to 6 scale)
*Notes: maximum for nightmares/week = 14, so scale is 0 to 14. Don't use Q2. Score > 10 usually indicate a nightmare disorder.

Wake after Sleep Onset & Sleep Onset Latency from Sleep Diaries

WAKETIME

Keep by Bed - Please Fill this out First Thing in the Morning.

Today is: Sun M T W Th F Sat Today's date is: _____

Last night I got into bed at ___:___ PM AM

I actually tried to go to sleep at ___:___ PM AM

I think it took me about _____ minutes to fall asleep

This morning, I finally woke at ___:___ AM PM

I actually got out of bed to start my day at ___:___ AM PM

My final awakening this morning was caused by (check one):

alarm clock/radio ☐ noises ☐
someone woke me ☐ I just woke up ☐

==========

Last night after I finally fell asleep, I woke up this many times during the night (circle one)

0 1 2 3 4 5 or more.

Altogether, these awakenings lasted _____ minutes.

Of these awakenings (circle one for each line):

I woke to use the bathroom	0	1	2	3	4	5 or more times.
I woke due to noises, child, or bedpartner	0	1	2	3	4	5 or more times.
I woke due to discomfort or a physical complaint	0	1	2	3	4	5 or more times.
I woke due to another or no special reason	0	1	2	3	4	5 or more times.
Last night I remember that I had	0	1	2	3	4	5 or more dreams.

==========

Please place an X on the following lines where it best describes your feelings:

The quality of my sleep last night was:

Very Bad _____ Very Good

My mood when I finally woke up this morning was:

Very Tense _____ Very Calm

My alertness when I finally woke up this morning was:

Very Sleepy _____ Very Alert

In general, my dreams last night were: *(answer only if you had dreams)*

Very Unpleasant _____ Very Pleasant

Not at all Intense _____ Very Intense

Suicidal Behavior and Risk

Patient Name _____ Date of Visit _____

Instructions: Please check the number beside the statement or phrase that best applies to you.

1. Have you ever thought about or attempted to kill yourself? (check one only)

- ☐ 1. Never
- ☐ 2. It was just a brief passing thought
- ☐ 3a. I have had a plan at least once to kill myself but did not try to do it
- ☐ 3b. I have had a plan at least once to kill myself and really wanted to die
- ☐ 4a. I have attempted to kill myself, but did not want to die
- ☐ 4b. I have attempted to kill myself, and really hoped to die

2. How often have you thought about killing yourself in the past year? (check one only)

- ☐ 1. Never
- ☐ 2. Rarely (1 time)
- ☐ 3. Sometimes (2 times)
- ☐ 4. Often (3-4 times)
- ☐ 5. Very Often (5 or more times)

3. Have you ever told someone that you were going to commit suicide, or that you might do it? (check one only)

- ☐ 1. No
- ☐ 2a. Yes, at one time, but did not really want to die
- ☐ 2b. Yes, at one time, and really wanted to die
- ☐ 3a. Yes, more than once, but did not want to do it
- ☐ 3b. Yes, more than once, and really wanted to do it

4. How likely is it that you will attempt suicide someday? (check one only)

- ☐ 0. Never
- ☐ 1. No chance at all
- ☐ 2. Rather unlikely
- ☐ 3. Unlikely
- ☐ 4. Likely
- ☐ 5. Rather likely
- ☐ 6. Very likely

Frequency of Suicidal Ideation

Item	
1.	Over the past year, how often have you thought about hurting yourself?
2.	Over the past year, how often have you believed that your life was not worth living?
3.	Over the past year, how often have you wondered what would happen if you ended your own life?
4.	Over the past year, how often have you thought about committing suicide?
5.	Over the past year, how often have you wished you did not exist?

Emotional Distress – Anxiety

PROMIS® Item Bank v1.0 – Emotional Distress – Anxiety – Short Form 8a

Emotional Distress – Anxiety – Short Form 8a

Please respond to each question or statement by marking one box per row.

In the past 7 days…

		Never	Rarely	Sometimes	Often	Always
EDANX01	I felt fearful	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX40	I found it hard to focus on anything other than my anxiety	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX41	My worries overwhelmed me	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX53	I felt uneasy	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX46	I felt nervous	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX07	I felt like I needed help for my anxiety	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX05	I felt anxious	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
EDANX54	I felt tense	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Depression

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✔" to indicate your answer)*	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING 0 + _____ + _____ + _____

=Total Score: _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	**Somewhat difficult**	**Very difficult**	**Extremely difficult**
☐	☐	☐	☐