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A Biopsychosocial Model of Chronic Posttraumatic Nightmares

by

Maegan M. Paxton Willing

Dissertation proposal submitted to the Faculty of the
Department of Medical and Clinical Psychology
Uniformed Services University of the Health Sciences
In partial fulfillment of the requirements for the degree of
Doctor of Philosophy 2021

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
SCHOOL OF MEDICINE GRADUATE PROGRAMS
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March 26, 2021

MEMORANDUM FOR: **DR. JOSHUA C. GRAY**
DR. DAVID S. RIGGS
DR. LAYNE BENNION
DR. TREVEN C. PICKETT

SUBJECT: Appointment to the Final Doctoral Examination Committee for Maegan M. Paxton Willing

In accordance with the School of Medicine Graduate Program Guidelines, you are formally appointed to the Final Examination Committee of Maegan M. Paxton Willing, doctoral student in the Department of Medical and Clinical Psychology.

This Committee will evaluate the scope and quality of the student's Dissertation and certify the document's acceptability.

In addition, the Committee will conduct an Oral Examination of the student's scientific knowledge, as well as the knowledge and understanding of the research project and Dissertation. This examination constitutes the Private Defense.

The Private Defense for Maegan M. Paxton Willing will take place on Tuesday, April 6, 2021 at 10:00 AM via Zoom meeting.

Dr. David S. Riggs is appointed Chair of the Examination Committee. Dr. Riggs will oversee the examination. Passage of the Private Defense will be by majority vote. If corrections to the Dissertation are needed, the Chair may oversee this process and sign-off after the corrections are made.

The Committee Chair should return the signed and dated Final Examination/Private Defense Form and the Dissertation Approval Form to the Graduate Education Office.

GEO thanks you in advance for your participation in the SOM Graduate Program process.

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Saibal Dey, Ph.D.
Associate Dean for Graduate Education

Learning to Care for Those in Harm's Way

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FINAL EXAMINATION/PRIVATE DEFENSE FOR THE DEGREE OF DOCTOR OF PHILOSOPHY
IN THE DEPARTMENT OF MEDICAL AND CLINICAL PSYCHOLOGY

Name of Student: Maegan M. Paxton Willing

Date of Examination: April 6, 2021
Time: 10:00 AM

DECISION OF EXAMINATION COMMITTEE MEMBERS:

	PASS	FAIL
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APPROVAL OF THE DOCTORAL DISSERTATION IN THE DEPARTMENT OF MEDICAL AND CLINICAL PSYCHOLOGY

Title of Dissertation: "A Biopsychosocial Model of Chronic Posttraumatic Nightmares"

Name of Candidate: Maegan M. Paxton Willing
Doctor of Philosophy Degree
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I truly could not have made it to this point without you all!

DEDICATION

This work is dedicated to my Poppey whose years of service led me here. You'll always be my hero. And to my Nanny who always believed in us. I love you big much.

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Maegan M. Paxton Willing

May 14, 2021

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ABSTRACT

A Biopsychosocial Model of Chronic Posttraumatic Nightmares

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Doctoral Candidate, 2021

Dissertation directed by: David S. Riggs, PhD, Department of Medical and Clinical Psychology

Posttraumatic nightmares are estimated to be present in more than 90% of PTSD cases. Posttraumatic nightmares are associated with a number of deleterious effects such as decreased quality of life and increased risk of suicide. Despite the substantial impact on patients' lives, current treatments are often insufficient to resolve posttraumatic nightmares. Importantly, there is a dearth of knowledge regarding the underlying mechanisms involved in the initiation and maintenance of posttraumatic nightmares. Thus, an increased understanding into the possible mechanisms involved in their perpetuation may improve treatment strategies. Currently, proposed models conceptualize posttraumatic nightmares as the same as idiopathic nightmares. However, posttraumatic nightmares are related to a traumatic experience whereas idiopathic nightmares do not have a known cause. Although these two types of nightmares may share some overlap, it is unwise to assume aspects of the trauma experience or other distinctions between the two types of nightmares do not result in disparate pathways to chronicity. Some models

of posttraumatic nightmares exist; however, these models consider singular predictors of posttraumatic nightmares and lack the important perspective of a comprehensive approach. Therefore, the present project aimed to develop and examine a comprehensive biopsychosocial model of posttraumatic nightmares utilizing data from the clinical database of the Intensive Outpatient Program at the National Intrepid Center of Excellence. The first study examined psychological factors (i.e., PTSD, anxiety, depression) as they relate to posttraumatic nightmares, while controlling for relevant comorbid symptoms and demographic and military characteristics. Notable findings included mental health symptoms including PTSD, anxiety, and depression were related to a greater likelihood of posttraumatic nightmares but were relatively small compared to odds ratios associated with sleep disturbances including problems falling asleep, problems staying asleep, and pain that disrupted sleep. Conversely, patients who were special operators were substantially less likely to endorse posttraumatic nightmares. These findings provide support for the role of mental health symptoms and sleep disturbances in posttraumatic nightmares as well as the importance of considering patient factors. The second study sought to contribute to the understanding of the neurophysiology of posttraumatic nightmares through an examination of gray matter volume and cortical thickness associated with their occurrence. Contrary to our hypotheses, neither gray matter volume or cortical thickness were related to posttraumatic nightmares in our sample. Finally, the third study assessed the relationship of sleep and suicidal ideation to understand the outcomes of posttraumatic nightmares. This study provided support for the importance of considering posttraumatic nightmares as they were related to a nearly 10 times increased likelihood of suicidal ideation for patients

with significant posttraumatic nightmares. Additionally, findings support the need to consider posttraumatic and idiopathic nightmares separately. In addition to contributing to the paucity of literature examining the mechanisms of posttraumatic nightmares, these studies examine the viability of the proposed biopsychosocial model. The proposed biopsychosocial approach may provide opportunities for identifying pathways by which posttraumatic nightmares become chronic thus potentially leading to improved treatments. Additionally, the proposed project may encourage both researchers and providers to take a biopsychosocial approach to the study of posttraumatic nightmares as well as the conceptualization and treatment of patients seeking relief from posttraumatic nightmares.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1: Introduction

UNDERSTANDING POSTTRAUMATIC NIGHTMARES

Posttraumatic nightmares are extremely common among patients with posttraumatic stress disorder (PTSD). Indeed, some estimates suggest posttraumatic nightmares occur in 90% of patients with PTSD (Creamer et al., 2018) and may be the hallmark of the disorder (Writer et al., 2014). Additionally, a study of World War II veterans found patients continued to experience frequent posttraumatic nightmares more than 45 years after the trauma (Guerrero & Crocq, 1994). Despite the high prevalence of nightmares among people with PTSD, comparatively little research and theoretical work has addressed posttraumatic nightmares, factors that relate to their presence/severity, or their relation to other important aspects of adjustment following trauma.

Nightmares are known to cause significant distress (Lamis et al., 2018) and are associated with a number of deleterious effects. Nightmares are correlated with negative affect, which may be due to a decreased ability to self-regulate emotions or handle suffering (Cukrowicz et al., 2006). Further, posttraumatic nightmares influence psychological pain and worsen outcomes beyond their role in the intrusion category (Campbell & Germain, 2016). The nightmare content may result in heightened anguish and negative cognitions while awake. Nightmares affect many aspects of a patient's life including occupational and social functioning, energy, mood, and diet (Miró & Martínez, 2005) as well as their overall well-being (Blagrove et al., 2004; Miró & Martínez, 2005) and sleep (e.g., Lancee et al., 2010; Short et al., 2018). Therefore, it is not surprising that nightmares negatively affect quality of life (Kung et al., 2012), and treating them

improves reported QoL (Davis et al., 2011). Thus, there is a significant need to increase understanding of this phenomenon and its relation to other posttraumatic reactions such as PTSD.

PTSD occurs after one experiences a traumatic event related to actual or possible sexual violence, injury, or death through first-hand experience, observing the event, hearing about it happening to a close friend or family member, or recurring or severe exposure to aspects of the traumatic event (American Psychiatric Association, 2013). The corresponding symptoms are classified in four categories including intrusions (e.g., repeated bad dreams or nightmares of the traumatic event), avoidance (e.g., avoiding people or situations that are reminders of the event), negative cognitions and mood (e.g., feeling detached or excessively guilty), and arousal (e.g., hypervigilance; American Psychiatric Association, 2013). In order to be given a PTSD diagnosis, a patient must present with at least one intrusion and avoidance symptom as well as a minimum of two arousal and negative cognitions and mood related symptoms (American Psychiatric Association, 2013). Additionally, the patient must have experienced these symptoms for a minimum of one month and cause clinically significant distress or dysfunction in the patient's life.

Defining the Phenomena of Posttraumatic Nightmares

Oftentimes, bad dreams and nightmares are discussed interchangeably. However, these two phenomena are different and should be distinguished clinically and in research (e.g., Levin & Nielsen, 2007). Bad dreams are similar to nightmares in that they are distressing dreams that may be a negative experience; however, they do not wake the

patient up from sleep (Robert & Zadra, 2008). In addition to this important distinction, there are a number of subtypes of nightmares that require consideration.

To fully understand posttraumatic nightmares, it is imperative to first distinguish them from idiopathic nightmares. A posttraumatic nightmare is a distressing or frightening dream related to a traumatic experience that awakens the sleeper (Phelps et al., 2008). Conversely, idiopathic nightmares are not trauma related and, at this time, have no known cause (Nielsen & Levin, 2007). Patients may have posttraumatic dreams or posttraumatic anxiety dreams as well. Posttraumatic dreams and posttraumatic anxiety dreams differ from one another in that the latter is a *frightening* dream related to the traumatic event and posttraumatic dreams are simply a dream that the patient associates with a traumatic experience (Phelps et al., 2008). Posttraumatic anxiety dreams differ from posttraumatic nightmares in that anxiety dreams do not awaken the patient and, thus, may or may not be remembered in the morning when they awaken (Phelps et al., 2008).

Within the posttraumatic nightmare category, patients may experience replicative or nonreplicative posttraumatic nightmares (Nielsen & Levin, 2007; Phelps et al., 2008). In replicative posttraumatic nightmares, a patient essentially relives the traumatic experience. A nonreplicative posttraumatic nightmare is a nightmare that has content related to the traumatic event but is not an exact depiction of the event. Replicative posttraumatic nightmares are hypothesized to cause greater distress and disruption of emotion regulation than posttraumatic nightmares (Levin & Nielsen, 2007). It is important to distinguish among these categories when treating and diagnosing patients to

increase consistency and better elucidate distinctions for clinical and research purposes (Nielsen & Levin, 2007; Phelps et al., 2008).

Current Models

A number of psychological theories of dreaming exist. Although a thorough description of these theories is beyond the scope of the present proposal, a brief description of the most prominent ones will be provided in the Psychological Factors section below. For a more thorough review of the psychological theories, see Nielsen and Levin (2007). The present discussion will focus on the models specifically pertaining to posttraumatic nightmares.

A number of theorists have proposed posttraumatic nightmares serve to integrate a traumatic experience, and psychodynamic, cognitive, and physiological theorists concur that chronic posttraumatic nightmares are the result of inadequate adaptation and recovery after a traumatic experience (Germain, 2013). Psychodynamic theorists hypothesize that posttraumatic nightmares serve as an opportunity for integration of the trauma memory during sleep, as this represents a time when defense mechanisms are thought to be reduced (as cited in Germain, 2013). Freud posited posttraumatic nightmares serve to control the anxiety and guilt related to the traumatic experience (as cited in Germain, 2013). Similarly, Miller and colleagues (2017) proposed nightmares that occur soon after a trauma are the mind's attempt to integrate the trauma and chronic nightmares may be the result of a misstep in this process (Miller et al., 2017).

Two models of nightmares have been proposed (e.g., Levin & Nielsen, 2007, 2009; Nielsen & Levin, 2007; Phelps et al., 2008); however, the model by Levin and Nielsen (2007, 2009; Nielsen & Levin, 2007) conceptualize idiopathic and posttraumatic

nightmares as sharing a unified model. Idiopathic and posttraumatic nightmares differ in that posttraumatic nightmares involve the patient reexperiencing his or her traumatic experience in dream form. Idiopathic nightmares are unrelated to a traumatic experience and have no known cause (Nielsen & Levin, 2007). Therefore, it is necessary to develop a posttraumatic nightmare-specific model. Phelps and colleagues (2008) presented three individual proposed mechanisms for chronic posttraumatic nightmares; however, they neglected to provide a comprehensive or integrative model. These models are reviewed below.

Levin and Nielsen (2007, 2009; Nielsen & Levin, 2007) developed the "Neurocognitive Model of Dreaming," which presents a model of disturbing dreams, a term inclusive of both nightmares and bad dreams, with cognitive and neurophysiological components. This model posits affect load, a state factor, increases the propensity for disturbing dreams, while affect distress, a trait factor, increases the likelihood that disturbing dreams will result in daytime dysfunction such as increased anxiety (Levin & Nielsen, 2009). Affect load describes the sum of stressful and emotionally negative experiences that disrupt effective emotion regulation. Affect distress is one's innate likelihood to experience increased distress to emotional events (Levin & Nielsen, 2009). Affect distress is positively associated with nightmare frequency and severity (Levin & Nielsen, 2007).

Fear memory extinction, or the capacity to eliminate a conditioned fear (Zuj et al., 2016), is hypothesized to be an important component in limiting the perpetuation of posttraumatic nightmares. Levin and Nielsen (2009) propose that cognitively, dreams enable the fear memory learning and extinction processes through memory-element

activation and recombination as well as emotional expression. Memory element activation is the heightened accessibility of "memory elements" while dreaming, and memory-element recombination is the process of assembling these memory elements into a coherent dream (Levin & Nielsen, 2009). Emotional expression utilizes the neural processes to allow for decreasing the averse emotional response, thus facilitating fear extinction (Levin & Nielsen, 2009). These three processes may be particularly salient for the conceptualization of posttraumatic nightmares and the hypothesis that posttraumatic nightmares provide an opportunity for fear extinction and memory consolidation of the traumatic memory (described below). In terms of neurophysiology, this model highlights the role of the Amygdala, Medial Prefrontal Cortex, Hippocampus, and Anterior Cingulate Cortex, or AMPHAC (Levin & Nielsen, 2007; Nielsen & Levin, 2007). The application of these brain structures to posttraumatic nightmares is described in the Biological Factors section below.

Although Levin and Nielson do not distinguish between idiopathic and posttraumatic nightmares in their model, they do provide a discussion of some relevant considerations specific to posttraumatic nightmares (Levin & Nielsen, 2007, 2009; Nielsen & Levin, 2007). For example, the number and severity of trauma events are included as an avenue for increased affect distress and can be a cause of increased vulnerability to nightmares (Levin & Nielsen, 2007). The authors contend that the inextricable relationship between PTSD and posttraumatic nightmares provides substantial support for their hypothesis that affect distress (in this case PTSD) explains nightmare production. Additionally, posttraumatic nightmares, both trauma-related and replicative, are thought to have greater affect load and cause more affect distress than bad

dreams and idiopathic nightmares. Further, they postulate that trauma memories may be more resistant to fear memory extinction, thus resulting in the replicative nature of posttraumatic nightmares, either in part through themes and certain images or entirely as a replay of the traumatic event.

Phelps and colleagues (2008) summarized the state of the posttraumatic nightmare literature and called for a comprehensive model that would provide an explanation as to why some patients' nightmares resolve while others do not. The authors provided three distinct models for explaining posttraumatic nightmares. In the first, Phelps et al. (2008) hypothesize nightmares in the acute phase (i.e., the time period shortly after the trauma) take two forms: an intrusion and an adaptive dream. The former results in chronic posttraumatic nightmares and the latter leads to nightmare resolution. The authors suggest in their second model that the patient's response to the posttraumatic nightmare predicts whether the nightmare will resolve or continue. Specifically, when a patient negatively appraises the nightmare and thus responds with fear and avoidance, the nightmare will become chronic; however, if they appraise it neutrally or positively, the nightmare will resolve. Finally, Phelps and colleagues (2008) propose that if the posttraumatic nightmare is interrupted by awakening, thus disrupting the adaptive role of the dream, the nightmare will become chronic.

As there is at present a paucity of knowledge regarding the mechanisms, relations, precipitants, and maintainers of posttraumatic nightmares, developing a comprehensive model based only on those data is challenging. Therefore, related literature regarding biological, psychological, and social factors related to nightmares will be drawn upon to build the rationale. Of note, although it is important to distinguish between idiopathic and

posttraumatic nightmares, this is not always specified in the existing literature. Thus, in some cases, the more general term of "nightmares" will be used to reflect the ambiguity in the literature. Additionally, due to the specific interest of combat-related populations in the proposed studies, supporting literature will draw from military and veteran research, where possible.

IMPORTANCE OF SLEEP

Researchers propose that sleep disturbances may increase one's risk for developing PTSD (Koffel et al., 2013). As noted above, sleep disturbances prevent the critical mechanism of processing and reducing the affective severity of emotional events, which may increase one's susceptibility to these disorders (Koffel et al., 2013). Notably, rapid eye movement (REM) sleep plays an important role in decreasing emotional latency of memories through an overnight depotentiation of amygdala response to previously emotional experiences (Van Der Helm et al., 2011). The importance of REM sleep is discussed in more detail below.

Many service members return from deployment with sleep disturbances (Bramoweth & Germain, 2013). In fact, sleep disturbances are one of the most commonly reported symptoms of returning service members after deployment (Mysliwiec et al., 2013). Within a sample of post-deployment service members with sleep complaints, 88.2% were diagnosed with a sleep disorder (Mysliwiec et al., 2013). Additionally, service members report diagnoses of snoring and obstructive sleep apnea (OSA), insomnia, paradoxical insomnia, and behaviorally induced insufficient sleep syndrome (Mysliwiec et al., 2013).

Among service members being assessed for posttraumatic stress upon return from combat- and noncombat-related deployments, insomnia was one of the most frequently endorsed symptoms (Bramoweth & Germain, 2013). Service members returning from a combat deployment are at a greater risk of insomnia compared to noncombat deployments and civilian samples. Indeed, veterans of Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) report significantly greater rates of insomnia compared to civilian samples (Bramoweth & Germain, 2013).

Service members bring home stressors from deployment that increase their risk for insomnia (Bramoweth & Germain, 2013). These include, but are not limited to, combat experiences, traumatic brain injuries (TBI), as well as inconsistent sleep schedules. Additionally, they are experiencing further stressors during the reintegration process in readjusting at home and at work. For many service members, insomnia symptoms become chronic after returning from a deployment. These symptoms are often comorbid with common deployment-related stress reactions including PTSD, anxiety, and depression.

Service members who report symptoms of insomnia after returning from a deployment are more likely to develop PTSD (e.g., Germain et al., 2008; Wright et al., 2011). In veterans, insomnia severity at four months post-deployment predicted overall PTSD and intrusion symptom severity (including posttraumatic nightmares) at twelve months (Wright et al., 2011). Further, Wright and colleagues (2011) examined the relationship of insomnia severity to the PTSD symptom clusters and found insomnia was related only to the intrusion category of PTSD. Gerhart et al. (2014) found consistent

results: baseline sleep disturbances were predictive of PTSD and depression symptoms at the six month follow-up. The consistent finding that sleep dysfunction mediates the relationship of combat stressors to later psychiatric symptoms (Picchioni et al., 2010), provides support for the theory that sleep disturbances are an integral piece in the development of symptoms after a traumatic event. We propose these sleep disturbances also play a critical role in the initiation and continuation of posttraumatic nightmares. This relationship will be described in detail in future sections.

Rapid Eye Movement (REM)

Early life trauma experiences may serve as a risk factor for REM sleep disturbances associated with PTSD. In work conducted by Insana and colleagues (2012), early-life trauma was significantly associated with REM dysfunction in military veterans. Additionally, REM dysfunction, specifically REM fragmentation, was associated with disruptive nocturnal behaviors common in PTSD (Insana et al., 2012), which include hot flashes, nightmares, and sleep terrors (Germain et al., 2005). Notably, REM fragmentation was indirectly related to early-life trauma and the disruptive nocturnal behaviors reported by the sample of veterans (Insana et al., 2012). The authors further noted that REM fragmentation may account for the relationship of early-life trauma to later PTSD symptoms. Additional support for the role of REM sleep is seen in studies of prazosin, a hypertension medication. Many studies have found prazosin improves posttraumatic nightmares (e.g., Raskind et al., 2002) possibly through normalizing REM sleep to reduce nightmares (Boehnlein & Kinzie, 2007), suggesting a dysfunctional REM sleep mechanism may be responsible for recurrent posttraumatic nightmares.

Sleep Disruption and the Development of Trauma-Related Symptoms

Sleep deprivation appears to affect the trajectory of post-trauma symptom development through its effect on the processing of emotion, memory, and trauma. Two models have been presented that may explain this, both of which relate sleep processes to psychological treatment. Stickgold (2002) proposed that sleep is similar to cognitive restructuring therapy in that sleep allows for the integration and association of emotional memories. During proper sleep, these memories are allowed to associate with memories outside of their confined network, which results in emotional adaptation due to the cognitive perspective gained during sleep. In a second theory, Walker (2009) states that sleep allows for the "process of divorcing emotion from memory," which is similar to principles of systematic desensitization therapy. During sleep, the emotional valence is decreased. When this process fails, further attempts to decrease the emotional valence, or complete the fear learning process, occur in following nights. The failure of this process is a hypothesized risk factor for the development of PTSD. These two theories, although different, are not mutually exclusive and may work together to explain the important role sleep plays in the prevention of PTSD.

Kobayashi et al. (2012) highlighted the literature suggesting REM fragmentation is associated with the development of PTSD and concluded sleep disturbances are both a risk factor for development of PTSD and a key trait of the disorder. A number of studies provide support for the relationship between REM sleep disruptions and PTSD, including greater frequency of awakenings from REM sleep in patients with PTSD (Habukawa et al., 2007) and more REM periods and shorter REM segments predicted development of PTSD (Mellman et al., 2002). Kleim and colleagues (2016) found that sleep in the night

after a trauma protected against intrusion symptoms and, in a follow-up study, aimed to replicate this finding in naps rather than a full night's sleep (Kleim, 2018). Females were randomized to a 90-minute nap or wake groups after watching a distressing film, which was used as a trauma analog. Women who achieved REM sleep during the nap experienced fewer intrusion symptoms than those who did not nap or who napped without REM sleep. Thus, a nap with REM sleep may be protective against intrusion symptoms, adding to the growing evidence that REM sleep may be protective against trauma symptoms. We propose it is the disruption of REM sleep, specifically, that results in a failure to extinguish the fear memory thus perpetuating the posttraumatic nightmares. Importantly, we further propose posttraumatic nightmares themselves may disrupt REM sleep contributing to the cycle of chronic posttraumatic nightmares.

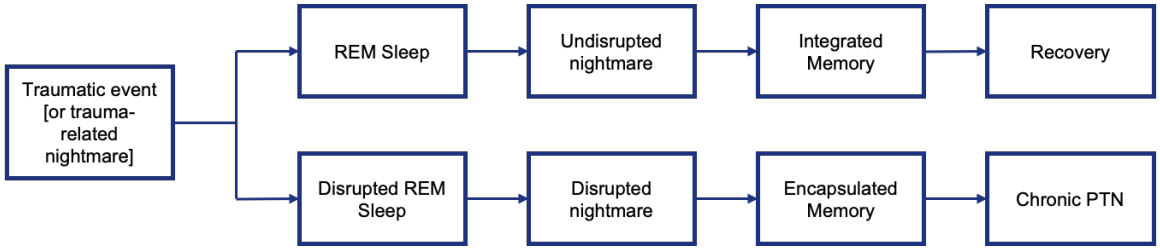

Figure 1. Role of REM sleep in the maintenance of chronic posttraumatic nightmares (Model adapted from Phelps et al., 2008).

Cycle of Sleep and Symptom Severity

As noted previously, sleep deprivation affects a number of processes, such as fear learning and processing. Therefore, it is not surprising that sleep deprivation has a cyclical relationship with multiple aspects of symptom development and maintenance. First, the necessary vigilance and arousal related to combat experiences disrupt sleep, which then further deregulates arousal (Bramoweth & Germain, 2013). PTSD also has a

cyclic relationship with sleep deprivation. When decreases in REM occur with hyperarousal during REM, this leads to the hyperadrenic tone of PTSD (Krause et al., 2017). Hyperadrenic tone refers to hyperarousal, reexperiencing, anxiety, elevated heart rate, and sweatiness associated with PTSD (Kelmendi et al., 2016). Chronic hyperadrenic activity due to PTSD while awake worsens sleep quality and quantity, thus contributing to the cycle of decreased REM sleep leading to increased PTSD hyperadrenic tone leading to further sleep disruptions (Krause et al., 2017). Harvey and colleagues (2011) proposed an additional relationship hypothesizing that sleep dysfunction disrupts emotion regulation. The resulting emotional arousal that occurs throughout the period of wakefulness then negatively impacts sleep quality. When taken in conjunction with our knowledge of fear learning disruption due to sleep disturbances, it is possible this cycle of symptoms may be in part responsible for the continuation of posttraumatic nightmares.

BIOPSYCHOSOCIAL FACTORS RELATED TO THE MODEL

Biological Factors

At this time, there is a dearth of knowledge regarding the physiology of posttraumatic nightmares. Much of what is known comes from older studies, studies that include both posttraumatic and idiopathic nightmares. Additional information arises from clinical trials of medications being tested for their ability to reduce posttraumatic nightmares. The lack of substantial knowledge highlights the need for additional research into the physiological aspects of posttraumatic nightmares. Because we lack meaningful data on the physiological underpinnings of posttraumatic nightmares, the following will present several hypothesized mechanisms requiring further study.

The Stress Response

It is thought that nightmares occur when a patient's threshold for anxiety is surpassed and autonomic activation (i.e., decreased heart rate, respiratory rate, and eye movement activity; Nielsen & Zadra, 2005) occurs (Nielsen & Levin, 2007). In a study of patients with idiopathic and posttraumatic nightmares, some subjects demonstrated moderately elevated heart rates and respiration rates (e.g., sympathetic arousal); however, others had low heart rates and respiration rates during their nightmares (Fisher et al., 1970). These findings, although older, suggest patients experience changes in arousal during nightmares but that they may vary in the characterization and intensity of those changes. Additional research is needed to elucidate which patients experience increased arousal and which experience decreased arousal. Further, research should examine differences in the arousal response of patients experiencing posttraumatic nightmares and those experiencing idiopathic nightmares, as this may account for the different patient responses.

Women with posttraumatic nightmares demonstrate changes in waking stress response during loud tone procedures (i.e., participants are asked to keep their eyes closed while sudden, loud tones are played; Tanev et al., 2017). Posttraumatic nightmares were significantly correlated with heart rate response even when controlling for all other PTSD symptoms. However, posttraumatic nightmares were not significantly related to skin conductance. This suggests nightmares may be associated with a decreased parasympathetic tone. Additionally, when coupled with Porges' polyvagal theory (2001), these findings indicate that posttraumatic nightmares may be related to the constraints placed on the heart's "vagal break" and may disinhibit the effect of the sympathetic

nervous system on the heart. Studies of nightmares in non-PTSD populations also suggest nightmares may be associated with decreased parasympathetic tone through reduced heart-rate variability (Simor et al., 2014) as well as greater sympathetic influence, reduced parasympathetic influence, and greater sympathovagal ratio (Nielsen et al., 2010). In addition to a blunted parasympathetic response, nightmares may be associated with a decrease in hypothalamus pituitary adrenal (HPA) axis reactivity as suggested by a diminished cortisol awakening response in women with frequent nightmares when controlling for demographics, mental health, and lifestyle (Nagy et al., 2015).

Adrenergic Stimulation

Adrenergic stimulation may be partially responsible for the pathophysiology of posttraumatic nightmares (Peskind et al., 2003). This is notable because early studies suggest increased postsynaptic adrenergic receptor responsiveness to norepinephrine from the central nervous system may be partially responsible for the physiology of PTSD (Southwick et al., 1993), and specifically relevant for the nighttime symptoms (Mellman et al., 1995). This mechanism also provides insight into the possible biological underpinnings of posttraumatic nightmares. However, though some studies have indicated prazosin, an alpha-1 adrenergic receptor antagonist, may provide relief from posttraumatic nightmares (e.g., Kung et al., 2012), others, including a large-scale randomized control trial (Raskind et al., 2018), with null findings have led the VA and DoD to neither recommend for or against the use of Prazosin (Veterans Health Administration and Department of Defense, 2017).

Hypothesized Neural Components

To our knowledge, no prior studies have examined neural correlates of posttraumatic nightmares. Thus, our current hypotheses are largely formed from our understanding of the neurobiology of PTSD and sleep as well as a proposed model of disturbing dreams. Please note, sample size and study groups are described in Appendix B.

Structural Correlates

PTSD is related to decreased volume reduced grey matter volume (Logue et al., 2018; Morey et al., 2019; Nelson & Tumpap, 2017; O'Doherty et al., 2017; Xie et al., 2018) and density (Kasai et al., 2008) of the hippocampus. Of note, Morey and colleagues (2019) found the relationship between PTSD diagnosis and hippocampal volume was stronger in females compared to males. Kasai et al. (2008) found reductions in right hippocampal gray matter density in combat-exposed veterans with PTSD compared to combat-exposed veterans without PTSD, and Crombie and colleagues (2021) identified reduced cortical thickness in the right parahippocampus in women with PTSD compared to healthy controls without a trauma history. Further, one study (Akiki et al., 2017) found abnormalities (i.e., indentations) in the anterior of the right hippocampus and the dorsal region of the amygdala in combat-exposed veterans with more severe PTSD symptoms compared to those with fewer symptoms. PTSD also is related to decreased volume in the amygdala (e.g., Logue et al., 2018; Morey et al., 2020; Morey et al., 2019; O'Doherty et al., 2017). Notably, the amygdala, in particular, has been implicated in PTSD symptoms in veterans (e.g., Akiki et al., 2017; Morey et al.,

2020; Pieper et al., 2020). Reduced amygdala subnucleus volume, shape distortions (Morey et al., 2020), and indentations (Akiki et al., 2017) have been identified in relation to PTSD symptoms in veterans. However, one study of active duty service members and veterans found *greater* volume in the amygdala of participants with comorbid mTBI and PTSD compared to participants with only a history of mTBI (Pieper et al., 2020).

Volume (Herringa et al., 2012; O'Doherty et al., 2017; Woodward et al., 2006; Young et al., 2018) and gray matter density (Kasai et al., 2008) of the anterior cingulate cortex are reduced in patients with PTSD, and in veterans these reductions were related to greater physiological arousal (Young et al., 2018). Patients with PTSD also exhibit a diminished medial frontal cortex compared to trauma-exposed controls (O'Doherty et al., 2017). Finally, PTSD diagnosis and symptom severity is related to reduced volume (Herringa et al., 2012), cortical volume (Wang et al., 2020), and gray matter density (Kasai et al., 2008) in the insular cortex. Wang and colleagues (2020) also found reductions in cortical volume in the left and right lateral orbitofrontal gyrus, left superior temporal gyrus, and lingual and superior parietal gyri in a mega-analysis of over 1,300 patients with PTSD and nearly 2,200 controls.

Reexperiencing or intrusion symptoms of PTSD (e.g., posttraumatic nightmares) have been linked to a number of regions. In patients with PTSD related to a sexual assault, gray matter density of the lingual parietal gyri was negatively associated with re-experiencing symptoms. Additionally, reexperiencing symptoms are associated with reduced gray matter density in the temporal, parietal, and occipital regions (Kroes et al., 2011) and the insula (Kasai et al., 2008) as well as decreased gray matter volume in the hippocampus (O'Doherty et al., 2017; Xie et al., 2018) and lingual gyrus (Berman et al.,

2018). In a trauma analog study, patients with less insula gyrus volume reported more early intrusive memories related to the film (Gvozdanovic et al., 2020). In regards to cortical thickness, reductions of the inferior and middle temporal gyrus as well as the parahippocampus are related to greater reexperiencing symptoms (Crombie et al., 2021). Furthermore, shape of regions also may be involved in posttraumatic nightmares, as indentations of the right amygdala were largely explained by reexperiencing symptoms in veterans (Akiki et al., 2017).

Functional Correlates

Research suggests functional and structural associations are distinct and each require consideration (e.g., Owens et al., 2018). For instance, emotional and memory processing regions have a strong relationship to PTSD. In patients with PTSD who experienced a morally injurious event, patients demonstrated hyperarousal of the insula and anterior cingulate cortex (Lloyd et al., 2020). Patients with PTSD also show increased activation of the insula and decreased activation of the anterior cingulate cortex in response to Affective Stroop trials (Fani et al., 2019). PTSD is related to increased activity in the amygdala as well (Badura-Brack et al., 2018; Shin et al., 2006). Additionally, amygdala reactivity after trauma (i.e., 5-12 weeks) predicts PTSD symptoms 12 months post-trauma (Stevens et al., 2017). Decreased functioning of the hippocampus and responsiveness of the medial prefrontal cortex is associated with PTSD (Shin et al., 2006), with decreased activation of the medial prefrontal cortex to personal, stressful images in patients with PTSD (Dahlgren et al., 2018). Additionally, habituation to fearful stimuli, as evidenced by decreased activation of the anterior cingulate cortex, predicts poor PTSD recovery (Stevens et al., 2017). PTSD is related to.

Research suggests neural function is related to reexperiencing symptoms as well. Neural connectivity has been implicated such that reexperiencing symptoms are related to reductions of functional connectivity of the lingual parietal gyri in patients with PTSD (Berman et al., 2018). Reexperiencing symptoms also are associated with greater functional connectivity of the amygdala and lateral orbitofrontal cortex in response to punishment on a gambling choice game in patients with posttraumatic stress symptoms (Ben-Zion et al., 2021). Finally, activation of the amygdala (Ben-Zion et al., 2021) and prefrontal cortices may be associated with increased reexperiencing symptoms (Henigsberg et al., 2019). Further, fear acquisition and extinction in healthy controls indicated activation of the insula, anterior cingulate cortex, hippocampus, and medial frontal cortex, among others is positively associated with reexperiencing symptoms, suggesting extinction learning may, in part, be responsible for reexperiencing symptoms such as posttraumatic nightmares (Miedl et al., 2020).

A meta-analysis of trauma-related autobiographical memories in patients with PTSD concluded diminished activation of the prefrontal cortices may indicate a greater propensity for reexperiencing symptoms (Thome et al., 2020) such as posttraumatic nightmares. Levin and Nielsen (2007) proposed emotion regulation to be a critical component for the initiation of disturbing dreams, and emotion dysregulation has been identified in connection to hypoactivity of the ventromedial prefrontal cortex (Etkin & Wager, 2007). Thus, hypoactivity of the ventromedial prefrontal cortex, in particular, may increase the propensity for posttraumatic nightmares through a failure of adequate emotion regulation. A review by Fitzgerald and colleagues (2018) suggested this emotion dysregulation is the result of dysfunction of the neurocircuitry involving the amygdala,

insula, hippocampus, anterior cingulate cortex, and prefrontal cortex. They suggest it is the amygdala and insula's response to emotional stimuli as well as abnormal anterior cingulate and prefrontal cortices leading to inadequate appraisal, resolution, and management of these emotional stimuli that results in the emotional dysregulation observed in patients with PTSD (Fitzgerald et al., 2018). Notably, cooccurring sleep disturbances, such as insomnia, may further disrupt emotion regulation in patients (Leerssen et al., 2020) thus necessitating consideration of their compounding effect on emotion regulation in patients with posttraumatic nightmares.

Hyperactivity in the amygdala, which is common in PTSD (e.g., Badura-Brack et al., 2018), may increase the occurrence of nightmares (Levin & Nielsen, 2007). Germain and colleagues (2008) proposed that hyperactivity of the amygdala *and* hypoactivity of the medial prefrontal cortex intensified by REM sleep may promote nightmare occurrence. The hippocampus and amygdala, specifically, are implicated in the production of dreams and thus may be involved in nightmare production as well. These brain areas also are involved in state and trait emotional responses and emotion-based disorders including PTSD and have been shown to be more active during REM sleep compared to non-REM sleep and waking. Therefore, these regions may play a critical role in the physiological basis of normal dreaming and may influence the emotional imagery present in normal, bad dreams, and nightmares (Levin & Nielsen, 2007).

Many of these brain regions have been implicated in sleep disturbances as well. Patients with insomnia have reduced hippocampal volume (e.g., Spiegelhalder et al., 2013). Indeed, sleep quality, sleep efficiency, sleep problems, and sleepiness predict atrophy of the hippocampus (Fjell et al., 2019). Females with poor sleep quality

demonstrate reduced gray matter volume of the right parahippocampus and right hippocampus (Neumann et al., 2020). Localized atrophy of the amygdala was found in patients with chronic insomnia disorder (Gong et al., 2019). Cortical thinning and of the anterior cingulate cortex and gray matter reduction of the anterior cingulate gyri are related to idiopathic rapid eye movement sleep behavior disorder (Rahayel et al., 2018). Finally, associations have been found among persons with disrupted sleep and decreased cerebral glucose metabolism in the anterior cingulate cortex and medial prefrontal cortex (e.g., Nofzinger et al., 2004), atypical connectivity of the amygdala (e.g., Huang et al., 2012), and decreased activity in the insular cortex (e.g., Liu et al., 2016).

Leerssen et al. (2020) argue that although one may be tempted to consider the neurophysiology of insomnia symptoms as consistent across psychiatric conditions, there may be distinct differences in the mechanisms of these analogous sleep disturbances. Indeed, results of their study comparing the neurobiology of patients with insomnia, healthy controls, and clinical controls (i.e., patients with bipolar disorder) suggest the neurobiological profiles differ among groups (Leerssen et al., 2020). This suggests sleep related brain differences differ with comorbid psychological conditions requiring careful consideration when making assumptions regarding associated brain regions of findings in patients with other underlying psychological conditions. Importantly, posttraumatic nightmares represent an intersection between PTSD and sleep disturbances. Thus, it is important to consider regions that are implicated in both PTSD and sleep disturbances.

Proposed Models of Neurobiological Correlates of Posttraumatic Nightmares

The Amygdala, Medial Prefrontal Cortex, Hippocampus, and Anterior Cingulate Cortex, or AMPHAC, Model is a hypothesized neurophysiological model of nightmare

formation proposed by Levin and Nielsen (2007). This model was created with a unified theory of nightmares in mind. Phrased differently, idiopathic and posttraumatic nightmares are hypothesized to share a model. Although, this model may not be entirely representative of the posttraumatic nightmare, the model provides a framework in which to begin examining neural correlates of posttraumatic nightmares. Additional theorists (e.g., Nardo et al., 2015) also have hypothesized the amygdala, hippocampus, and anterior cingulate cortex may play a role in posttraumatic nightmares.

Levin and Nielsen (2007) provided several reasons as to why these neural regions, in particular, should be studied further for their role in nightmare production. First, the AMPHAC regions are implicated in state and trait emotional responses and emotion-based disorders including PTSD (Levin & Nielsen, 2007). These regions also have been shown to be more active during REM sleep compared to non-REM sleep and waking (Levin & Nielsen, 2007). Finally, these neural areas are associated with identifying, creating, sustaining, and remembering fear and other emotions (Levin & Nielsen, 2007). Specifically, the amygdala is involved in the physical response typically associated with the sympathetic nervous system's stress response by increasing blood pressure, heart rate, and respiration (Levin & Nielsen, 2007), and the anterior cingulate cortex may play a critical role in modulation of activity in the amygdala (Nielsen & Levin, 2007). The medial prefrontal cortex and hippocampus are crucial for fear conditioning and fear extinction, and the anterior cingulate cortex is involved in emotional distress, which may be related to the perpetuation of the nightmare cycle.

Hyperactivity in the amygdala, which is common in PTSD (e.g., Badura-Brack et al., 2018), is thought to increase the occurrence of nightmares (Levin & Nielsen, 2007);

however, Germain and colleagues (2008) proposed that hyperactivity of the amygdala *and* hypoactivity of the medial prefrontal cortex intensified by REM sleep may promote nightmare occurrence. Gilbert and colleagues (2015) implicated reduced activity specifically in the dorsal region of the medial prefrontal cortex in the generation of posttraumatic nightmares given its role in regulating activity in the amygdala during REM sleep. The hippocampus-amygdala complex, specifically, is implicated in the emotional load of dreams and thus may be involved in nightmare production as well (Cipolli et al., 2017). Therefore, these regions may be "a vital component of the physiological infrastructure of normal dreaming and is likely influential in shaping emotional imagery during both normal and disturbed dreaming" (Levin & Nielsen, 2007, p. 505).

SUPPORT FOR THE AMPHAC MODEL

As discussed above, the amygdala, hippocampus, anterior cingulate cortex, and medial prefrontal cortex have a strong relationship to PTSD (e.g., Logue et al., 2018; Morey et al., 2019; O'Doherty et al., 2017; Wang et al., 2020; Young et al., 2018). Notably, two studies provide further support for the role of these regions through examination of sleep in patients with PTSD (Germain et al., 2013; Nardo et al., 2015). Germain and colleagues (2013) examined neural correlates in patients with combat-related PTSD and found hypermetabolism of glucose consumption in a number of regions during REM sleep including the amygdala, hippocampus, anterior cingulate cortex, medial prefrontal cortex, and locus coeruleus compared to veterans without PTSD. Nardo et al. (2015) examined brain volume in relation to sleep disturbances, including nightmares, in patients with PTSD using voxel-based morphometry and single-photon

emission computerized tomography (SPECT); however, sleep disturbances were assessed as a single construct comprised of symptoms of insomnia and nightmares. Their results indicated regional reductions in gray matter volume of the amygdala, hippocampus, anterior cingulate cortex, and insula were related to sleep disturbances in patients developing PTSD compared to those not developing PTSD (Nardo et al., 2015). Further examination using whole-brain voxel-based morphometry suggested reduced gray matter volume in the right anterior cingulate cortex, bilateral insular cortex, amygdala, hippocampus, parahippocampal cortex, left striatum, and the right dorsolateral prefrontal cortex. Finally, the severity of sleep disturbances was related to the increased dorsal midbrain, precuneus, and insula activity and decreased activity in anterior cingulate cortex, dorsolateral prefrontal cortex, and orbitofrontal cortex during an "individualized autobiographical script-driven symptom-provocation procedure" (Nardo et al., 2015, p. 4). These results provide initial support for the amygdala, hippocampus, and anterior cingulate cortex in the AMPHAC Model proposed by Levin and Nielsen (2007).

Although larger studies of neural correlates of PTSD (Wang et al., 2020) do not provide support for these regions, we hypothesize they remain relevant and important to investigate for two primary reasons. First, these regions were identified in the only model of disturbing dreams (Levin & Nielsen, 2007, 2009; Nielsen & Levin, 2007) currently in the literature. To comprehensively assess possible correlates, an examination of the neurophysiology of posttraumatic nightmares should include consideration of the historical context in development of hypotheses. Second, studies by Germain et al. (2013) and Nardo et al. (2015) provide support for these regions. Of note, these studies, albeit smaller and older than the Wang et al. (2020) article, are arguably as relevant to the study

of posttraumatic nightmares as larger, more recent articles because of the examination of sleep in patients with PTSD rather than PTSD as a single construct, as we suggest sleep is an important component in the cycle of posttraumatic nightmares. It also is possible that differences related to posttraumatic stress severity, broadly, will not correspond to differences related to posttraumatic nightmares, specifically. Thus, Germain et al. (2013) and Nardo et al. (2015) may be more indicative of true differences between patients with and without posttraumatic nightmares.

Psychological Factors

As with many psychological disorders and symptoms, the etiology of posttraumatic nightmares is not solely biological. A number of psychological etiological mechanisms have been hypothesized from a variety of perspectives including psychoanalysis, personality, contextualization, and threat stimulations. A brief description of prominent theories follows.

Clinical Theories of Dreaming

Freud is one of the most famous dream theorists in psychotherapy and believed the unsatisfied wishes and desires of one's day emerge in dreams (Freud, 2005). Freud posited that dreams can perform two functions: a physiological purpose and a psychological purpose. Physiologically, Freud believed that dreams functioned to protect one's sleep from disturbance (Guénolé et al., 2013). Also, dreams serve a psychological purpose of fulfilling the dreamer's wishes and desires from their waking life (Malinowski, 2016). Some of these wishes are considered too taboo, forbidden, or

distasteful and are thus suppressed by our unconscious mind (Malinowski, 2016). Notably, these desires may present in a distorted or unrecognizable way in dreams.

Many researchers have worked to test Freud's theories using a variety of techniques including galvanic skin response, Rorschach cards, and sleep studies. In a study of galvanic skin response and secondary revision of dreams, Fancher and Strahan (1971) concluded that participant responses were contrary to Freud's hypothesis that forgotten content is more anxiety provoking, instead finding that this material was less emotional and likely less important. In a second study, patients were given Rorschach images to dream about under hypnosis (Wiseman & Reyher, 1973). They found support for Freud's theories with an increase of drives, overtness of their representation, primary processing, and defensiveness, suggesting that Freud's theories should be tested as a cohesive set of constructs rather than individually. In a more recent study of dreams' protective factors, researchers found support for the theory when studying sleep problems in patients with brain damage (Guénolé et al., 2013). However, this protective factor is limited to non-rapid eye movement (NREM) sleep, as rapid eye movement (REM) sleep is a time of arousal.

Carl Jung was in agreement about Freud's theories of dreams (Zhu, 2013). Specifically, he agreed on Freud's classifications of dreams, as well as the physiological protective feature of dreams (Zhu, 2013). However, Jung also presented an alternative theory that dreams are a typical and creative manifestation of the unconscious (Hill & Knox, 2010). He also believed that dreams may be an expression of things avoided during waking life, allowing for a unification of the conscious and unconscious.

Alfred Adler stated that there is no difference between the conscious and the unconscious mind (Hill & Knox, 2010). This means that the conscious mind is also echoed in the dream state and can be reassuring or protective against injury to one's self-worth (Hill & Knox, 2010). Notably, Adler was particularly concerned with the emotion caused by the dream and the problem-solving role that it fulfilled.

Cognitive theorists also have integrated dream work into psychotherapy. Similar to Adler, Beck theorized that dreams match the waking mind and can be affected by the waking thoughts (Hill & Knox, 2010). Beck believed that dreams serve many roles including revealing a patient's automatic thoughts, and although some dreams may not serve to provide insight into one's problems, others offer clarity to problems or may suggest dysfunctional attitudes (Hill & Knox, 2010).

Finally, evolutionary psychologists have proposed dreaming serves to allow the dreamer to encounter and tackle hazards in their environment (Revonsuo, 2000). During dreaming, one is able to rehearse ways of confronting these threats, thus better equipping the dreamer for addressing the threat when faced in reality (Revonsuo, 2000).

Traumatic Experience

Posttraumatic nightmares are related to a traumatic experience; however, not everyone who experiences a traumatic event will develop posttraumatic nightmares (Breslau, 2009). For some patients, they are able to successfully integrate the traumatic experience and do not have a negative response to the event. However, others will develop chronic posttraumatic nightmares. Posttraumatic nightmares are one of the many disruptive nocturnal behaviors (e.g., hot flashes and nervousness) that frequently occur in PTSD (Germain et al., 2005). These symptoms are so integral to PTSD that the

Pittsburgh Sleep Quality Index Addendum for PTSD (Germain et al., 2005), which assess these disruptive nocturnal behaviors, is able to accurately identify patients with PTSD with 93% positive predictive value. Their presence prior to deployment is a risk factor for the addition of further PTSD symptoms (van Liempt et al., 2013), influence the trajectory of symptom development, and are positively correlated with PTSD severity and depression (Pigeon et al., 2013).

The re-experiencing aspect of nightmares also may result in an increase in PTSD hypervigilance symptoms. This may be due to an increase in upsetting thoughts and events that are reexperienced through nightmares, increasing a patient's reactivity to reminders and the associated feelings while awake (Cukrowicz et al., 2006). Poor sleep may function to inhibit a patient's ability to control their emotions and decrease their ability to endure suffering, thus worsening symptom severity (Cukrowicz et al., 2006).

Ecological momentary assessment (EMA) studies have further elucidated this complex bi-directional relationship: baseline and daily PTSD significantly increased nightmares (Short et al., 2018). Furthermore, patients with nightmares had more severe PTSD, and these nightmares influenced the trajectory of PTSD symptom development. Researchers hypothesize nightmares are associated with increased PTSD symptoms due to their role in inhibiting fear extinction memory consolidation (van Liempt et al., 2013) and further suggest nightmares may be an effective treatment target to improve psychological outcomes and increase resiliency if done before or soon following a deployment (Campbell & Germain, 2016).

Disruption of Fear Processes

Sleep is necessary for the processing and encoding of affective memories while simultaneously reducing the emotional strength of the memory (Walker & van Der Helm, 2009). It is hypothesized that posttraumatic nightmares may become chronic due to dysfunctional encoding of the emotionally latent trauma memory due to existing sleep disturbances, such as insomnia, that can disrupt the memory processes that occur during sleep (Nissen et al., 2011). Due to this ineffective encoding, there also are disturbances in assimilating these memories. This may be due to sleep disturbances, as sleep is thought to be integral to the incorporation of new memories (e.g., Walker & van Der Helm, 2009). Therefore, when sleep disruption occurs, the emotional aspects of the memory are over-consolidated, possibly leading to an increased risk of PTSD symptoms such as posttraumatic nightmares. Walker (2009) further hypothesized that over a period of several sleeps, sleep may reattempt to consolidate these memories, thus decreasing distress. Therefore, disruptions of sleep and the associated memory consolidation processes not only affects the encoding of the initial event, but they also may disrupt extinction learning thereby increasing the risk for chronic PTSD symptoms (Spoormaker et al., 2010).

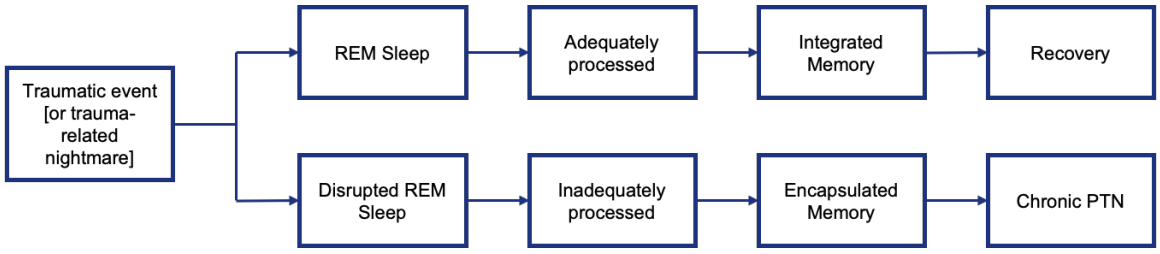

Figure 2. Role of disrupted fear memory processing in posttraumatic nightmares (Model adapted from Phelps et al., 2008).

Psychological factors for the model

There is a strong relationship between mental health disorders and sleep dysfunction. Researchers hypothesize sleep distress may increase the risk for developing an internalizing disorder such as PTSD or depression (Koffel et al., 2013). This may be because sleep disturbances prevent the critical mechanism of processing and reduce the affective severity of emotional incidents, which may increase one's susceptibility to these disorders (Koffel et al., 2013). Additionally, sleep disturbances may disrupt normal processes of emotional adaptation and regulation, thus increasing the likelihood of developing PTSD (Mellman, 2006).

Although little is known about the etiology or physiology of nightmares, it seems that they create a susceptibility to further development of disorders. In addition to PTSD severity as described above, nightmares are positively correlated with depression severity (DeViva et al., 2004; Pigeon et al., 2013). Furthermore, nightmares and insomnia independently increase depression symptoms, and this effect is strengthened when these two co-occur (Nakajima et al., 2014). Additionally, PTSD, depression, and anxiety commonly cooccur with dysfunctional sleep in service members. Each of these disorders are associated with decreased sleep quantity (e.g., Taylor et al., 2014) and quality (e.g., Rice & Schroeder, 2019).

Objective measures of sleep, such as polysomnographic recordings, indicate patients with anxiety experience significant sleep related issues including increased arousals, alertness, increased time to fall asleep as well as decreased time asleep and slow-wave sleep (Bourdet & Goldenberg, 1994). However, nightmares were found to be independent of and not related to anxiety (Wood & Bootzin, 1990).

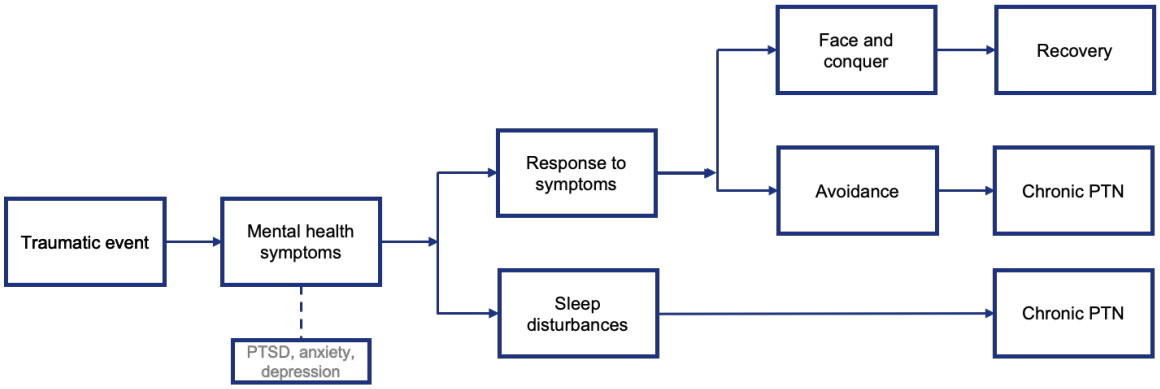

Figure 3. The role of mental health symptoms in the posttraumatic nightmare cycle.

In summary, we propose sleep problems, such as insomnia and nightmares, may predate the traumatic experience. After the trauma occurs, the patient may experience disrupted sleep and acute nightmares leading to the development and exacerbation of mental health symptoms including PTSD, anxiety, and depression. Through a number of mechanisms (e.g., disrupted sleep, psychological symptoms), posttraumatic nightmares continue, which disrupts sleep resulting in a cycle of sleep disturbances increasing mental health symptoms that increase the propensity for disturbed sleep.

Social Factors

Maercker and Horn (2013) proposed three levels of socio-interpersonal factors related to the development of PTSD (see Figure 5). The first level considers social affective changes and encompasses factors such as shame, guilt, anger, and revenge. The second level examines close social relationships including social support, and the third level includes distant social contexts (Maercker & Horn, 2013). These categories will be used to guide the social factors of posttraumatic nightmares.

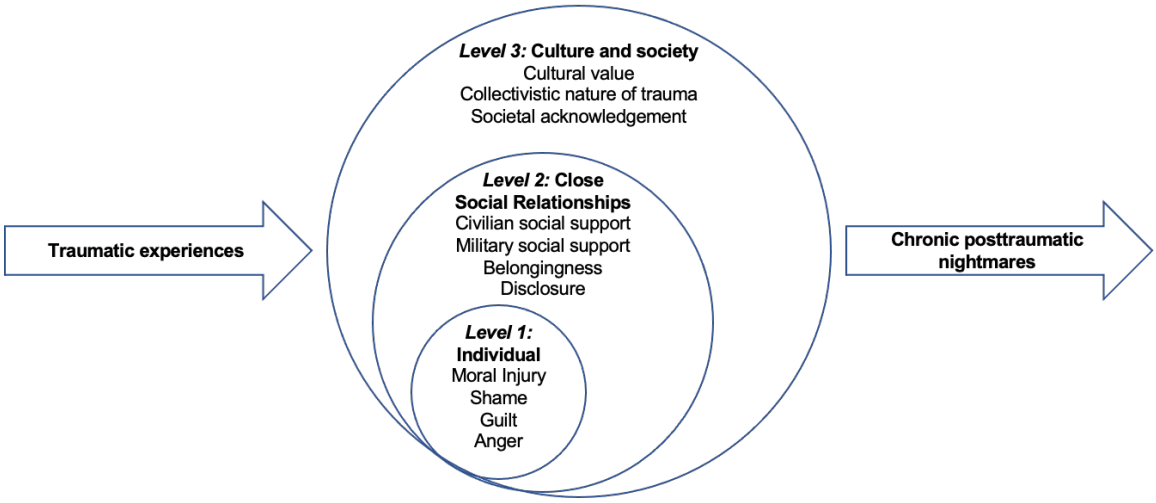

Figure 4. Social influences of posttraumatic nightmares. Model adapted from the socio-interpersonal model (Maercker & Horn, 2013).

Level 1: Individual and Social-affective Factors

As with the proposed biological mechanisms of posttraumatic nightmares, there is a dearth of literature regarding social factors related to posttraumatic nightmares. Therefore, the following discussion will begin with a general discussion of the individual social mechanisms in PTSD before proposing potential mechanisms specific to posttraumatic nightmares.

Maercker and Horn (2013) posited shame, guilt, and anger are important social considerations in the development of PTSD. Notably, these symptoms are central components of moral injury (Evans et al., 2020; Molendijk, 2018). Thus, it is possible that moral injury may play a central role in the development of chronic posttraumatic nightmares, as it has been suggested moral injury may be, in part, responsible for the perpetuation of PTSD after a combat-related trauma (Koenig et al., 2019). Indeed, Nash and Litz (2013) suggest the distress felt from these core features of moral injury (i.e.,

shame, guilt, and anger) are demonstrated through re-experiencing symptoms such as posttraumatic nightmares. Research supports this theory as combat-related guilt is related to both reexperiencing and avoidance symptoms of PTSD (Henning & Frueh, 1997).

Moral injury may be particularly salient for combat-related traumas. Indeed, a majority of service members with military-related PTSD have symptoms of moral injury (Koenig et al., 2019). Two forms of moral injury are recognized: moral injury by self and moral injury by others. Moral injury by self refers to an act in violation of one's moral or ethical code, such as killing a civilian during war (Stein et al., 2012). Conversely, moral injury by others is when one witnesses or is the victim of an act in violation of one's moral or ethical code, such as a sexual assault (Stein et al., 2012). Moral injury by self and by others are differentially related to PTSD symptoms, with the former more strongly related to intrusion symptoms and the latter to anger (Stein et al., 2012). Stein and colleagues (2012) hypothesized this may be due to these events conflicting with individuals' self-schema and thus are more challenging to process resulting in intrusions. Consistent with the social-cognitive theory, it is hypothesized that as one struggles to integrate the morally injurious event into their view of themselves, others, and the world, they may experience guilt, shame, anxiety, and increased avoidance and intrusions (Litz et al., 2009). Thus, treatment to resolve posttraumatic nightmares may require specific targeting of addressing the guilt associated with violations of their worldview.

There is a significant dearth of research examining these constructs as they relate to posttraumatic nightmares. Treatment studies of Imagery Rehearsal Therapy (e.g., Krakow & Zadra, 2006), a cognitive-behavioral treatment for posttraumatic nightmares, have identified guilt as a component or cooccurring symptom with posttraumatic

nightmares (e.g., Harb et al., 2012). However, primary support for the link between moral injury, the associated emotions, and posttraumatic nightmares is provided by a study from Dedert and colleagues (2019). In this study, the researchers examined guilt cognitions, trauma-related sleep disturbances, and posttraumatic nightmares in a sample of veterans with PTSD who were seeking combined treatment for PTSD and smoking cessation. Guilt cognitions were measured using the Trauma-Related Guilt Inventory (TRGI; Kubany et al., 1996), which has subscales for hindsight bias (e.g., one's responsibility for knowing the result prior to it happening), perceived wrongdoing (e.g., thoughts, feelings, or behaviors during the event that violated one's values), and lack of justification for one's actions. Notably, the hindsight bias and perceived wrongdoing subscales are related to measures of moral injury (Stein et al., 2012). Dedert and colleagues (2019) found perceived wrongdoing completely mediated the relationship of both combat exposure to self-reported trauma-related sleep disturbances and the relationship of combat exposure to nightmare severity, as measured by the Clinician Administered PTSD Scale for DSM-5 (CAPS-5; Weathers, Blake, et al., 2013), accounting for 62% and 24% of the variance, respectively (Dedert et al., 2019). This study provides support for the hypothesized relationship of guilt and posttraumatic nightmares; however, due to the small sample size (N = 50) and the smoking cessation focus of the study, these relations should be examined in additional samples. Further, as guilt only explained 24% of the variance in posttraumatic nightmares, there remain many unexplained aspects of posttraumatic nightmares thus requiring consideration of additional factors.

Level 2: Social Support

Social support is a critical component in understanding the development of posttraumatic stress symptoms (e.g., Brewin et al., 2000). Social support has repeatedly been identified as an important factor in the development (Pietrzak et al., 2010; Wilcox, 2010), severity (Brewin et al., 2000; Gros et al., 2016), and maintenance of PTSD (Schnurr et al., 2004). A meta-analytic review of PTSD risk factors identified low social support as one of the strongest predictors of PTSD; furthermore, poor social support was associated with more adverse psychological reactions in military personnel as compared to civilian trauma survivors (Brewin et al., 2000).

Previous research suggests that Veterans differentiate support received from civilian and military sources (Wilcox, 2010) and that these sources are differentially related to psychological outcomes (Smith et al., 2013). Therefore, in the present review, perceived social support will be described as it relates to civilian social support (i.e., friends, family, community) and military social support (e.g., fellow service members and perceived unit cohesion). Clearly, this distinction is arbitrary and some sources of support may provide both civilian and military support. For example, some service members may be in a dual military relationship or have military-affiliated romantic partners, friends, and family members. However, these sources of support will be considered under the heading of civilian social support to be most consistent with the current literature. However, it should be remembered that these individuals, functioning in their roles as fellow service members, may provide sources of military support as well.

Studies of veterans have found a relationship between PTSD diagnosis and social support. For example, among National Guard veterans, patients with probable PTSD

reported less social support than those without a probable diagnosis (Pietrzak et al., 2010). Similarly, veterans with PTSD were found to have less social support from friends, family, and community as well as worse social functioning than veterans without PTSD (Tsai et al., 2012). Additionally, veterans with PTSD had more problems in their romantic relationship and less family cohesion. In addition to finding that low social support increased risk of PTSD, Tsai and colleagues (2012) identified low community social support as a mediator of the relationship between PTSD and decreased social functioning. Among active duty Marines completing an intensive training program, civilian social support was related to decreased posttraumatic stress symptoms, but only when the perception of the stressor was low. This suggests that civilian social support may be more meaningful when stressors are low but becomes less important as stressors increase in severity (Smith et al., 2013); however, this relationship may be specific to females. For female Marines civilian social support predicts less severe posttraumatic stress symptoms regardless of the severity of the stressor, but the relationship between civilian social support and posttraumatic stress symptoms in male Marines was not significant (Smith et al., 2013).

Social support received after deployment is associated with decreased PTSD severity in both active duty and National Guard Soldiers; however, increased PTSD symptoms can decrease support. In a second study of National Guard Soldiers who recently returned from deployment, PTSD severity predicted reduced social support (Shallcross et al., 2016). Most applicable to the present model, PTSD intrusion symptoms, such as posttraumatic nightmares, are consistently predictive of decreased social support at later time points (Shallcross et al., 2016). However, decreased social

support also predicts greater intrusion symptoms (Shallcross et al., 2016), indicating a bidirectional relationship. Notably, the role of social support may change over time. The relationship between social support and PTSD severity is stronger when the traumatic event happened more than 3 years before, suggesting social support may have cumulative effects (Ozer et al., 2003).

Military social support is an important consideration in PTSD symptom development in service members. Specifically, fellow veterans are an important part of the social network for veterans with PTSD (Laffaye et al., 2008). For veterans with PTSD, their fellow veterans not only make up the largest portion of their social network, but they also provide more instrumental support compared to relatives and more emotional support than any other source of support (i.e., spouse, relatives and nonveteran friends) suggesting veterans seek emotional support more often from other veterans (Laffaye et al., 2008). Importantly, these participants reported high levels of support with low interpersonal stress in relationships with fellow veterans; however, their spouses were both fairly equivalent sources of support and interpersonal stress. Thus, we hypothesize the increased interpersonal stress from the spouse may account for why veterans are more likely to seek support from fellow veterans.

In addition to receiving individual support from fellow service members, unit support also may mitigate PTSD development. Low unit social support is associated with probable PTSD diagnosis in veterans (Pietrzak et al., 2010), and military unit social support is associated with decreased PTSD both as stressors occur (e.g., Smith et al., 2013) and with earlier life stressors (Brailey et al., 2007). In active duty Soldiers, unit support during deployment, but not prior to deployment, is related to decreased PTSD

severity; however, unit social support was not associated with PTSD severity before or after deployment for National Guard Soldiers (Han et al., 2014). Military social support moderated the relationship between stressfulness of military experiences and posttraumatic stress symptoms for Marines undergoing extensive military training, with military support attenuating the association between military stress and symptoms (Smith et al., 2013). For male Marines, military social support was related to decreased posttraumatic stress symptoms but not in female Marines (Smith et al., 2013). Unit cohesion also diminishes the relationship between earlier life stressors and PTSD symptom severity prior to deployment (Brailey et al., 2007).

Research into social support and PTSD in firefighters may provide additional insight into the role service specific support can play. Perceived social support from supervisors, coworkers, and civilian sources was related to decreased PTSD severity; however, support from supervisors was the only factor that remained associated with decreased symptom severity when all three sources were placed into a single model (Stanley et al., 2019). Only service specific sources (i.e., supervisors and coworkers) were associated with less reexperiencing symptom severity. As with overall PTSD severity, only support from supervisors remained significant. Perceived belongingness also is related to decreased overall PTSD symptoms as well as reexperiencing, avoidance, numbing, and hyperarousal symptoms in firefighters (Stanley et al., 2019). Thus, when service members identify themselves as an integral part of the military system, they may

be less likely to develop severe PTSD symptoms. Importantly, social support can increase one's feelings of belongness (Stanley et al., 2019).

We hypothesize social support from both civilian and military sources may decrease posttraumatic nightmare severity much the same as it provides a buffering effect for PTSD.

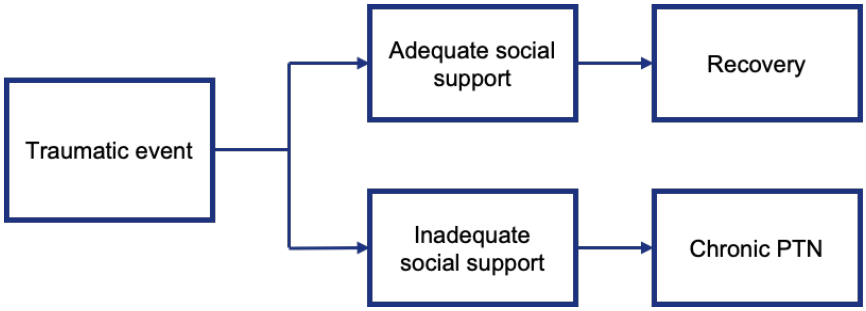

Figure 5. Role of social support in the cycle of posttraumatic nightmares.

Level 3: Distant Social Contexts

It is imperative to consider cultural implications when understanding the dream experience, imagery and symbolism, disclosure, and interpretation and meaning because every dream is influenced by the patient's culture (Lohmann, 2000). Of the many cultures present in the world, approximately 90 percent find meaning and usefulness in dreams. In many cultures, dreams are considered another form of one's reality or may serve as a source of knowledge (Lohmann, 2000). Therefore, a patient's culture may influence the emphasis on and interpretation of the posttraumatic nightmare.

Many modern societies teach children from a young age that dreams are not real and should be ignored (Laughlin & Rock, 2014). These monophasic societies teach that knowledge shared through dreams is not applicable to daily life, though they may be useful during psychotherapy. Ultimately, monophasic societies need the dream to be

reasonable to the waking mind to be understandable (Laughlin & Rock, 2014). In polyphasic cultures one's sense of identity is formed through the integration of experiences in dreams, altered states of being, and waking (Laughlin & Rock, 2014). These cultures emphasize the belief that dream content can provide knowledge that shapes the society's views about the self and the world.

It is important to be aware of the many interpretations of dreams across cultures. For example, Tahitian dreamers believe that their dreams signify the meanderings of the soul and provide a view of the supernatural world (Lohmann, 2000). The Asabano people believe the presence of mythological creatures in dreams are confirmation of their existence in real life (Lohmann, 2000). The Ilahita Arapesh use this same principle in providing evidence of ghosts or spirits (Lohmann, 2000). A "classic" interpretation of dreams is seen among the Raramuri of Mexico, who believe that one's soul leaves the body to explore and use this opportunity to gain important cosmological knowledge (Lohmann, 2000).

Notably, posttraumatic nightmares occur at a much higher rate in Native American populations than in others. In a study of Northern Plains tribes, 100 percent of individuals reporting at least one traumatic event reported experiencing nightmares (Shore et al., 2009). Native Americans may have a higher prevalence of nightmares due to the cultural emphasis placed on dreams. It is hypothesized that this may be because they are more mindful of their dreams and the content, thus, making them more likely to recall them (Shore et al., 2009).

Although many Native American tribes place significance on dreams, their interpretation varies among tribes. Two tribes will be presented to highlight this: The

Indigenous peoples of the Great Plains and Canadian Prairies, or Plains Indians, and the Diegueño. Among the Plains Indians, dreaming can possess a "transformative effect" on the person (Irwin, 1994). While dreaming, the present and past are no longer mutually exclusive, and these lines blur to create new knowledge and understanding for the dreamer (Irwin, 1994). Dreaming is considered a significant source of information and power among the Plains Indians.

The act of dreaming and the following interpretations are essential to the culture of the Diegueño (Toffelmier & Luomala, 2006). They believe that dreams are essential to the treatment of mental health conditions because they are able to expose the person's problems and wishes. One Diegueño dream doctor described three classifications of dreams: the accident, the standard, and the significant (Toffelmier & Luomala, 2006). "The meaningless or 'accident' dreams are those of the average healthy woman and child and those due to passing physical complaints" (Toffelmier & Luomala, 2006, p. 218). Standard dreams are usually related to symbols of good or bad luck and typically require no interpretation because of their easily discerned meaning. Finally, significant dreams are dreams that cause significant distress leading the patient to consult the dream doctor or are the dreams of a patient with a mental disorder (Toffelmier & Luomala, 2006). Standard interpretations have been given for some specific wish-fulfillment dreams in the tribe. However, it has been suggested that dream content has been altered due to the acculturation to white culture (Toffelmier & Luomala, 2006).

The current Eurocentric definition of dreaming, as described in the Psychological section above, should not be dismissed; however, the current view is too restrictive. Typically, in psychotherapy dreams are considered more fantasy than fact; however, this

is opposite of the belief of many cultures that view dreams as variable levels of reality that are impacted through cultural knowledge (Lohmann, 2000). A patient's culture is critical to understanding chronic posttraumatic nightmares because the patient's cultural interpretation of their posttraumatic nightmare may influence their distress, interpretation of the trauma, and appraisal of the posttraumatic nightmare.

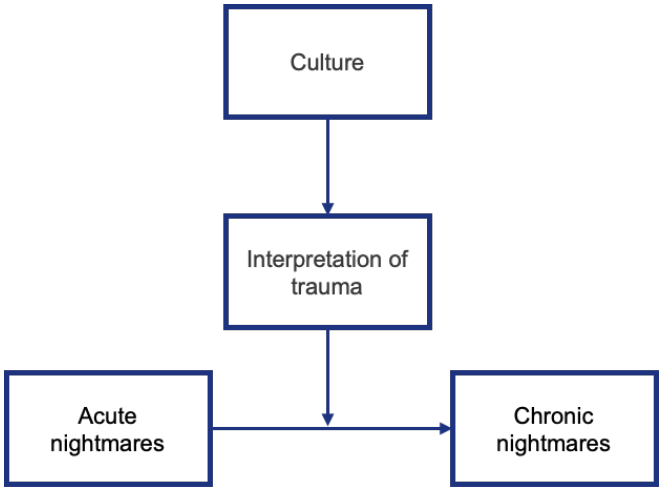

Figure 6. Culture and interpretation of trauma moderates the development of chronic nightmares.

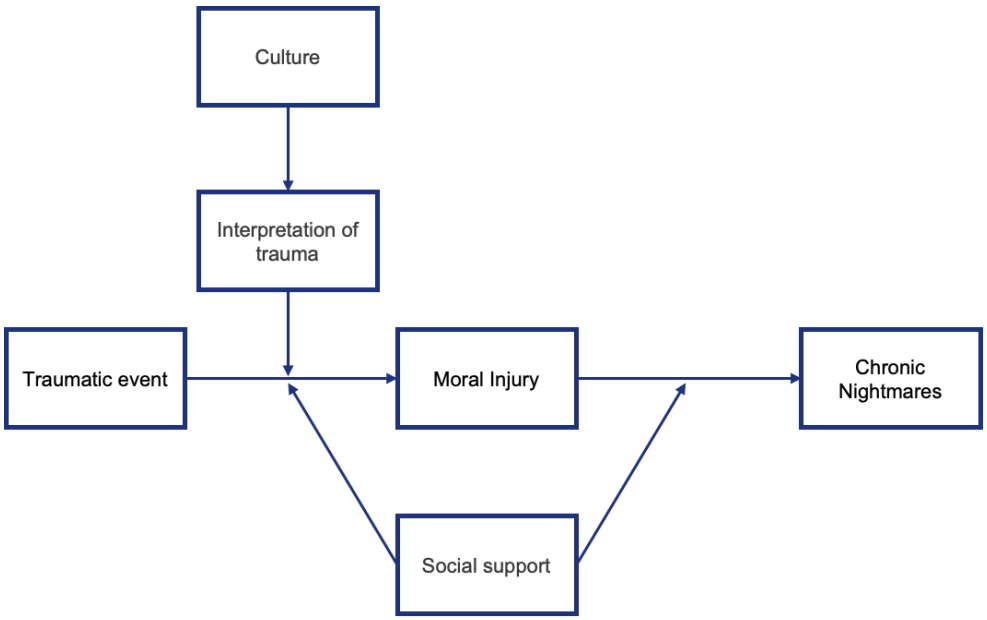

Figure 7. Social factors in the cycle of posttraumatic nightmares.

Summary of Proposed Model

The proposed model (presented in Figure 7) depicts the hypothesized role of the previously discussed biological, psychological, and social factors in perpetuating and maintaining posttraumatic nightmares. The cyclical and bidirectional aspects of the model are considered key to the maintenance of posttraumatic nightmares.

The model begins with the occurrence of a traumatic event; however, the effect of prior factors — including, but not limited to, trauma history, mental health history, family history, culture, and genetic predisposition — are important patient factors in understanding the trauma response. Trauma-related nightmares are a common response in the acute phase after a trauma, with estimates as high as 90% and are thought to aid in fear-memory extinction (Levin & Nielsen, 2007). These trauma-related nightmares are different than the chronic posttraumatic nightmares that are the focus of the current model. For patients who experience disrupted REM sleep during the immediate aftermath of a trauma, which may or may not be related to a trauma-related nightmare, the typical fear learning and memory processing that occurs during REM sleep is disrupted. This disruption of fear learning and memory processing leads to a dysregulated stress response, mental health symptoms, and moral injury, which ultimately leads to chronic posttraumatic nightmares. Notably, a patient's appraisal of the trauma and/or the posttraumatic nightmare, which is influenced by the patient's culture, and subsequent response (i.e., avoid or face and conquer) can prevent the sequela of disrupted fear learning and memory processing.

The biological processes involved in the model are largely initiated by the dysregulated stress response, which is associated with both disrupted hormones and

disrupted sleep, both generally and specifically REM sleep. Hormone disruption and sleep disruption are bidirectionally related, and both are bidirectionally related to mental health symptoms. Importantly, this model is proposed as a cycle rather than as a linear process, and this process begins again through disrupted sleep continuing to disrupt fear learning and memory processing, eventually leading to chronic posttraumatic nightmares (cycle depicted in abbreviated form in Figure 8).

Disrupted fear learning and memory processing is bidirectionally related to mental health symptoms, which is also bidirectionally related to chronic posttraumatic nightmares. Affect distress is thought to mediate the relationship between mental health symptoms and chronic posttraumatic nightmares. Finally, as previously mentioned, disrupted fear learning and memory processing leads to symptoms of moral injury; however, this relationship is moderated by the patient's interpretation of trauma, which is influenced by their culture. Symptoms of moral injury result in increased mental health symptoms and chronic posttraumatic nightmares.

Although the proposed model focuses on understanding the pathway to chronic posttraumatic nightmares, it is equally important to understand the effect of chronic posttraumatic nightmares in a patient's life. Thus, the model also depicts the deleterious effects of chronic posttraumatic nightmares including increased suicidal ideation and substance use, decreased cognition and satisfaction with life, and worse subjective and objective sleep.

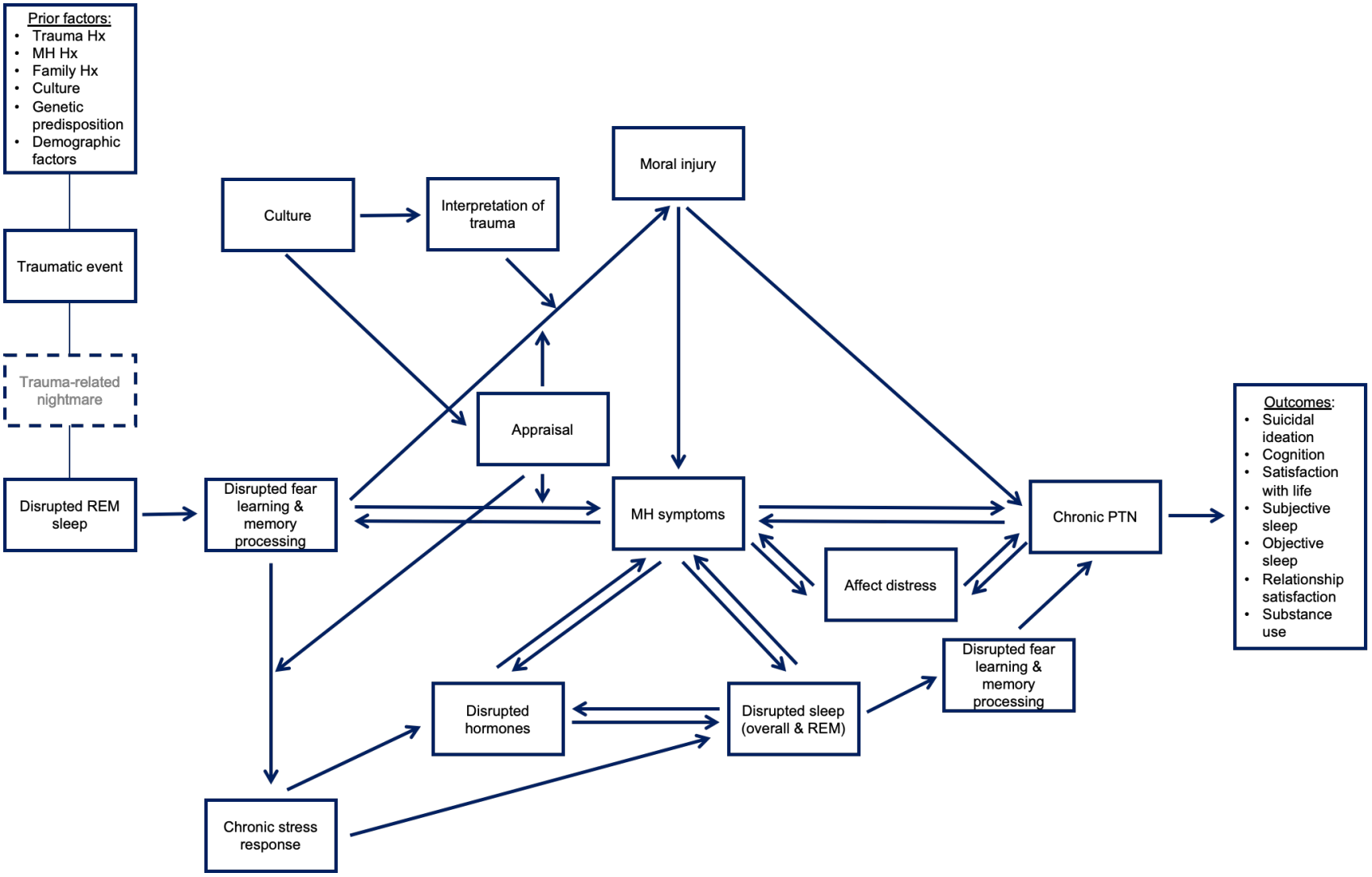

Figure 8. Proposed biopsychosocial model of posttraumatic nightmares.

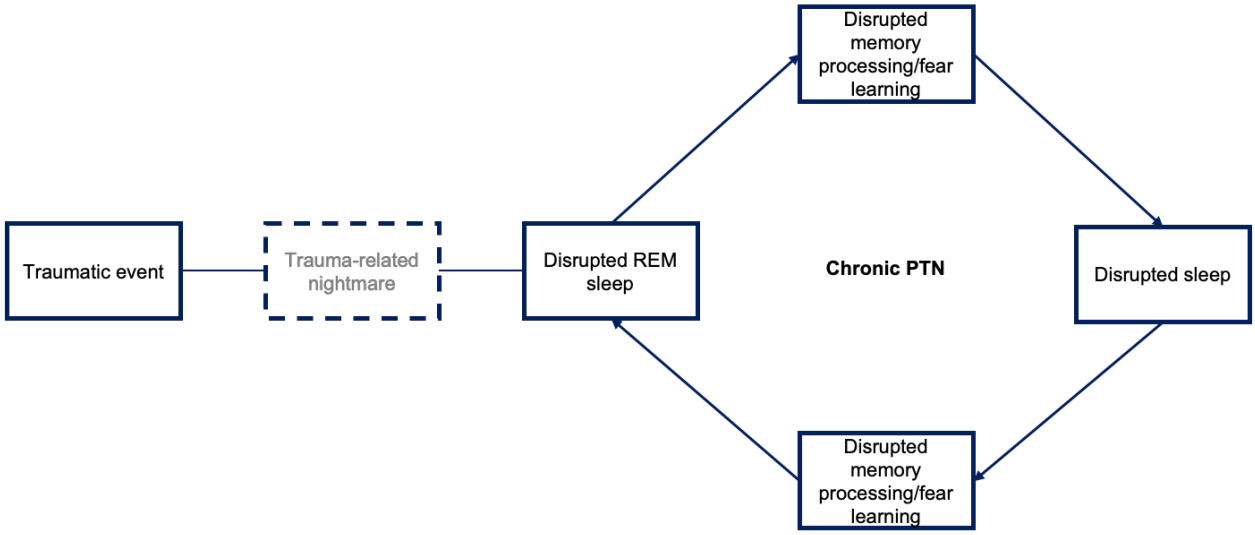

Figure 9. Cyclical nature of posttraumatic nightmares.

Current Research Gaps

There are a number of significant gaps in the literature. Presently, one group (Levin & Nielsen, 2007; Nielsen & Levin, 2007) has proposed an integrated model of nightmares; however, there are three primary reasons a new model is needed. First, and most notable, the model proposed by Nielsen and Levin (2007) presents a single, unified model of nightmares that includes both idiopathic and trauma-related nightmares. This is problematic because idiopathic and trauma-related nightmares have different origins, thus by considering them as a single construct, the model neglects important pieces of the traumatic stress experience (e.g., stress-related hormones, avoidance) that necessitate consideration. Second, Nielsen and Levin's (2007) model neglects consideration of social factors that may influence the development and/or perpetuation of posttraumatic nightmares. Finally, there have been advancements in our understanding of both PTSD and sleep over the last 14 years that require consideration in an updated model. Through a better understanding of mechanisms of posttraumatic nightmares, we can improve patient

outcomes and decrease suffering. Additionally, this information will contribute to military readiness by improving the psychological health of service members with these symptoms.

Proposed Series of Studies

A series of studies is proposed to address some of the identified gaps in the literature and to begin constructing a data-informed model of posttraumatic nightmares (see Appendix A). The first study will contribute to the psychological understanding of posttraumatic nightmares by examining the relationship of PTSD, anxiety, and depression to posttraumatic nightmares while controlling for relevant covariates (e.g., demographics, military characteristics, and self-reported symptoms). The second study will examine neurophysiological correlates of posttraumatic nightmares using magnetic resonance imaging data to examine possible biological underpinnings of posttraumatic nightmares. The third study will examine the relationship of posttraumatic nightmares and other sleep indices to suicidal ideation in order to highlight the importance of increasing our understanding of posttraumatic nightmares. All three studies will utilize data from the National Intrepid Center of Excellence. These studies will provide initial support for the proposed biopsychosocial model that will serve as the basis for a programmatic line of research focused on further testing this model.

CHAPTER 2: Modeling the Association of Mental Health Symptoms to Posttraumatic Nightmares in Active Duty Service Members

STUDY OVERVIEW

Authorship

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Brief Summary & Relationship to Larger Proposal

The present study examines the relationship of mental health symptoms (i.e., PTSD, anxiety, and depression) to posttraumatic nightmares. The forward stepwise regressions consider relevant covariates including comorbid symptoms (e.g., problems staying asleep), demographic characteristics (e.g., marital status), and military characteristics (e.g., military branch).

This study seeks to examine the psychological factors identified in the preceding review. Specifically, we seek to examine the piece of the conceptual model suggesting a relationship of mental health symptoms to posttraumatic nightmares (highlighted in the figure below).

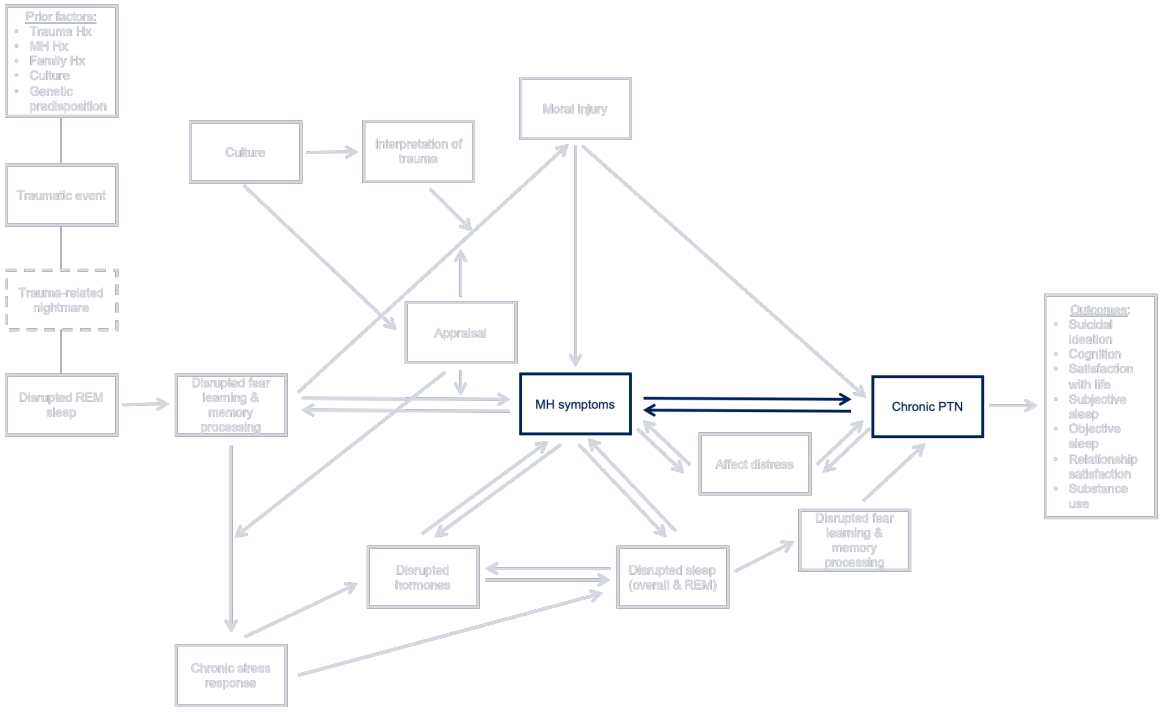

Figure 10. Role of Study 1 in overall project.

Statistical Considerations

Bujang et al. (2018) states a minimum sample size of 500 is required to sufficiently power a logistic regression. Alternatively, a power equation is provided: $n = 100 + 50i$, with i representing the number of independent variables. Thus, the present sample size (n = 684, 856, and 902) would provide adequate power for 11 to 16 independent variables.

Additionally, as discussed below independent analyses were conducted for PTSS, anxiety, and depression due to issues of multicollinearity. A correlation table depicting these relationships is provided in Appendix B.

Study Involvement and Status

Study 1 is in review by the journal *Military Behavioral Health* (see Appendix C). Mrs. Willing designed the study, cleaned and analyzed the data, interpreted the findings, and generated the manuscript under the primary guidance of Drs. Riggs and Pickett. Additional documentation (e.g., emails) of Mrs. Willing's role on this project is available upon request.

Manuscript Title Page

The Association of Mental Health Symptoms to Posttraumatic Nightmares Among Active Duty Service Members Seeking Treatment

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Author Note:

The views expressed in this abstract are those of the authors and do not reflect the official policy of the Uniformed Services University, Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Department of Army/Navy/Air Force, Department of Defense, or U.S. Government. The identification of specific products, scientific instrumentation, or organizations is considered an integral part of the scientific endeavor and does not constitute endorsement or implied endorsement on the part of the authors, DoD, or any component agency. Additionally, the authors have no conflicts of interest to report. Correspondence: Maegan M. Paxton Willing, megan.paxton.ctr@usuhs.edu; Phone: (301) 816-4748; Fax: (301) 816-4765

MANUSCRIPT ABSTRACT AND KEYWORDS

Abstract

Posttraumatic nightmares (PTN) are a common experience among service members with a history of combat or mission-related trauma and are associated with decreased well-being and increased risk of developing PTSD. The present study sought to examine the potential contribution of comorbid symptoms, such as posttraumatic stress, depression, and anxiety, to the development and maintenance of PTN in an effort to inform and improve treatment outcomes. Data were collected as part of standard procedures for an intensive outpatient program for service members with history of TBI and/or psychological health conditions. Separate models were created for posttraumatic stress symptoms, depression, and anxiety inclusive of comorbid psychological symptoms, patient demographics, and military characteristics, with some variance in covariates among final models. Results demonstrated that these, and other related mental health symptoms (i.e., pain that disrupts sleep, early awakenings, sleep onset latency, postconcussive symptoms), were associated with incremental increases in odds of PTN. Findings suggest treating co-occurring symptoms may decrease the distress associated with PTN. Consideration of the association of comorbid symptoms and relevant military characteristics (e.g., special operator status) is important for a more complete understanding of these co-occurring presentations. Future research utilizing longitudinal methods may inform the temporal aspects of these relationships.

Words: 200/200

Keywords: military, posttraumatic nightmares, PTSD, depression, anxiety, sleep

THE ASSOCIATION OF MENTAL HEALTH SYMPTOMS TO POSTTRAUMATIC NIGHTMARES AMONG ACTIVE DUTY SERVICE MEMBERS SEEKING TREATMENT

More than 90% of patients with posttraumatic stress disorder (PTSD) report nightmares and other sleep-related disturbances (Creamer et al., 2018). Because of this high prevalence, these difficulties have been labeled the "hallmark" symptoms of PTSD (Germain, 2013). Posttraumatic nightmares are often chronic and can negatively affect individuals' mental health (Pigeon et al., 2013) and quality of life (Kung et al., 2012). In fact, a study of World War II veterans found patients continued to experience frequent posttraumatic nightmares more than 45 years after the trauma (Guerrero & Crocq, 1994).

Presently, posttraumatic nightmares are not well-understood and often persist even after the use of behavioral or pharmacologic treatment for PTSD (e.g., Tripp et al., 2020) and pharmacological interventions specifically targeting posttraumatic nightmares (i.e., prazosin; Raskind et al., 2018). Posttraumatic nightmares are positively correlated with other mental health difficulties including anxiety (Short et al., 2018), posttraumatic stress symptoms (PTSS), and depression (Pigeon et al., 2013; Short et al., 2018), and it is possible these comorbidities complicate treatment for posttraumatic nightmares. Unfortunately, beyond establishing an association between mental health symptoms and posttraumatic nightmares, the existing literature falls short of a more comprehensive understanding of additional associations between PTN and other comorbidities, demographic variables, functioning, and quality of life. Therefore, we undertook the present study to better understand these potential associations among treatment-seeking individuals with history of TBI and co-occurring mental health conditions.

PTSD, anxiety, and depression frequently co-occur with alcohol use disorder (e.g, Brière et al., 2014; Debell et al., 2014; Vorspan et al., 2015) and are often associated with sleep disturbances (Pigeon et al., 2013; Taylor et al., 2005), suicidal ideation (e.g., Hyman et al., 2012), neurobehavioral difficulties (e.g., Tate et al., 2020), and decreased quality of life (e.g., Fang et al., 2015). More specifically, PTSD (Pigeon et al., 2013), anxiety disorders (Taylor et al., 2005), and major depressive disorder (Pigeon et al., 2013; Taylor et al., 2005) often present with co-occurring insomnia, which is related to decreased sleep quality (Mellinger et al., 1985) and sleepiness (Hurlston et al., 2019). Additionally, PTSD (e.g., Hyman et al., 2012), anxiety (Sareen et al., 2005), and depression (LeardMann et al., 2013) are associated with increased risk of suicide. These disorders also are linked to cognitive dysfunction, including decreased cognitive performance (Tate et al., 2020), episodic memory and executive functioning (Airaksinen et al., 2005), and attention (Farrin et al., 2003). Decreased quality of life has been associated with PTSD (e.g., Fang et al., 2015; Schnurr et al., 2006), depression (e.g., IsHak et al., 2011; Strine et al., 2009), and anxiety (e.g., Beard et al., 2010). Consideration of these associated factors is important as a pretext for understanding the role of various other mental health symptoms on distress and functioning in the presence of posttraumatic nightmares.

Among veterans and military service members, demographic differences have been found in the prevalence of mental health symptoms, including sex (Cohen et al., 2010; King et al., 2013), race (McClendon et al., 2019), marital status (Watkins et al., 2017), and military characteristics (Cohen et al., 2010). In veterans of Operation Iraqi Freedom and Operation Enduring Freedom, females had greater rates of depression,

adjustment disorder, and anxiety disorders; however, males had greater rates of PTSD (Cohen et al., 2010). In a multi-year examination of PTSD diagnostic rates in active duty service members receiving care in the Military Health System, men were diagnosed at a greater rate than women at the beginning of the time-period (i.e., 2008); however, rates in women continually increased and surpassed rates in men in 2010 (Cook et al., 2020). In regards to race, PTSD rates are higher in Black and Hispanic/Latinx active duty service members (Kaczkurkin et al., 2016) and Black, Hispanic/Latinx, and multiracial veterans (McClendon et al., 2019) as compared to their White counterparts. White service members had greater depression symptom severity than Black service members, after controlling for PTSD symptom severity (Kaczkurkin et al., 2016). Marital status also may be an important consideration. An examination of diagnostic rates within the U.S. Military Health System revealed married service members had a greater incidence of PTSD diagnosis than any other marital status (Cook et al., 2020). A second study similarly found married service members reported greater PTSD symptoms, possibly due to the increased familial obligations or low marital satisfaction (Watkins et al., 2017).

Finally, characteristics especially pertinent to the military may be important in considerations, such as rank and branch. A study of Iraq and Afghanistan veterans identified those who were in the Army and the Marine Corps as well as those of enlisted rank had greater rates of PTSD diagnosis (Cohen et al., 2010). A similar trend is seen in active duty service members. Army Soldiers and Marines had the highest rates of PTSD diagnosis compared to all other military branches, and rates were higher in enlisted personnel compared to officers, with the highest rates in junior enlisted personnel (Cook et al., 2020).

To date, research has examined posttraumatic nightmares as a predictor of subsequent mental health symptoms rather than an outcome of these symptoms (e.g., PTSS, anxiety, depression). Examining the effect of mental health conditions on posttraumatic nightmares is also important as current treatments for posttraumatic nightmares are often inadequate (e.g., Lu et al., 2009) and identifying symptoms that may exacerbate posttraumatic nightmares may be important for more targeted treatments. Further, it is important to consider the context (i.e., demographics, life situation) in which nightmares occur. To further our understanding of posttraumatic nightmares, the present study examined the association of PTSS, anxiety, and depression to posttraumatic nightmares to better understand their interrelations and consider the potential implications for nightmare treatments.

METHOD

Data for the present study were obtained from the Clinical Database Protocol at the National Intrepid Center of Excellence (NICoE) at Walter Reed National Military Medical Center. Data were collected between October 2010 and March 2020 as part of standard clinical procedures of a four-week interdisciplinary intensive outpatient program (IOP) for evaluation and treatment of symptoms related to traumatic brain injuries (TBI) and/or psychological health conditions (DeGraba et al. (2021). Patients (N = 1,550) enrolled in this program were active duty service members with combat or mission-related brain trauma. Patients had a mean age of approximately 38 years and were predominately male (98%) and White (77%). Enlisted service members made up 80% of the sample and nearly half (49%) were in the United States Navy. The study sample included one member of the Coast Guard and one cadet. To protect patient identities,

their data were collapsed into the Navy branch and Officer rank categories, respectively. Please see Paxton Willing et al. (in press) for additional details of study procedures. Under a Walter Reed National Military Medical Center Institutional Review Board (IRB)-approved data use protocol, study analyses were performed utilizing de-identified data from the clinical database in accordance with all Federal laws, regulations and standards of practice as well as those of the DoD and the Departments of Army/Navy/Air Force.

Measures

As part of standard care, patients enrolled in the IOP underwent a number of diagnostic tests and completed a battery of intake measures on the first day of the program. Demographic characteristics were assessed at intake and included age, gender, race/ethnicity, education, marital status, rank, branch, and special operator status (yes/no). The following measures were included for analyses in the present study.

The PTSD Checklist-Military version (PCL-M) is a 17-item self-report measure of PTSD symptoms related to a stressful military experience (Weathers et al., 1993a). This measure is commonly used in the literature and has demonstrated appropriate psychometric properties (Weathers et al., 1993a). Patients rate how "bothered" they are by certain PTSD symptoms on a five-point scale (1 = Not at all, 2 = A little bit, 3 = Moderately, 4 = Quite a bit, 5 = Extremely; Weathers et al., 1993a). The PCL-M was employed to measure both posttraumatic nightmares and PTSS. More specifically, a binary measure (0 = "Not at all" bothered; 1 = bothered "A little bit" to "Extremely") of posttraumatic nightmares was assessed using item 2 of the PCL-M ("Repeated, disturbing dreams of a stressful experience from the past?"), consistent with extant literature (e.g.,

Greenbaum et al., 2017; Pigeon et al., 2013). To assess PTSS severity, the remainder of the PCL-M items were totaled. In other words, item 2 was removed from the PTSS total score to prevent artificially inflated results due to the redundancy of the item. The modified measure demonstrated excellent levels of internal consistency comparable to that of the full measure (Modified: Cronbach's alpha = .94; Full PCL-M: Cronbach's alpha = .94). Further, the adapted measure was highly correlated with the full measure ($r = 1.00$, $p < .001$).

The General Anxiety Disorder-7 (GAD-7; Spitzer et al., 2006) is a 7-item scale that was used to assess anxiety in the present study. Respondents rate how much they are bothered by certain anxiety symptoms on a four-point scale (0 = "Not at all," 1 = "Several Days," 2 = "More than half the days", and 3 = "Nearly every day"). Total scores of 5, 10, and 15 represent cut points for mild, moderate, and severe anxiety respectively. The GAD-7 has demonstrated appropriate psychometric properties (Löwe et al., 2008).

The Patient Health Questionnaire-9 (PHQ-9; Kroenke et al., 2001), a 9-item self-report scale, was employed as a measure of depression. Each item is rated on a 4-point scale (0 = "Not at all," 1 = "Several Days," 2 = "More than half the days," and 3 = "Nearly every day"), with respondents endorsing how much they are bothered by each item. The PHQ-9 has a total score range of 0-27; scores of 1-4, 5-9, 10-14, 15-19, and 20-27 represent cutoff scores for minimal, mild, moderate, moderately severe, and severe depression, respectively. The PHQ-9 has demonstrated reliability and validity (Kroenke et al., 2001).

The Pittsburgh Sleep Quality Index (PSQI) is a 10-item self-administered questionnaire evaluating subjective sleep quality, sleep latency, sleep duration, sleep

disturbances, use of sleeping medication, and daytime cognitive dysfunction (Buysse et al., 1989). The 7 component scores yield a global score of 0-21 indicating sleep dysfunction, a score of 5 or more representing poor sleep. The PSQI has shown good psychometric properties (Backhaus et al., 2002). The PSQI provides a measure of sleep quality and endorsement of sleep disturbances and allows for consideration of reduced sleep quality, which is associated with PTSD, anxiety, and depression.

The Satisfaction with Life Scale (SWLS) is a 5-item measures examining life satisfaction (Diener et al., 1985). The SWLS has shown appropriate psychometric properties. Participants rate agreement with statements on a scale of 1 ("strongly disagree") to 7 ("strongly agree"). Responses are summed for a total score ranging from 5 to 35, with lower scores indicating dissatisfaction and greater scores representing satisfaction with life. Satisfaction with life was included due to the known deleterious effects of PTSD, anxiety, and depression on quality of life.

The Neurobehavioral Symptom Inventory (NSI) examines post-concussion symptoms via 22 self-report items (Cicerone & Kalmar, 1995). The NSI has high internal consistency (King et al., 2012). As many of the patients enrolled in the IOP have a history of TBI, the NSI was included to account for postconcussive symptoms associated with TBIs.

The Epworth Sleepiness Scale measures general daytime sleepiness through eight items assessing the likelihood of falling asleep in a number of situations using a 4-point scale (0 = "Would never nod off," 1 = "Slight chance of nodding off," 2 = "Moderate chance of nodding off," 3 = "High chance of nodding off;" Johns, 1991). A score greater than or equal to 10 represents dysfunction. The Epworth Sleepiness Scale is a reliable

measure of sleepiness (Johns, 1992) and allows for consideration of sleepiness caused by sleep disturbances.

Data Analysis

Analyses were conducted using SPSS 25. Three Forward Likelihood Ratio (LR) logistic regression analyses were conducted with PTSS, anxiety, and depression, respectively, as the independent variable in Step 1 while controlling for prazosin use, with covariates included in Step 2 for consideration in the final model. Indicator groups were consistent across all analyses. To mitigate against the risk of multicollinearity, PTSS, anxiety, and depression could not be included in a single analysis thus requiring individual consideration. For demographic variables, male sex, White race/ethnicity, non-special operators, married, enlisted rank, and US Navy were selected as the indicator. For other categorical variables including some sleep measures, not present was the indicator.

Due to missing data, education, suicidal ideation, alcohol use, history of TBI, and the PSQI Global Score of sleep quality were excluded from final model testing. Additionally, patients who were widowed were excluded for this reason. In place of the PSQI Global Score, nine individual items were added (i.e., self-reported hours in bed; difficulty falling asleep within 30 minutes; early awakenings; use of sleep medication; lack of enthusiasm; perceived sleep quality; and trouble sleeping due to problems breathing comfortably, coughing or snoring, or pain). The final model analyses also included demographic variables including marital status, sex, race/ethnicity, and age; military characteristics including rank category (i.e., enlisted and officer), time in service,

special operations status, branch; and comorbid symptoms including sleepiness, satisfaction with life, and postconcussive symptoms.

RESULTS

PTSS Model

PTSS was associated with increased odds of posttraumatic nightmares when controlling for prazosin (OR = 1.13, 95% CI: 1.12, 1.15). The model examining the relation of PTSS to posttraumatic nightmares included four iterations at step 2. Each step provided a significant improvement to the previous model. Across the four steps, pain that disrupted sleep, postconcussive symptoms, special operator status, and early awakenings were added to the model. The final model accounted for a significant amount of variance in the presence/absence of posttraumatic nightmares, (χ^2 (10, 902) = 405.72, $p < .001$; Table 2). In the final model, PTSS was associated with an increase in odds of posttraumatic nightmares (OR = 1.15, 95% CI: 1.12, 1.18). Patients reporting pain that disrupted sleep one or two times per week, as measured by the PSQI, had 2.04 times greater odds of posttraumatic nightmares (95% CI: 1.16, 3.58). Further, patients reporting pain that disrupted sleep three or more times per week had 2.66 times greater odds of posttraumatic nightmares than patients without pain preventing sleep (95% CI: 1.56, 4.53). Postconcussive symptoms were significantly related to posttraumatic nightmares such that greater postconcussive symptoms were associated with fewer posttraumatic nightmares (OR = 0.97, 95% CI: 0.96, 0.99). Similarly, patients who were special operators had decreased odds of posttraumatic nightmares (OR = 0.62, 95% CI: 0.41, 0.95). Finally, patients reporting early awakenings three or more times a week were 4.07

times more likely to report posttraumatic nightmares than patients who did not experience early awakenings (95% CI: 1.06, 15.57).

Anxiety Model

Anxiety also was related to increased odds of posttraumatic nightmares when controlling for prazosin (OR = 1.19, 95% CI: 1.15, 1.24). Likewise, the model examining the relation of anxiety to posttraumatic nightmares included four iterations of the model at step 2, with significant improvement to each step. The models added postconcussive symptoms, pain that disrupted sleep, special operator status, and prazosin use, respectively. The fourth iteration of the model accounted for a significant amount of variance (χ^2 (7, 684) = 186.54, $p < .001$; Table 3). Anxiety also was associated with increased odds of posttraumatic nightmares in the final model (OR = 1.12, 95% CI: 1.07, 1.17). Postconcussive symptoms were related to increased odds of posttraumatic nightmares (OR = 1.03, 95% CI: 1.01, 1.05). Patients reporting pain that disrupted sleep were more likely to report posttraumatic nightmares than patients without pain that disrupted sleep (less than once a week: OR = 2.00, 95% CI: 1.11, 3.59; once or twice a week: OR = 2.57, 95% CI: 1.48, 4.46; three or more times per week: OR = 3.03, 95% CI: 1.80, 5.12). Special operators had an approximately 46% decrease in odds of posttraumatic nightmares compared to non-special operators (OR = 0.54, 95% CI: 0.35, 0.85). Finally, prazosin use was associated with a seven times increase in odds of posttraumatic nightmares (OR = 7.19; 95% CI: 1.50, 34.53).

Depression Model

Finally, symptoms of depression were related to greater likelihood of posttraumatic nightmares (OR = 1.19, 95% CI: 1.15, 1.23). The depression model underwent five iterations at step 2, with postconcussive symptoms, pain that disrupted sleep, special operating status, difficulty falling asleep within 30 minutes, and prazosin use being included. The final model accounted for a significant amount of variance in the presence/absence of posttraumatic nightmares (χ^2 (10, 856) = 220.87, $p < .001$; Table 4). As in the PTSS and anxiety models, depression was related to an increase in odds of posttraumatic nightmares in the final model (OR = 1.09, 95% CI: 1.04, 1.14). Postconcussive symptoms were positively associated with posttraumatic nightmares (OR = 1.03, 95% CI: 1.01, 1.05). Pain that disrupts sleep was associated with greater odds of posttraumatic nightmares (less than once a week: OR = 1.78, 95% CI: 1.03, 3.08; once or twice a week: OR = 2.26, 95% CI: 1.37, 3.72; three or more times per week: OR = 2.56, 95% CI: 1.60, 4.12). As in the PTSS and anxiety models, special operators had decreased odds of posttraumatic nightmares compared to patients who were not (OR = 0.57, 95% CI: 0.39, 0.84). Patients with problems fallings asleep within thirty minutes more than once a week had greater odds of posttraumatic nightmares compared to those who did not (once or twice a week: OR = 1.71, 95% CI: 1.01, 2.89; three or more times per week: OR = 1.85, 95% CI: 1.13, 3.05). Finally, prazosin use was associated with a five times greater likelihood of posttraumatic nightmares (OR = 5.07, 95% CI: 1.11, 23.17).

DISCUSSION

In each of the final models, the mental health symptoms of interest (i.e., PTSS, anxiety, and depression) were related to a small increase in odds of posttraumatic nightmares. However, the amount was often less than that of other factors in the model, including sleep disturbances (i.e., early awakenings and pain that disrupts sleep) and special operator status, when controlling for prazosin use, a medication prescribed for the treatment of posttraumatic nightmares (George et al., 2016). This suggests these other factors may be more related to posttraumatic nightmares than the presence of symptoms of PTSD, anxiety, and depression. Additionally, postconcussive symptoms were assessed due to their relation to mental health symptoms and posttraumatic nightmares. Results showed that these symptoms were significantly related to posttraumatic nightmares in all three models; however, the odds ratios were quite small suggesting these symptoms may not have a clinically meaningful impact on the perceived burden of posttraumatic nightmares. Additionally, the direction of impact was not consistent across the models: in the model of PTSS, postconcussive symptoms were related to decreased odds of posttraumatic nightmares; conversely, in the anxiety and depression models, they were related to increased odds of posttraumatic nightmares. Results from this study suggest exploration of these relationships as they relate to the subscales of the NSI (e.g., somatic/sensory, affective, and cognitive) would be useful in gaining further understanding of these patterns. The present results emphasize the importance of considering co-occurring symptoms and military factors in the understanding of posttraumatic nightmares.

Sleep disturbances were consistently associated with increased odds of posttraumatic nightmares, and we hypothesize these sleep disturbances play a critical role in the initiation and maintenance of posttraumatic nightmares. A number of studies provide support for the relationship between sleep disruptions and PTSD, including insomnia predicting PTSD and intrusion (e.g., posttraumatic nightmare) symptom severity (Wright et al., 2011), greater frequency of awakenings from REM sleep in patients with PTSD (Habukawa et al., 2007), and more REM periods and shorter REM segments in the prediction of PTSD (Mellman et al., 2002). Additionally, REM dysfunction, specifically REM fragmentation, is associated with disruptive nocturnal behaviors common in PTSD, such as posttraumatic nightmares (Insana et al., 2012). Some have conjectured that sleep disturbances interfere with the a critical mechanism of the cognitive processing of events during sleep that help to reduce the affective intensity of stressful incidents, which may increase one's susceptibility to PTSD symptoms such as posttraumatic nightmares (Koffel et al., 2013). Taken together, we propose it is the disruption of REM sleep, specifically, that results in a failure to extinguish the fear memory thus perpetuating the posttraumatic nightmares. However, additional research is needed to interrogate this hypothesis.

Notably, pain that interfered with sleep was related to increased odds of posttraumatic nightmares in all models. Perhaps physical pain and emotional pain may be related, such that feeling pain during sleep may trigger emotional pain or memories associated with their trauma that lead to the posttraumatic nightmares. This may be particularly true for patients whose physical pain is related to an injury sustained during their index traumatic event. Additionally, physical pain might trigger memories of the

traumatic event, resulting in a posttraumatic nightmare. This theory is supported by research suggesting a relationship between physical pain and PTSS, specifically re-experiencing symptoms. A study by Liedl and colleagues (2010) found pain maintenance and development were predictive of PTSD development and maintenance. Notably, the majority of participants' index trauma resulted in a physical injury. Thus, they hypothesized the traumatic memory may have a physical pain aspect. Further, pain mediated the relationship of acute reexperiencing symptoms and reexperiencing symptoms at 12 months suggesting pain memories may induce memories of the traumatic event (Liedl et al., 2010). However, it also is possible that posttraumatic nightmares may induce a pain memory. In a case study of a survivor of the 2005 London bombings, the patient reported experiencing pain when reliving the traumatic memory (Whalley et al., 2007), providing support for a connection between reexperiencing and pain sensation.

Additionally, patients who were special operators had decreased odds of posttraumatic nightmares across all models. We suggest this may be related to specific military training for special operators or may be related to innate factors such as personality or resiliency, including innate character and training that affects sympathetic and parasympathetic tone, which have been postulated to influence nightmares (Simor et al., 2014). Of note, in our clinical observations, service members who are special operators demonstrate a vast difference in cerebral vasomotor reactivity and parasympathetic tone compared to service members who are not special operators. Additional research on the effect of training as well as personality differences may provide important avenues for prevention of posttraumatic nightmares. It is also possible that the findings may be influenced by a variance in the culture in warrior ethos between

military groups that results in a reduced perception of severity of symptoms recorded in self-report scales.

Strengths, Limitations, and Future Directions

The present study benefited from a large sample of active duty patients representing a diverse group of military branches and ranks. Additionally, this sample had a large number of special operators, which allowed examination of differences between patients who are and are not in special operations. However, demographic characteristics including sex and race were largely homogenous. This is important as these patients may experience different exposures to traumatic events, receive different training, and may have other personal differences (e.g., personality differences, marital status). Finally, the present sample is a treatment seeking sample, which allows these results to inform clinical interventions. However, it is important to consider that these results may not be generalizable to all patients with posttraumatic nightmares and as such exploration of the models covered in this manuscript should ideally be replicated in other populations. Differences in military status, experience with previous treatment, and history of TBI should be considered.

The present models were able to take a comprehensive approach to the understanding of posttraumatic nightmares. To understand the effect of comorbid mental health symptoms, it is important to consider biological factors such as sex differences as well as pain that may interfere with sleep. In addition to the mental health symptoms that were the focus of these analyses, the models also considered the effect of comorbid psychological and self-reported sleep symptoms. Finally, social and environmental factors including marital status and military branch and rank provided a better

understanding of the relationship of mental health and posttraumatic nightmares. However, the present study utilized cross-sectional data and, thus, cannot consider the temporal relationship of these factors. Future studies would benefit from a longitudinal or ecological momentary assessment approach to examine the effect of these symptoms on the development and severity of posttraumatic nightmares.

The cross-sectional nature of the data allows examination of these cooccurring symptoms as they would present in the clinic, potentially informing treatment strategies. The present study suggests sleep disturbances, including problems falling asleep or staying asleep and pain that disrupts sleep, are related to posttraumatic nightmares and may be more closely related than symptoms of posttraumatic stress, anxiety, and depression. Thus, attention to cooccurring sleep disturbances may be important to consider in treating posttraumatic nightmares. Specifically, treatment of sleep and pain through treatments such as cognitive behavioral therapy for insomnia and/or chronic pain may improve the effectiveness of psychological treatments for posttraumatic nightmares such as imagery rehearsal therapy (IRT; e.g, Krakow & Zadra, 2006; Krakow & Zadra, 2010) and exposure, relaxation, and rescripting therapy (ERRT; e.g., Balliett et al., 2015). Future research should examine the usefulness of treating sleep disturbances and chronic pain in conjunction with treatment for posttraumatic nightmares to improve patient outcomes.

CHAPTER 3: Examination of the AMPHAC Model of Disturbing Dreams in Male Active Duty Service Members

STUDY OVERVIEW

Authorship

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Brief Summary & Relationship to Larger Proposal

This study seeks to examine neurophysiological correlates of posttraumatic nightmares. Specifically, we aim to examine gray matter volume in a series of regions hypothesized to be associated with posttraumatic nightmares, including the amygdala, hippocampus, medial prefrontal cortex, anterior cingulate cortex, and the insular cortex in a large sample of active duty service members. These regions were theory driven as they have been implicated in disturbing dream production (e.g., Levin & Nielsen, 2007) and were identified as related to sleep disturbances in patients with PTSD (Germain et al.,

2013; Nardo et al., 2015). This process is depicted in Appendix A. Additionally, regions identified in a mega-analysis of the neurophysiology of PTSD (Wang et al., 2020) were included in analyses. This study seeks to contribute to the literature regarding the biological components of posttraumatic nightmares.

Power analysis

The present analyses were powered to detect a small effect size (f^2 = .03) in analyses with three predictors (i.e., posttraumatic nightmares, age, and history of mTBI), an alpha level of .05, and 80% power. Bonferroni comparisons were planned; however, no results met significance precluding further consideration.

Study Involvement and Status

Mrs. Willing designed the study, cleaned the non-imaging data, analyzed the data, interpreted the findings, and generated the manuscript under the primary guidance of Dr. Rhodes and Mr. Srikanchana. This study is in review by coauthors. Additional documentation (e.g., emails) of Mrs. Willing's role on this project is available upon request.

Manuscript Title Page

Examination of the AMPHAC Model of Disturbing Dreams in Male Active Duty Service Members

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endeavor and does not constitute endorsement or implied endorsement on the part of the authors, DoD, or any component agency. Additionally, the authors have no conflicts of interest to report.

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MANUSCRIPT ABSTRACT AND KEYWORDS

Abstract

Posttraumatic nightmares commonly occur after a traumatic experience. Despite the significant deleterious effects on well-being and their role in posttraumatic stress disorder, posttraumatic nightmares remain understudied. The AMPHAC model (Levin & Nielsen, 2007) implicates neuroanatomical structures such as the amygdala, medial prefrontal cortex, hippocampus, and anterior cingulate cortex in the neurophysiology of disturbing dreams, though to date this model has not been validated using neuroimaging data. The present study sought to elucidate whether there are structural differences in these identified AMPHAC regions in relation to posttraumatic nightmares. Data were obtained from male active duty service members ($N = 351$) who had received treatment at an intensive outpatient program for traumatic brain injury (TBI) and/or psychological health conditions. Posttraumatic nightmares were not significantly related to gray matter volume or cortical thickness of any of the identified neuroanatomical regions when controlling for age and history of mild TBI. Although the present analyses do not support structural association of the AMPHAC Model to posttraumatic nightmares, we suggest that functional differences within and/or between these brain regions may be involved in posttraumatic nightmares and that future research is needed to more fully determine whether these functional differences may be associated with posttraumatic nightmares.

Words: 199/200

Keywords: military, MRI, PTSD, sleep, disturbing dreams

EXAMINATION OF THE AMPHAC MODEL OF DISTURBING DREAMS IN MALE ACTIVE DUTY SERVICE MEMBERS

Posttraumatic nightmares commonly occur in patients with posttraumatic stress disorder (PTSD). Indeed, posttraumatic nightmares have been estimated to occur in 90% of patients with PTSD (Creamer et al., 2018) and many consider posttraumatic nightmares to be the hallmark of the disorder (Writer et al., 2014). However, little is known about the neurophysiology behind posttraumatic nightmares. To our knowledge, no prior studies have examined neuroanatomical correlates of posttraumatic nightmares. Thus, the current hypotheses about potential neuroanatomical structures involved are largely informed by our understanding of the neurobiology of PTSD and sleep architecture as well as an extant model.

Proposed Models of Neurobiological Correlates of Posttraumatic Nightmares

The Amygdala, Medial Prefrontal Cortex, Hippocampus, and Anterior Cingulate Cortex (AMPHAC) Model is a hypothesized neurophysiological model of disturbing dream formation created by Levin and Nielsen (2007, 2009; Nielsen & Levin, 2007). Levin and Nielsen (2007, 2009; Nielsen & Levin, 2007) offer reasons as to why these neural regions, in particular, should be studied to determine their potential roles in nightmare production. According to the AMPHAC model, identified regions are involved in state and trait emotional responses as well as disorders including PTSD. The model also predicts higher activity of these regions during REM sleep as compared to non-REM sleep and wake states. Finally, AMPHAC areas have been associated with identifying, creating, sustaining, and remembering fear and other emotions. Specifically, the

amygdala is involved in the physical responses typically associated with the sympathetic nervous system's stress response by increasing blood pressure, heart rate, and respiration. The anterior cingulate cortex has been proposed to play a critical role in modulation of activity in the amygdala and is involved in emotional distress, which may be related to the perpetuation of the nightmare cycle. The medial prefrontal cortex and hippocampus are crucial for fear conditioning and fear extinction (Nielsen & Levin, 2007).

The AMPHAC model was created with a unified theory of disturbing dreams in mind. Phrased differently, idiopathic (nightmares with an unknown origin) and posttraumatic nightmares (nightmares related to a traumatic event) are hypothesized to share a model. Additionally, the AMPHAC model considers both bad dreams and nightmares (distinguished by the awakening associated with nightmares). Although, this model is more generalized and thus may not be entirely representative of posttraumatic nightmares, it offers a framework from which to begin examining neural correlates of posttraumatic nightmares. Additional theorists (e.g., Nardo et al., 2015) have hypothesized that the amygdala, hippocampus, and anterior cingulate cortex play a role in posttraumatic nightmares.

Support for the AMPHAC Model

Some studies have found an association between the presence of PTSD and reduced grey matter volume (Logue et al., 2018; Morey et al., 2019; Nelson & Tumpap, 2017; O'Doherty et al., 2017; Xie et al., 2018) and density (Kasai et al., 2008) of the hippocampus. Kasai et al. (2008) found reductions in right hippocampal gray matter density in combat-exposed veterans with PTSD compared to combat-exposed veterans without PTSD, and Crombie and colleagues (2021) identified reduced cortical thickness

in the right parahippocampus in women with PTSD compared to healthy controls without a trauma history. Further, one study (Akiki et al., 2017) found abnormalities (i.e., indentations) in the anterior of the right hippocampus and the dorsal region of the amygdala in combat-exposed veterans with more severe PTSD symptoms compared to those with fewer symptoms. PTSD also is related to decreased volume in the amygdala (e.g., Logue et al., 2018; Morey et al., 2020; Morey et al., 2019; O'Doherty et al., 2017). Notably, the amygdala, in particular, has been implicated in PTSD symptoms in veterans (e.g., Akiki et al., 2017; Morey et al., 2020; Pieper et al., 2020). Reduced amygdala subnucleus volume, shape distortions (Morey et al., 2020), and indentations (Akiki et al., 2017) have been identified in relation to PTSD symptoms in veterans. However, one study of active duty service members and veterans found *greater* volume in the amygdala of participants with comorbid mild traumatic brain injury (mTBI) and PTSD compared to participants with only a history of mTBI (Pieper et al., 2020).

Volume (Herringa et al., 2012; O'Doherty et al., 2017; Woodward et al., 2006; Young et al., 2018) and gray matter density (Kasai et al., 2008) of the anterior cingulate cortex are reduced in patients with PTSD, and in veterans these reductions were related to greater physiological arousal (Young et al., 2018). Patients with PTSD also exhibit a diminished medial frontal cortex compared to trauma-exposed controls (O'Doherty et al., 2017). Finally, PTSD diagnosis and symptom severity is related to reduced volume (Herringa et al., 2012), cortical volume (Wang et al., 2020), and gray matter density (Kasai et al., 2008) in the insular cortex.

Reexperiencing symptoms of PTSD (e.g., posttraumatic nightmares) have been linked to a number of regions. Reexperiencing symptoms are associated with reduced

gray matter density in the insula (Kasai et al., 2008) as well as decreased gray matter volume in the hippocampus (O'Doherty et al., 2017; Xie et al., 2018) and lingual gyrus (Berman et al., 2018). In a trauma analog study, patients with less insula gyrus volume reported more early intrusive memories related to the traumatic film (Gvozdanovic et al., 2020). In regards to cortical thickness, reductions of the parahippocampus are related to greater reexperiencing symptoms (Crombie et al., 2021). Furthermore, shape of regions also may be involved in posttraumatic nightmares, as indentations of the right amygdala were largely explained by reexperiencing symptoms in veterans (Akiki et al., 2017).

Germain and colleagues (2013) examined neural correlates in patients with combat-related PTSD and found hypermetabolism of glucose consumption in a number of regions during REM sleep including the amygdala, hippocampus, anterior cingulate cortex, medial prefrontal cortex, and locus coeruleus. Nardo et al. (2015) examined brain volume in relation to sleep disturbances, including nightmares, in patients with PTSD using voxel-based morphometry and single-photon emission computerized tomography (SPECT); however, sleep disturbances were assessed as a single construct comprised of symptoms of insomnia and nightmares. Their results indicated regional reductions in gray matter volume of the amygdala, hippocampus, anterior cingulate cortex, and insula were related to sleep disturbances in patients with PTSD (Nardo et al., 2015). Further examination using whole-brain voxel-based morphometry suggested reduced gray matter volume in the right anterior cingulate cortex, bilateral insular cortex, amygdala, hippocampus, parahippocampal cortex, left striatum, and the right dorsolateral prefrontal cortex. These results provide initial support for the involvement of the amygdala,

hippocampus, and anterior cingulate cortex in cooccurring sleep disturbances and PTSD, supporting the AMPHAC Model proposed by Levin and Nielsen (2007).

Rationale

We sought to examine the neurobiology of patients with posttraumatic nightmares informed by the extant literature using volumetric and cortical thickness measures obtained from structural MR imaging. Given the largest overlap across the Nardo et al. (2015) and Germain et al. (2013) studies as well as their hypothesized functional roles in the models proposed by Levin and Nielsen (2007), we proposed the amygdala, hippocampus, medial prefrontal cortex, anterior cingulate cortex, and insular cortex would be implicated in posttraumatic nightmares. Specifically, we hypothesized significant decreases in gray matter volume and cortical thickness in the amygdala, hippocampus, medial prefrontal cortex, anterior cingulate cortex, and the insular cortex in patients with posttraumatic nightmares compared to those without posttraumatic nightmares. Previous research suggests brain volume and cortical thickness represent discrete biological processes (e.g., Leerssen et al., 2020) thus consideration of both measures is important to increase understanding of the role of these regions.

METHOD

The present data were obtained from a larger, ongoing study exploring associations between advanced neuroimaging sequences, traumatic brain injury (TBI) history, behavioral outcomes, and blood biomarkers as part of the TBI Neuroimaging Core Protocol at the National Intrepid Center of Excellence (NICoE; $N = 399$). Data were collected between 2017 and 2020. All patients were enrolled in an intensive outpatient

program (IOP) for treatment of TBI and/or psychological health conditions. For the present analyses, patients were excluded for history of moderate (n = 5) or severe (n = 2) TBI, for missing posttraumatic nightmare data (n = 17), or imaging that failed quality assurance checks (n = 24; reasons included skull strip errors, intensity normalization errors, white matter segmentation errors, topological defect, and pial surface misplacement). Included patients (n = 351) were male and were on average approximately 40 years old, white (54.1%), married (84.6%), enlisted rank (78.9%), in the United States Navy/Coast Guard (60.1%), and had a history of mTBI (86.9%). Complete demographic breakdown as well as the demographics of excluded patients are available in Table 1. Included and excluded patients did not significantly differ in regards to demographic characteristics.

A complete description of the standard clinical procedures and the IOP treatment program can be found in DeGraba et al. (2021). All patients provided written informed consent prior to participation. The present analyses were conducted as part of a Walter Reed National Military Medical Center Institutional Review Board (IRB)-approved protocol in accordance with all Federal laws, regulations and standards of practice as well as those of the DoD and the Departments of Army/Navy/Air Force.

Measures

PTSD Checklist-Civilian (PCL-C)

The PCL-C is a commonly used measure of posttraumatic stress symptoms with appropriate psychometric properties (Weathers et al., 1993b). This 17-item self-report assesses symptoms related to a traumatic experience. Consistent with previous research

(e.g., Greenbaum et al., 2017; Pigeon et al., 2013), item two of the PCL-C ("Repeated, disturbing dreams of a stressful experience from the past;" Weathers et al., 1993b) was used as a measure of posttraumatic nightmares.

Ohio State University TBI Identification Method

The Ohio State University TBI Identification Method is a structured interview utilized to identify the number, type, severity, effects, and timing of TBIs incurred over a patient's lifetime (Corrigan & Bogner, 2007). This measure has demonstrated strong reliability (Corrigan & Bogner, 2007). Final determination of mTBI history was made via consensus meeting including both clinical and research team members. mTBI was defined using Veterans Affairs/Department of Defense guidelines: loss of consciousness (LOC) < 30 minutes and/or post-traumatic amnesia/alteration of consciousness (AOC) <24 hours (Assistant Secretary of Defense, 2015). LOC was required to be witnessed by an additional person at the time of the event, and AOC needed to be substantiated by a clear disruption in cognitive functioning.

Image and Data Processing

Images were acquired on GE Discovery MR 750 3T MRI scanner (GE Healthcare, Waukesha, WI) with a 32-channel phased array head coil (Nova Medical, Wilmington, MA). The high resolution structural T1-weighted magnetic resonance imaging (MRI) scan was acquired in the sagittal plane with a 3D BRAVO sequence (TI/TR/TE = 450/9.6/4.12ms, FA = 12°, voxel size = 0.47mm x 0.47mm x 0.6mm). Volumetric segmentation, cortical surface reconstruction, and thickness measurement were performed using the FreeSurfer software package

(https://surfer.nmr.mgh.harvard.edu), Version 6.0. All results were visually inspected as part of quality assurance to check for inaccuracies during the cortical reconstruction. Briefly, the automated image processing steps include intensity normalization (Sled et al., 1998), registration to MNI305 atlas (Collins et al., 1994), removal of non-brain tissue using a hybrid watershed/surface deformation procedure (Ségonne et al., 2004), segmentation of the subcortical white matter/deep gray matter volumetric structures, tessellation of the gray matter/white matter boundary, automated topology correction, and surface deformation (Fischl et al., 2002; Fischl et al., 2004). The surface deformation enables the detection of tissue boundaries, and the cortical thickness is calculated as the distance between the white and pial surface that gives us the thickness at each location of the cortex (Fischl & Dale, 2000).

Based on the AMPHAC Model of nightmares, subcortical, left hemisphere, right hemisphere, total cortical, and total gray matter volume were extracted, and cortical thickness were extracted for the amygdala, hippocampus, medial prefrontal cortex, anterior cingulate cortex, and the insular cortex.

Statistical Analysis

IBM SPSS 25.0 was used to conduct all analyses. Prior to conducting analyses, tests of normality were performed and nonparametric data were transformed using a natural log transformation. Linear regressions were conducted to compare gray matter volume using the estimated total intracranial volume (eTIV) and cortical thickness measurements in patients with and without posttraumatic nightmares while controlling for age and history of mTBI. Normalizing structural volumes with an eTIV compensates for overall brain size, thus controlling for head size.

Results and Discussion

Gray matter volume and cortical thickness measures were compared in patients with (n = 177) and without (n = 174) posttraumatic nightmares. All analyses were nonsignificant when controlling for age and mTBI precluding further consideration such as correcting for multiple comparisons or controlling for additional covariates. Results for gray matter volume and cortical thickness analyses are depicted in Tables 2 and 3, respectively. A recent mega-analysis of cortical volume in patients with PTSD found reduced volume in the left and right lateral orbitofrontal gyri; left superior temporal gyrus; and right insular, lingual, and superior parietal gyri (Wang et al., 2020). Secondary analyses were performed with hopes to replicate these findings in relation to posttraumatic nightmares. These results also were nonsignificant when controlling for age and mTBI history (see Table 4).

The present study sought to evaluate the AMPHAC model of disturbing dreams proposed by Levin and Nielsen (2007, 2009; Nielsen & Levin, 2007). To our knowledge, this is the first study to examine volumetric or cortical thickness in patients with posttraumatic nightmares. Thus, these results suggest the regional volume of the bilateral amygdala, medial prefrontal cortex, hippocampus, anterior cingulate cortex, and insular cortex are not significantly associated with the presence of posttraumatic nightmares in male active duty service members. Of note, Morey and colleagues (2019) found the relationship between PTSD diagnosis and hippocampal volume was stronger in females compared to males. These sex differences may offer some explanation for these null findings. The present findings are inconsistent with previous literature suggesting a relationship between PTSD and the amygdala, medial prefrontal cortex, hippocampus,

anterior cingulate cortex, and insular cortex (e.g., Logue et al., 2018; Morey et al., 2019; O'Doherty et al., 2017; Wang et al., 2020; Young et al., 2018). It is important to note that these previous studies found support for these regions in relation to PTSD, and these findings may not be generalizable to posttraumatic nightmares, which represents a distinct symptom within PTSD that occurs during sleep. It also is suggested that the problem of inadequate power in neuroimaging studies has led to an overestimation of effect sizes and may account for the large variability in replication efforts (Button et al., 2013; Cremers et al., 2017). Indeed, Button and colleagues (2013) estimate a median of 8% power in studies examining brain volume abnormalities. These results did not find support for the AMPHAC model of disturbing dreams despite a large sample size that provided sufficient power to detect small effect sizes ($f^2 \leq .03$ at $a = .05$ and 80% power).

In contrast to many previous studies (e.g., Logue et al., 2018; Morey et al., 2019; O'Doherty et al., 2017; Wang et al., 2020; Young et al., 2018), the present analyses controlled for history of mTBI. We hypothesize this statistical adjustment may in part explain the current findings. In service members, PTSD and TBI commonly cooccur. Hoge and colleagues (2008) found that approximately 44% of active duty soldiers who sustained an injury with loss of consciousness and approximately 27% of soldiers who experienced an altered mental status due to an injury had comorbid PTSD, compared to only 9% of soldiers who did not sustain an injury (Hoge et al., 2008). In the present sample, nearly 87% of patients had a history of mTBI, and approximately 65% had clinically significant posttraumatic stress symptoms (defined as a PCL total score of ≥ 35 as recommended by the National Center for PTSD (2012)). It has been suggested that the increased levels of threat and utilization of improvised explosive devices during the

ongoing conflicts in Iraq and Afghanistan may offer some explanation for this comorbidity (Kaplan et al., 2017). Notably, blast-related mTBIs, such as those obtained from improvised explosive devices or heavy artillery, are related to greater decreases in cortical thickness compared to non-blast-related mTBIs (Eierud et al., 2019). Importantly, one review of the pathophysiology of TBI and PTSD concluded that neurologically this comorbidity has a "unique signature" (Kaplan et al., 2017, p. 213), and TBI is, therefore, an important consideration when examining neurologic differences in patients with a trauma history. It is possible TBI history accounts for some variance in previous studies.

Although the present analyses do not support structural associations of these regions to posttraumatic nightmares, there remains room to explore whether there may be functional differences in the activity of the individual regions, as well as how the regions communicate with each other, during waking and sleep. Indeed, studies suggest functional and structural associations are distinct (e.g., Owens et al., 2018). For instance, emotional and memory processing regions have a strong relationship to PTSD. Patients with PTSD show increased activation of the insula and decreased activation of the anterior cingulate cortex in response to Affective Stroop trials (Fani et al., 2019). In Nardo and colleagues' (2015) study of sleep disturbances in patients with PTSD, the severity of sleep disturbances was related to the increased activity in the dorsal midbrain, precuneus, and insula but decreased activity in anterior cingulate cortex, dorsolateral prefrontal cortex, and orbitofrontal cortex. Reexperiencing or intrusion symptoms of PTSD (e.g., posttraumatic nightmares) have been linked to a number of regions. Hyperactivation of the amygdala (Ben-Zion et al., 2021) and prefrontal cortices may be associated with increased reexperiencing symptoms (Henigsberg et al., 2019). Further,

fear acquisition and extinction in healthy subjects indicated hyperactivation of the insula, anterior cingulate cortex, hippocampus, and medial frontal cortex, among others is positively associated with reexperiencing symptoms, suggesting extinction learning may, in part, be responsible for reexperiencing symptoms such as posttraumatic nightmares (Miedl et al., 2020).

A meta-analysis of trauma-related autobiographical memories in patients with PTSD concluded diminished activation of the prefrontal cortices may indicate a greater propensity for reexperiencing symptoms (Thome et al., 2020) such as posttraumatic nightmares. Levin and Nielsen (2007) proposed emotion regulation to be a critical component for the initiation of disturbing dreams, and emotion dysregulation has been identified in connection to hypoactivity of the ventromedial prefrontal cortex (Etkin & Wager, 2007). Thus, hypoactivity of the ventromedial prefrontal cortex, in particular, may increase the propensity for posttraumatic nightmares through a failure of adequate emotion regulation. A review by Fitzgerald and colleagues (2018) suggested this emotion dysregulation is the result of dysfunction of the neurocircuitry involving the amygdala, insula, hippocampus, anterior cingulate cortex, and prefrontal cortex. They suggest it is the amygdala and insula's response to emotional stimuli as well as abnormal anterior cingulate and prefrontal cortices leading to inadequate appraisal, resolution, and management of these emotional stimuli that results in the emotional dysregulation observed in patients with PTSD (Fitzgerald et al., 2018). Notably, cooccurring sleep disturbances, such as insomnia, may further disrupt emotion regulation in patients (Leerssen et al., 2020) thus necessitating consideration of their compounding effect on emotion regulation in patients with posttraumatic nightmares.

Future studies should examine functional differences in patients with and without posttraumatic nightmares. Hyperactivity in these regions, which is common in PTSD (e.g., Badura-Brack et al., 2018), is hypothesized to increase the occurrence of disturbing dreams (Levin & Nielsen, 2007). Germain and colleagues (2008) proposed that hyperactivity of the amygdala *and* hypoactivity of the medial prefrontal cortex intensified by REM sleep may promote nightmare occurrence. The hippocampus and amygdala, specifically, are implicated in the production of dreams and thus may be involved in nightmare production as well. These brain areas also are involved in state and trait emotional responses and emotion-based disorders including PTSD and have been shown to be more active during REM sleep compared to non-REM sleep and waking. Therefore, these regions may play a critical role in the physiological basis of normal dreaming and may influence the emotional imagery present (Levin & Nielsen, 2007). Although the current findings did not identify structural differences within the AMPAHC regions in patients with posttraumatic nightmares, there remains room for future studies to elucidate whether there are meaningful functional differences within, or between, these regions in patients with and without posttraumatic nightmares.

CHAPTER 4: Understanding the Role of Sleep on Suicidal Ideation in Active Duty Service Members: Implications for Clinical Practice

STUDY OVERVIEW

Authorship

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Brief Summary & Relationship to Larger Proposal

The present study examined the association of sleep indices — both subjective and objectives measures — to suicidal ideation in active duty service members. Of particular relevance to the larger study, both posttraumatic nightmares and a generic measure of bad dreams/nightmares (the Pittsburgh Sleep Quality Index Item 5H) were assessed. In addition to further elucidating the association of sleep and suicidal ideation, this study provides support for the importance of considering the impact of posttraumatic nightmares in a patient's life.

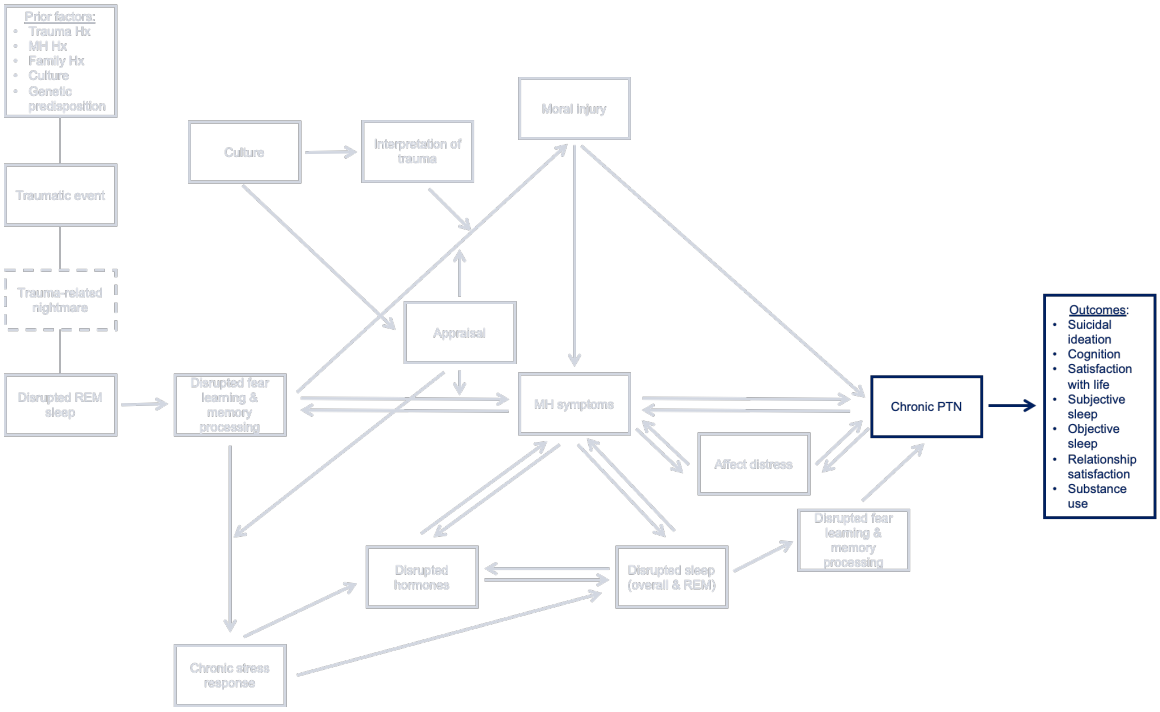

Figure 11. Role of Study 3 in examining the proposed conceptual model.

Statistical Considerations

Power was calculated using through the power equation provided in Bujang et al. (2018): $n = 100 + 50i$, i representing the number of independent variables. Thus, the present sample size ($n \geq 489$) is sufficiently powered to detect significant relationships.

Study Involvement and Status

Study 3 has been accepted for publication in *Practice Innovations.* Copies of manuscript acceptance and publication proofs are available in Appendices D and E, respectively. Mrs. Willing designed the study, cleaned and analyzed the data, interpreted the findings, and generated the manuscript under the primary guidance of Drs. Pickett and Riggs. Additional documentation (e.g., emails) of Mrs. Willing's role on this project is available upon request.

MANUSCRIPT TITLE PAGE

Understanding the Role of Sleep on Suicidal Ideation in Active Duty Service Members: Implications for Clinical Practice

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Author Note:

The views expressed in this abstract are those of the authors and do not reflect the official policy of the Uniformed Services University, Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Department of Army/Navy/Air Force, Department of Defense, or U.S. Government. The identification of specific products, scientific instrumentation, or organizations is considered an integral part of the scientific endeavor and does not constitute endorsement or implied endorsement on the part of the authors, DoD, or any component agency. Additionally, the authors have no conflicts of interest to report. Correspondence: Maegan M. Paxton Willing, megan.paxton.ctr@usuhs.edu; Phone: (301) 816-4748; Fax: (301) 816-4765

MANUSCRIPT ABSTRACT, KEYWORDS, AND CLINICAL IMPACT STATEMENT

Abstract

Suicide is a significant public health concern, particularly within the U.S. military. Sleep difficulties are hypothesized to elevate risk, yet this association is not well understood. Presently, there is some support for a positive association between subjective reports of sleep disturbances and suicidal ideation (SI); however, research regarding the relation of SI and objective measures of sleep is sparse. The present study aimed to examine the association of subjective and objectives measures of sleep on SI in a sample of active duty service members and provide recommendations to changes in clinical care. Data were obtained from the National Intrepid Center of Excellence's clinical database. Patients (*N*=1,550) were predominantly male, Navy/Coast Guard, and enlisted rank, with a mean age of 38 years. Patients underwent a sleep study and completed a battery of measures as part of standard clinical care. SI was coded as a binary variable, and odds ratios were calculated using logistic regression. Of the 14 objective sleep indices examined, REM latency and time in sleep stage N2 were related to SI. Subjective reports, including sleep quality, sleepiness, bad dreams, and traumatic bad dreams and nightmares, were all significantly associated with increased odds of SI. Notably, subjective reports of sleep were the only measures with meaningful odds ratios, with traumatic bad dreams producing the greatest odds ratios. The present findings suggest subjective reports of sleep disturbance are important when evaluating SI in active duty service members and may represent an important point of intervention for patients experiencing SI.

Words: 248/250

Keywords: military, suicidal ideation, sleep, nightmares, polysomnography

Clinical Impact Statement

The present study adds to the literature on the role of sleep, both objective and subjective, on suicidal ideation in service members. These results provide support for the need to evaluate self-reported sleep disturbances during suicide risk assessments, with a particular focus on the need to consider bad dreams and posttraumatic nightmares.

UNDERSTANDING THE ROLE OF SLEEP ON SUICIDAL IDEATION IN ACTIVE DUTY SERVICE MEMBERS: IMPLICATIONS FOR CLINICAL PRACTICE

Suicide is a significantly increasing public health concern. In the United States, it is the tenth leading cause of death nationwide and occurs at a rate of 14.2 per 100,000 people (Hedegaard et al., 2020), with one person attempting suicide every 31 seconds (Center for Deployment Psychology, n.d.). Suicide is also a substantial problem facing the U.S. military, with a rate of 24.8 suicide deaths per 100,000 active duty service members, 22.9 per 100,000 reservists, and 30.6 per 100,000 National Guardsmen (Tucker et al., 2019). This suggests a critical need to identify opportunities for intervention. It is, therefore, imperative to identify factors associated with increased risk of suicide in service members. Sleep disturbances, in particular, have been identified as one such determinant requiring further study. With the high prevalence of sleep disturbances in the U.S. military (e.g., Plumb et al., 2014), it is particularly important to increase the understanding of the role sleep plays in suicide risk among active duty service members.

Some sleep disorders, including sleep apnea and insomnia, have been shown to be related to increased suicidal ideation and attempts. In a sample of patients who underwent a one-night polysomnography (PSG) evaluation, approximately 20% of those diagnosed with obstructive sleep apnea (OSA) reported suicidal ideation (Timkova et al., 2018). Patients with sleep apnea also have been found to have increased odds of suicidal ideation and suicidal planning, even when controlling for relevant demographics, substance use, and depression; however, they did not have increased odds of suicidal attempts (Bishop et al., 2018). In contrast, Bishop and colleagues (2019) examined suicide attempts and psychiatric diagnoses among veterans seeking care in the

Department of Veterans Affairs (VA) and found sleep-related breathing disorders, such as OSA, were positively associated with suicide attempts when controlling for age, gender, utilization of sleep or mental health services, and comorbid sleep disorders. However, this association was no longer significant when further controlling for PTSD, depression, anxiety disorders, schizophrenia, bipolar disorder, and substance use disorder.

Insomnia also has been implicated in the relationship of sleep to suicide. It is important to note insomnia is both a diagnosis as well as a symptom. To highlight the differences, we will discuss the literature as it relates to both the disorder and as a self-reported symptom (below). In a large review of VA medical records, a diagnosis of insomnia was found to be associated with having attempted suicide, even when controlling for patient age, gender, sleep or mental health treatment utilization, and other sleep disorders (Bishop et al., 2019). This relationship remained significant after controlling for relevant mental health disorders and medical comorbidities. Pompili et al. (2013) examined patients who were admitted to an emergency room after seeking psychiatric care and found those with a diagnosis of insomnia were *less* likely to have attempted suicide in the last 24 hours. However, for those patients with insomnia who *had* attempted suicide within this timeframe, they were more likely to have used a violent method.

Objective Measures of Sleep

Little research has examined objective measures of sleep in relation to suicide. In a study of civilians with PTSD who were receiving an at home sleep apnea test, respiratory disturbance index (RDI), apnea-hypopnea index (AHI), and oxygen desaturation index were positively associated with suicidal ideation (Gupta & Jarosz,

2018). In this study, OSA severity was measured by RDI, thus suggesting OSA severity is associated with increased suicidal ideation. One study (Bernert, Hom, et al., 2017) examined objective measures of sleep as measured by actigraphy in relation to suicidal ideation. Time of sleep onset was predictive of suicidal ideation, but not sleep onset latency (SOL), total sleep time, wake after sleep onset, sleep efficiency, or sleep offsets (i.e., time of final awakening; Bernert, Hom, et al., 2017). Notably, this study included only patients with high suicide risk, and, therefore, should be replicated with patients of other suicidal risk levels.

Bernert, Luckenbaugh, et al. (2017) compared patients with and without suicidal ideation on objective sleep measures (e.g., sleep efficiency (SE), rapid eye movement (REM) latency, wake after sleep onset (WASO), total sleep time (TST), percent of time spent in REM, and time spent in non-rapid eye movement (NREM; Stages 1-4) during an electroencephalograph (EEG) sleep study. Patients with suicidal ideation had less NREM Stage 4 sleep and lower SE but greater WASO when controlling for depressive symptoms and a diagnosis of bipolar disorder or major depressive disorder (Bernert, Luckenbaugh, et al., 2017). This study employed a sample of treatment-seeking patients with treatment-resistant depression, underscoring the need for replication in additional populations.

Subjective Sleep Reports

Subjective sleep reports have been associated with increased suicidal ideation (e.g., Bernert et al., 2014; Tae et al., 2019). In a study of treatment-seeking patients with depression, subjective reports of sleep quality as measured by the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) were positively associated with suicidal ideation (Tae et al., 2019). This study further identified that each of the seven

components of the PSQI (i.e., sleep quality, sleep latency, time asleep, sleep efficiency, sleep disturbances, use of sleep medication, and impact on daytime functioning) were positively correlated with suicidal ideation. Additionally, results demonstrated coughing or snoring loudly, as reported on the PSQI, to be associated with greater suicidal ideation, when controlling for age, depression symptoms, and marital status. Sleep quality also has been found to predict suicide risk at 10-year follow up in older adults (Bernert et al., 2014). In a study of Afghanistan and Iraq era veterans receiving care in the VA, subjectively-reported poor sleep quality was related to suicidal ideation, but self-reported sleep duration was not (Swinkels et al., 2013). However, a separate study found self-reported short sleep duration was associated with suicide risk in a study of veterans recently home from deployment (Luxton et al., 2011).

Self-reported insomnia symptoms also have been shown to be related to suicidal ideation. In patients with a history of suicidal ideation, plan, or attempt, prior levels of insomnia symptoms were positively associated with subsequent increases in suicidal ideation (Zuromski et al., 2017). In undergraduate students with high suicide risk, subjective reports of insomnia and nightmares were each predictive of increased suicidal ideation (Bernert, Hom, et al., 2017). Sleep quality also has been found to be longitudinally associated with a greater risk of death by suicide, which remained when controlling for depressive symptoms (Bernert et al., 2014).

A number of studies have examined the role of bad dreams and/or nightmares in suicidal ideation (e.g., Bishop et al., 2018; Sandman et al., 2017; Tae et al., 2019). It is important to examine both idiopathic (without known origin) and traumatic (related to a traumatic event) bad dreams and nightmares, as there may be a differential effect on

suicidal ideation. Idiopathic bad dreams were positively associated with suicidal ideation in patients with depression when controlling for age, depression symptoms, and marital status (Tae et al., 2019). Posttraumatic nightmares have been associated with increased suicidal ideation in a study of civilians with PTSD receiving an in-home diagnostic test for OSA (Gupta & Jarosz, 2018). Additionally, in an examination of data from VA patients, nightmare disorder and suspected posttraumatic nightmares also were found to be associated with a suicide attempt when controlling for patient age, gender, sleep or mental health treatment utilization, and sleep disorders; however, this relationship did not remain when controlling for mental health diagnoses including PTSD, depression, anxiety disorders, schizophrenia, bipolar disorder, and substance use disorder (Bishop et al., 2019). This study classified patients as having nightmares if they had a nightmare disorder diagnosis or a PTSD diagnosis and also had been prescribed prazosin (Bishop et al., 2019), a commonly used medication for the treatment of posttraumatic nightmares (Taylor et al., 2008). This operational definition likely omitted a number of other patients who experienced nightmares and, thus, supports future studies that incorporate patient reports rather than relying solely on diagnoses documented in medical records.

To date, research has focused on the role of subjective sleep reports (e.g., sleep quality; Tae et al., 2019) and common sleep disorders (Bishop et al., 2018; Timkova et al., 2018) on increased suicidal ideation, but has largely neglected consideration of objective measures of sleep. Additionally, much of the extant research has been conducted in civilian samples and, thus, requires replication in military samples to increase the generalizability of results. The present study, therefore, aims to examine the association of various sleep indices, both subjective and objective, in relation to suicidal

ideation among active duty military personnel in order to provide empirically-informed recommendations for clinical practice.

METHOD

Participants

Patients included in the present study were active duty service members enrolled in a 4-week interdisciplinary intensive outpatient program (IOP) at the National Intrepid Center of Excellence (NICoE), Walter Reed National Military Medical Center (WRNMMC), Bethesda, Maryland, for treatment of unresolved persisting neurobehavioral symptoms related to traumatic brain injury (e.g., cognitive, pain, or sleep problems) and co-morbid psychological health problems. Service members from all branches of the military including the National Guard were eligible for referral to the program by a provider at their duty station. Inclusion criteria for the 4-week IOP included being active duty, sustained exposure to forces or event that provisionally resulted in a TBI, available to attend the 4-week care program in-person, able to participate in a structured discharge plan upon return to their duty station, not pose a risk to self or others, not be at risk of alcohol or narcotic withdrawal, not require monitoring or nursing care beyond what can be provided in an outpatient facility, and not have any legal issues pending. If prior psychiatric or inpatient care for substance use had been previously required, treatment must have been completed at least 30 days before their referral to NICoE. Please see DeGraba et al. (2021) for a description of the methods and outcomes of the IOP treatment program.

All patients included in the study were enrolled in the program between October 2010 and March 2020. Service members engaged in a standardized assessment from providers in up to 17 co-located disciplines to develop a comprehensive initial characterization of each patient's clinical neurological and behavioral health status at the start of the program. Patients had an average age of 38.01 years, were approximately 98% male, and approximately 77% white (see Table 1 for complete demographic breakdown). In regards to military characteristics, approximately 80% were enlisted, 49% were United States Navy or Coast Guard, and 56% were special operators. There was one patient who was a member of the Coast Guard and one patient who was a cadet. To prevent patient identification, these patients were collapsed into the Navy branch and officer rank, respectively.

Procedures

All service members signed informed consent through IRB-approved protocols at WRNMMC that allowed for standard of care clinical data to be prospectively collected and available for retrospective analysis. Demographic data were collected from intake questionnaires, and baseline behavioral health assessments on the first day of admission included self-report scales of PTSD Checklist Military Version (PCL-M), Generalized Anxiety Disorder-7 (GAD-7), and the Patient Health Questionnaire (PHQ-9) for posttraumatic stress, anxiety, and depression, respectively. Behavioral health diagnoses were confirmed through in-depth in-person evaluation by the team's psychiatrist. Further, in the first week of the program, all service members underwent a comprehensive consultation by a sleep neurologist, which included a thorough sleep history, polysomnography, and a five-day actigraphy recording to characterize any sleep

disturbance. In all, over 105 patient-provider encounters occurred in the evaluation and treatment of the patients in the 4-week IOP including blood work, neuroimaging, electrophysiological and physiological assessments, and vision and hearing assessments. All information is captured and stored in "The National Intrepid Center of Excellence (NICoE) Clinical Research Database to Study the Natural History of Traumatic Brain Injury and Psychological Health Outcomes in Military Personnel" protocol, from which the present data were obtained.

The present study was conducted at NICoE in accordance with all Department of Defense; Departments of the Army, Navy, and Air Force; and federal laws, regulations, and standards after review and approval by the Institutional Review Board at Walter Reed National Military Medical Center, Bethesda, Maryland. All data for analysis were de-identified and analyzed in batch to assure patient confidentiality.

Measures

Polysomnography

Polysomnography continually records neurophysiologic, cardiopulmonary, and other physiological measures typically over an entire night to identify abnormalities of sleep, wakefulness, sleep-wake transition, and organ functioning during sleep such as apneas (Jafari & Mohsenin, 2010). These readings produce measures of time spent in sleep stages, sleep latency, respiratory functioning, and heart rate, among others, and were used as measures of objective sleep functioning in the present study.

Pittsburgh Sleep Quality Index (PSQI)

The PSQI comprehensively examines sleep over a one-month period (Buysse et al., 1989). This 10-item self-report measure evaluates self-reported sleep efficiency and sleep quality. The PSQI is made up of seven components that are combined into a global score of sleep quality, with higher scores indicating lower sleep quality. This measure demonstrates good psychometric properties (Backhaus et al., 2002). Additionally, the PSQI assesses frequency of problems sleeping caused by bad dreams, which was used in the present study as a measure of idiopathic bad dreams and nightmares.

Epworth Sleepiness Scale

The Epworth Sleepiness Scale is an eight-item self-report questionnaire designed to measure a patient's general daytime sleepiness (Johns, 1991). Items assess how likely the patient is to fall asleep in a number of contexts including sitting and talking to someone or as a passenger in a vehicle. This scale has demonstrated a high-level of reliability (Johns, 1992).

PTSD Checklist-Military (PCL-M)

This 17-item self-report assessment is a common measure of PTSD symptoms and has demonstrated adequate psychometric properties (Weathers et al., 1993a). The military version of the PCL assesses PTSD symptoms specifically related to a military experience. For the present study, posttraumatic bad dreams and nightmares were measured using item two of the PCL-M ("Repeated, disturbing dreams of a stressful

experience from the past;" (Weathers et al., 1993a). This approach is consistent with previous studies (e.g., Greenbaum et al., 2017; Pigeon et al., 2013).

Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 (Kroenke & Spitzer, 2002) is a nine-item depression measure that has been found to have excellent reliability and strong validity (Kroenke et al., 2001). Item nine (i.e. "thoughts that you would be better off dead or of hurting yourself in some way") of the PHQ-9 was used as a binary measure of suicidal ideation (Kroenke & Spitzer, 2002, p. 6). This use is consistent with past literature and has been found to be related to increased suicide risk in veterans (Louzon et al., 2016).

Data Analysis

All analyses were conducted using IBM SPSS 25.0. T-tests or appropriate non-parametric tests were used to compare demographics of patients with and without suicidal ideation. Odds of suicidal ideation were obtained via logistic regression. To assess the relationship of traumatic bad dreams to suicidal ideation, the lowest item rating on the PCL-M ("Not during the past month") was used as the referent group; each of the other levels of response to this item was compared to this response. For traumatic bad dreams, patients who reported being "not at all" bothered by bad dreams related to their traumatic event were the referent group. Analyses of bad dreams or nightmares controlled for the use of prazosin, an alpha-1 receptor antagonist associated with improvement of posttraumatic nightmares (George et al., 2016). Complete data were not available for all patients due to the nature of the clinical database, which precluded running analyses to control for all relevant covariates. Therefore, analyses were conducted on individual

items to preserve power and prevent overmatching and multicollinearity. Furthermore, this approach allowed individual symptoms to be analyzed in an effort to understand the role of each sleep symptom within the context of the many other factors that may contribute to suicidal ideation in service members.

RESULTS

Among the objective measures of sleep examined, two were significant at $p < .05$ (Table 2). REM latency was associated with increased odds of suicidal ideation (OR = 1.00, 95% CI: 1.00, 1.01). Time in Stage N2 Sleep was related to decreased odds of suicidal ideation (OR = 0.98, 95% CI: 0.96, 1.00). Nonsignificant objective measures are described in Table 2. The association of subjective sleep measures to suicidal ideation also was examined with all showing a significant association to suicidal ideation. For every one unit increase in sleep quality (PSQI), the odds of suicidal ideation increase by 1.17 (95% CI: 1.06, 1.29). The odds of suicidal ideation increased by 1.05 (95% CI: 1.01. 1.09) for every unit of increase in sleepiness (ESS).

Patients who reported bad dreams "once or twice per week" on the PSQI had increased odds of 4.39 (95% CI: 2.23, 8.65) for suicidal ideation compared to patients who did not report bad dreams in the last month. For patients reporting bad dreams "three or more times per week," odds of suicidal ideation increased by 7.89 (95% CI: 4.04, 15.40) compared to the referent group. By comparison patients reporting bad dreams "less than once a week" were no more likely to report suicidal ideation that were those in the referent group (OR = 1.98, 95% CI: 0.93, 4.21). The use of prazosin was controlled for in all of these analyses.

Patients who reported being “moderately bothered” by traumatic bad dreams had an increased odds of 4.20 (95% CI: 2.19, 8.04) compared to the referent group. Patients who reported being bothered “quite a bit” by traumatic bad dreams had an increased odds of suicidal ideation compared to patients who were “not at all” bothered by bad dreams of their trauma (OR = 5.04, 95% CI: 2.62, 9.67). For patients reporting being “extremely bothered” by traumatic bad dreams, the odds of suicidal ideation increased by 9.90 (95% CI: 4.71, 20.83) compared to the referent group. However, patients who reported being bothered by bad dreams or nightmares of their traumatic event “a little bit” did not differ significantly from the referent group (OR = 1.49, 95% CI: 0.76, 2.95). Again, each analysis controlled for the use of prazosin.

DISCUSSION

The present results add to the nascent body of research examining objectively measured sleep quality as it relates to suicidal ideation (Bernert, Hom, et al., 2017; Bernert, Luckenbaugh, et al., 2017; Gupta & Jarosz, 2018). To our knowledge, this was the first study to find REM latency and time spent in Stage N2 to be significantly related to suicidal ideation. However, these relations were small suggesting these factors do not play a meaningful role in suicidal ideation. Further, there was no evidence of a relationship between objectively measured sleep indices previous identified as suicide correlates in the literature. Variables including respiratory disturbance index, apnea-hypopnea index, oxygen desaturation index, wake after sleep onset, time spent in Stage 4 sleep, and sleep efficiency did not significantly differ between patients with and without suicidal ideation. Further, although Bishop et al. (2019) identified a relationship between sleep-related breathing disorders, including OSA, and suicide attempts, the apnea-

hypopnea index, a measure of OSA severity (Caples et al., 2005) used in the present study, was not significant. Notably, patients in the NICoE IOP have reported anecdotally that they sleep better during their sleep studies than on a typical night in their own bed. Therefore, it is possible that results obtained during the polysomnography may not accurately reflect an average night's sleep.

Consistent with the extant literature (e.g., Bernert et al., 2014; Tae et al., 2019), all subjective sleep reports in the present study were significantly associated with suicidal ideation. These measures also were the only ones to produce meaningful odds ratios. Additional research is needed to better understand their possible role in suicidal ideation.

Bad dreams or nightmares, and specifically posttraumatic bad dreams and nightmares, were associated with large increases in odds of suicidal ideation. This may be explained in part by emotion regulation, as Ward-Ciesielski and colleagues (2018) found emotion regulation mediated the relationship of nightmares to both suicide risk and suicide attempts. However, these results were demonstrated in a sample recruited from Amazon's Mechanical Turk (MTurk), an online crowdsourcing website, and may not be generalizable to treatment-seeking or military samples such as in the present study. Self-reported sleep quality also showed increased odds of suicidal ideation. This may be explained by thwarted belongingness, or feelings of social disconnect, which has been found to mediate the relationship of insomnia symptoms to suicidal ideation (Chu et al., 2017).

This study was strengthened by the use of a large dataset of patients with diverse military characteristics. However, demographic characteristics, such as race and gender, as well as the treatment-seeking characteristics of the sample were rather homogenous.

Therefore, these results may not be generalizable to all patients and require replication in additional samples. The use of clinical data provides an understanding of these important relationships in a naturalistic setting and are more applicable to patients seeking care. However, the use of clinical data resulted in some variables not being available for all patients, as some measures were changed or updated over the course of nearly ten years of data collection. Thus, due to differences in available data, as well as issues with multicollinearity, the present study was unable to conduct analyses that controlled for possible covariates such as comorbid symptoms.

To our knowledge, this is the first study to examine objective measures of sleep in relation to suicidal ideation in active duty service members. The present study also replicated and expanded previous findings regarding the role of subjective sleep reports found in non-military samples (e.g., Bernert, Hom, et al., 2017; Gupta & Jarosz, 2018; Tae et al., 2019; Zuromski et al., 2017). The replication of these earlier findings strengthens the confidence in results of the present study. Future studies should examine the temporal relationship of nightmares and suicidal thoughts utilizing longitudinal or ecological momentary assessment methods.

Clinical Implications and Conclusion

These results also highlight the importance of the *subjective* view of sleep. A sleep study or period of monitoring via actigraphy may not be necessary to understand the impact of poor sleep on suicidal ideation; rather, it is the patient's subjective experience that appears critical to the evaluation of suicidal risk. Notably, in the present study bad dreams or nightmares, both idiopathic and traumatic, were related to a substantial increase in odds of suicidal ideation, suggesting these factors may be an

important inclusion for a comprehensive risk assessment. These results also may provide a secondary avenue for reduction of suicidal risk through sleep targeted treatments. The Departments of Defense and VA recommend Brief Behavioral Therapy for Insomnia (BBTI) and strongly recommend Cognitive Behavioral Therapy for Insomnia (CBT-I) for treatment and management of insomnia (Veterans Health Administration and Department of Defense, 2019). Additionally, they suggest the use of *short-term* pharmacotherapy. Incorporating sleep treatments in conjunction with treatment for suicidal ideation may aid in further reducing suicidal risk.

The impact of military factors on sleep should be considered when working to improve sleep for these patients in order to mitigate suicidal risk, particularly military-specific environmental and occupational ones. These can include, but are not limited to, characteristics related to sleeping in barracks or sleeping in a deployed environment where sleep is frequently disturbed, impacted by the warzone, and affected by missing a familiar bed partner. Shift work and working in environments that may negatively affect sleep, such as being stationed on a submarine, ship, or as part of an air crew, should be considered and may require tailored interventions.

In conclusion, subjective reports of sleep disturbances were found to be associated with increased odds of suicidal ideation and may provide a critical area for therapeutic intervention for patients with suicidal ideation. As suicide is a current public health crisis facing the U.S. military and nation as a whole, it is important that providers consider all possible avenues to mitigate suicidal risk. Therefore, as an adjunct to a provider's standard procedures when conducting a risk assessment, providers should evaluate subjective sleep symptoms, particularly bad dreams and nightmares, in combination with

comorbid conditions. In addition to being a provisionally important indicator for suicidal ideation, subjective sleep assessments also may serve as markers for efficacy of treatment. Clinic leaders and administrators may consider requiring regular screening for sleep disturbances and their inclusion in all suicide risk assessments. Though requiring replication, the present results suggest bad dreams and nightmares, particularly trauma-related ones, hold promise as a possible point of intervention to help reduce suicidal ideation in active duty service members.

Chapter 5: Conclusion

Summary of Studies

The present project serves as an initial foray into the testing and refinement of a comprehensive model of chronic posttraumatic nightmares. The proposed model hypothesizes posttraumatic nightmares and sleep are important considerations in the development of chronic PTSD, and thus are an important area of focus. Further, the model emphasizes the importance of considering the deleterious effects of posttraumatic nightmares, beyond their role in chronic PTSD, including their effect on suicidal ideation. We propose this model will be useful in understanding the mechanisms of posttraumatic nightmares and in improving patient outcomes and decreasing suffering, thereby increasing military readiness.

Study One

As hypothesized in the model, mental health symptoms including PTSD, anxiety, and depression were related to a greater likelihood of posttraumatic nightmares. Additionally, study 1 provided support for the role of sleep disturbances in increasing the likelihood of posttraumatic nightmares. Notably, these sleep disturbances (i.e., problems falling asleep, problems staying asleep, and pain that disrupted sleep) were related to substantial increases in odds of posttraumatic nightmares in contrast to the comparatively small increases found for PTSS, anxiety, and depression (odds ratios were less than or equal to 1.15 for mental health symptoms). Neurobehavioral symptoms were related to decreased odds of PTSS but increased odds of symptoms of anxiety and depression; however, these odds ratios were quite small and suggest they are of less clinical

significance than sleep disturbances. In contrast, patients who were special operators were substantially less likely to endorse posttraumatic nightmares. Consideration of military factors, such as special operators, will be discussed below.

Study Two

The second study sought to evaluate the AMPHAC model of disturbing dreams proposed by Levin and Nielsen (2007, 2009; Nielsen & Levin, 2007). To our knowledge, this is the first study to examine volumetric or cortical thickness in patients with posttraumatic nightmares. Thus, these results suggest the regional volume of the bilateral amygdala, medial prefrontal cortex, hippocampus, anterior cingulate cortex, and insular cortex are *not* associated with the presence of posttraumatic nightmares in male active duty service members. The present findings also are inconsistent with previous literature suggesting a relationship between PTSD and the amygdala, medial prefrontal cortex, hippocampus, anterior cingulate cortex, and insular cortex (e.g., Logue et al., 2018; Morey et al., 2019; O'Doherty et al., 2017; Wang et al., 2020; Young et al., 2018). We propose three reasons for these differences. First, Morey and colleagues (2019) found the relationship between PTSD diagnosis and hippocampal volume was stronger in females compared to males. As study two only included males, these sex differences may offer some explanation for these null findings. Further, it is suggested that the problem of inadequate power in neuroimaging studies has led to an overestimation of effect sizes and may account for the large variability in replication efforts (Button et al., 2013; Cremers et al., 2017). Indeed, Button and colleagues (2013) estimate a median of 8% to 31% power in the neuroscience literature. These results did not find support for the AMPHAC model of disturbing dreams despite a large sample size that provided sufficient power to detect

small effect sizes ($f^2 \leq .03$ at $a = .05$ and 80% power). Finally, in contrast to many previous studies (e.g., Logue et al., 2018; Morey et al., 2019; O'Doherty et al., 2017; Wang et al., 2020; Young et al., 2018), the present analyses controlled for history of mTBI. We hypothesize this statistical adjustment may in part explain the current findings. Importantly, one review of the pathophysiology of TBI and PTSD concluded that neurologically this comorbidity has a "unique signature" (Kaplan et al., 2017, p. 213), and TBI is, therefore, an important consideration when examining neurologic differences in patients with a trauma history.

Study Three

Finally, the third study provides support for the importance of furthering our understanding of posttraumatic nightmares. There is a general consensus that sleep disturbances may play an important role in understanding suicide; however, the field is not in agreement on what sleep disturbances increase suicidal behaviors and to what degree they are important. This study provides support for the general understanding of the relationship between sleep and suicidal ideation. Most important to the current project, posttraumatic nightmares were associated with a nearly 10 times increase in odds of suicidal ideation for patients with significant posttraumatic nightmares, revealing an important area for clinical concern and a promising area for future research to elucidate whether treatment of PTN also could help mitigate suicidal ideation. Additionally, posttraumatic nightmares were associated with a greater likelihood of suicidal ideation than idiopathic bad dreams (OR = 9.90 and 7.89, respectively) providing support for the importance of considering posttraumatic nightmares individually rather than as a single

disturbing dreams construct, as discussed previously (see "Defining the Phenomena of Posttraumatic Nightmares" above).

Integrating the Findings

Sleep disturbances serve a central role in the proposed model of posttraumatic nightmares. Many service members experience chronic symptoms of insomnia upon return from deployment (Bramoweth & Germain, 2013), and these sleep disturbances may serve as an important target for intervention for posttraumatic nightmares. We assert that it is the disruption of sleep, in particular REM sleep, that interferes with fear learning and memory consolidation processing, ultimately increasing the likelihood for chronic posttraumatic nightmare onset and sustainment. This assertion is supported by findings that sleep disturbances, including REM disturbances, prevent the processing of emotional events thereby increasing the risks for the development of mental health symptoms (Koffel et al., 2013; Van Der Helm et al., 2011). Additionally, researchers have found that sleep disturbances mediate the relationship between combat stressors and the development of mental health disorders (e.g., Picchioni et al., 2010), and that REM disturbances, specifically, are positively associated with PTSD (e.g., Habukawa et al., 2007; Kobayashi et al., 2012; Mellman et al., 2002). Taken together, these findings provide support for the theory that sleep disturbances may interfere with the normal resolution of symptoms after a traumatic event. Findings from study 1 are in general alignment with this theory. Specifically, we assert that sleep disturbances such as problems falling asleep, problems staying asleep, and pain that disrupts sleep, play important roles in the initiation and maintenance of posttraumatic nightmares.

Study two did not find support for our hypothesis that posttraumatic nightmares would be associated with structural differences in the amygdala, hippocampus, medial prefrontal cortex, and anterior cingulate cortex as theorized by Levin and Nielsen (2007, 2009; Nielsen & Levin, 2007) or the insular cortex, left and right lateral orbitofrontal gyri, left superior temporal gyrus, and lingual and superior parietal gyri as identified by Wang et al. (2020). Although the present analyses do not support structural associations of these regions to posttraumatic nightmares, we hypothesize there may be functional differences in the activity of the individual regions, as well as how the regions communicate with each other, during waking and sleep due to distinct associations of functional and structural neurophysiology (e.g., Owens et al., 2018).

Research supports the affect load theory posited by Levin and Nielsen (2009). Levin and Nielsen (2009) suggest the propensity for disturbing dreams is increased by affect load, which is the cumulation of the stressful and negative experiences that disrupt emotion regulation. Further, sleep disturbances (e.g., problems falling asleep or staying asleep) also may be responsible for disrupted emotion regulation (Harvey et al., 2011; Leerssen et al., 2020; Mellman, 2006) and are thought to interfere with one's ability to manage their emotions and endure suffering (Cukrowicz et al., 2006). Importantly, study one identified sleep disturbances, including pain that disrupts sleep, problems falling asleep, and early awakenings, were related to increased likelihood of posttraumatic nightmares. Ward-Ciesielski and colleagues' (2018) finding that emotion regulation mediates the relationship between nightmares and suicide risk and attempts aligns with this theory.

Emotion dysregulation has been identified in connection to hypoactivity of the ventromedial prefrontal cortex (Etkin & Wager, 2007). Thus, hypoactivity of the ventromedial prefrontal cortex, in particular, may increase the propensity for posttraumatic nightmares through a failure of adequate emotion regulation. A review by Fitzgerald and colleagues (2018) suggested this emotion dysregulation is the result of dysfunction of the neurocircuitry involving the amygdala, insula, hippocampus, anterior cingulate cortex, and prefrontal cortex. They suggest it is the amygdala and insula's response to emotional stimuli as well as abnormal anterior cingulate and prefrontal cortices leading to inadequate appraisal, resolution, and management of these emotional stimuli that results in the emotional dysregulation observed in patients with PTSD (Fitzgerald et al., 2018). Notably, cooccurring sleep disturbances, such as insomnia, may further disrupt emotion regulation in patients (Leerssen et al., 2020) thus necessitating consideration of their compounding effect on emotion regulation in patients with posttraumatic nightmares and the possible implications for understanding suicidal risk.

As discussed in study three, the significant relationship of posttraumatic nightmares to suicidal ideation may be in part explained by thwarted belongingness (Chu et al., 2017). Indeed, thwarted belongingness mediates the relationship between insomnia symptoms and suicidal ideation (Chu et al., 2017). As discussed previously, social support can increase one's perceived belongingness, which is associated with lower levels of overall and reexperiencing symptoms of PTSD (Stanley et al., 2019). By increasing social support and feelings of belongingness, patients may experience reduction in the frequency of posttraumatic nightmares and decreased suicidal ideation.

The hypothesized biopsychosocial model proposes symptoms of moral injury, and in particular guilt, may be partially responsible for chronic posttraumatic nightmares. This hypothesis is supported by Dedert and colleagues' (2019) finding that perceived wrongdoing, a component of moral injury, completely mediates the relationship between combat exposure and posttraumatic nightmares. Notably, guilt is related to increased suicidal ideation, and this relationship is strongest in service members with combat exposure compared to those without (Bryan et al., 2013). Social support and guilt, which are proposed socio-interpersonal aspects of the model of chronic posttraumatic nightmares, and emotion regulation may be relevant to our understanding of the relationship of posttraumatic nightmares and suicidal ideation.

Support for the Proposed Model

The present studies provide preliminary support for the proposed model. Study one supported the importance of consideration of patient factors (i.e., special operator status) as well as disturbed sleep and mental health symptoms (i.e., PTSD, anxiety, and depression) in increasing the likelihood of posttraumatic nightmares. Study two did not find support for a biological basis of posttraumatic nightmares. This study examined structural neural components, necessitating future study of functional differences in these regions. Additionally, other biological factors may exist including hormonal influences and biological sleep such as REM. Finally, study three details the importance of increasing our understanding of posttraumatic nightmares due to its strong relationship to suicidal ideation. Study three also lends support for the need to distinguish between idiopathic and posttraumatic bad dreams and nightmares, as these were differentially related to suicidal ideation. Figure 12 highlights the supported aspects of the model.

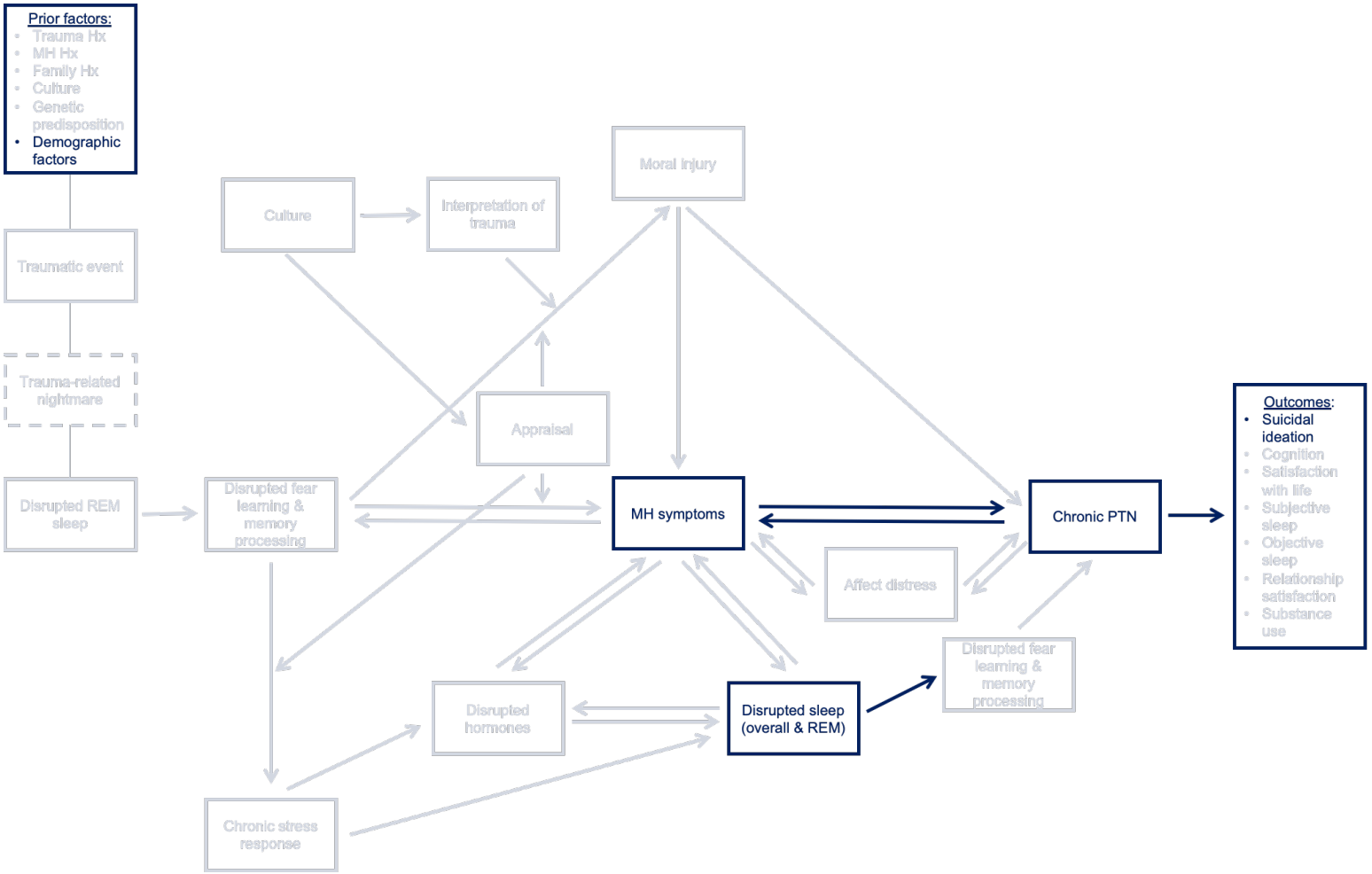

Figure 12. Significant relationships within the model

STRENGTHS AND LIMITATIONS

The present project has a number of strengths. First, this project builds on the extant literature to develop a comprehensive approach to posttraumatic nightmares. Specifically, the proposed model distinguishes itself from previous models (i.e., Levin & Nielsen, 2007, 2009; Nielsen & Levin, 2007; Phelps et al., 2008) through a targeted focus on posttraumatic nightmares, consideration of the interaction of factors, and utilization of a biopsychosocial approach to the understanding of posttraumatic nightmares. Posttraumatic nightmares are a significant problem for patients with PTSD. As stated above, some estimates suggest 90% of patients with PTSD experience posttraumatic nightmares (Creamer et al., 2018), and this symptom can continue for decades after the traumatic event (Guerrero & Crocq, 1994) causing significant distress and deleterious effects for the patient (e.g., Kung et al., 2012; Lamis et al., 2018). This model addresses a significant dearth in the conceptualization and understanding of posttraumatic nightmares and may eventually inform a new or modified approach to the treatment of posttraumatic nightmares.

The present project also begins testing the hypothesized relationships described in the proposed model through a series of three studies. The studies are strengthened by the use of a large dataset with diverse military characteristics. However, the sample is fairly homogenous in regards to patient demographics including sex and race. The use of the NICoE data provides important insight into a clinical population, specifically treatment-seeking service members. However, the use of clinical data provides methodological challenges including changes in measures over time, missing data, and the inability to change the methodology (discussed below). The present project contributes to the

growing need to address the significant dearth of literature examining the mechanisms of posttraumatic nightmares and begins interrogating a novel model of posttraumatic nightmares. Although the model was developed to be applicable to all patients, the nature of the present data may limit generalizability of the findings and requires replication in additional samples.

As noted above, the present studies utilized previously collected data, which have certain innate methodological challenges. If the data were prospectively collected with the current hypotheses in mind, study procedures would have included sampling of additional populations. This would ideally include non-treatment seeking service members, veterans, and civilians. Additionally, a longitudinal or ecological momentary assessment approach would be useful to examine the temporal and cyclical aspects depicted in the model.

Finally, prospective collection of data would include additional measures and assessment of time since trauma and duration of symptoms. In particular, inclusion of nightmare specific measures would strengthen the present analyses. Notably, the present study measures posttraumatic *nightmares* using Item 2 of the PCL, which asks "Repeated, disturbing *dreams* of a stressful military experience" on the PCL-M and "Repeated, disturbing *dreams* of a stressful experience from the past?" on the PCL-C (emphasis theirs; Weathers et al., 1993a). As noted previously, nightmares and bad dreams are discrete phenomena distinguished by awakening from a nightmare. Although the present data precluded consideration of nightmares versus bad dreams, our confidence in the use of the present item is supported by previous literature in which this item and a similar item from the CAPS are used to characterize posttraumatic nightmares (e.g., Don

Richardson et al., 2014; Don Richardson et al., 2018; Littlewood et al., 2016). Although it is important to consider the differences between bad dreams and nightmares in research and clinical work, we posit it is unlikely patients would be knowledgeable of the differences between the two. Indeed, patients have difficulty distinguishing between the various terms for nightmares and bad dreams (Krakow, 2006), and even medical providers are largely unfamiliar with the distinction between bad dreams and nightmares (Youngren et al., 2019). A discussion of common nightmare and/or dream measures is included in the "Future Directions" section below, and a discussion of considerations for assessing nightmares is included in the "Military Considerations" section below. The addition of clinician administered measures for PTSD, depression, anxiety, and sleep disturbances would increase confidence in the findings, as self-report measures can be biased or inaccurate. Finally, a multi-faceted measure of quality of life, such as the World Health Organization Quality of Life-BREF (WHOQOL Group, 1998), would offer a comprehensive view of the effect of posttraumatic nightmares in a patient's health-related, physical, psychological, social, environmental, and overall quality of life.

IMPLICATIONS AND MILITARY CONSIDERATIONS

Implications for Acute Trauma-Related Nightmares and Chronic Posttraumatic Nightmares

The proposed project may contribute to improved strategies both for the prevention and treatment of posttraumatic nightmares. Inherent in the proposed model is the assumption that there are distinct differences between acute trauma-related nightmares and chronic posttraumatic nightmares. As discussed previously, nightmares in

the acute phase after a traumatic event may serve a protective function (e.g., as cited in Germain, 2013; Miller et al., 2017); however, chronic posttraumatic nightmares are of clinical concern and both effect and are affected by a myriad of factors, including biological, psychological, and social factors. Although it is possible that these nightmares are qualitatively and biologically identical, we propose there are indeed differences. Namely, we propose differences related to a prolonged stress response, continued sleep disruptions, and chronic psychological distress related to chronic posttraumatic nightmares distinguish acute trauma-related nightmares from chronic posttraumatic nightmares. It is important to consider distinct implications for intervention strategies in patients with acute trauma-related nightmares and chronic posttraumatic nightmares.

Acute Trauma-Related Nightmares

Notably, service members who report sleep disruptions during deployment are at a significant risk for having comorbid PTSD, generalized anxiety disorder, or depression both during deployment (Taylor et al., 2014) and after deployment (Luxton et al., 2011). However, sleep disturbances also develop after a traumatic experience and occur more frequently in patients developing PTSD (Mellman, 2006) and predict the development and severity of PTSD (Wright et al., 2011). We propose sleep, and in particular REM sleep, is a protective factor against the detrimental effects of trauma. Further examination of REM sleep as prevention for negative outcomes, including PTSD and PTN, could increase military readiness.

Although ensuring adequate sleep may be protective against the deleterious effects following a traumatic event, ensuring proper sleep could be difficult for service members during deployment. The deployment experience causes significant disturbance

to sleep (Bramoweth & Germain, 2013). For some, these sleep disturbances may be related to a traumatic experience, but for others this may be related to other factors such as operations tempo, environmental factors, stressors at home, and combat zone-related factors, among others. Service members must adapt to different physical (e.g., different bed and pillow, combat zone) and social sleep environments (e.g., lack of bed partner, sharing space with others) than the ones they are accustomed to while at home. These factors have an additive effect and exacerbate the detrimental effects of common deployment sleep experiences (e.g., shift work, inconsistent sleep schedules). In a study of deployed Airmen, Peterson and colleagues (2008) reported 74% of service members had significantly worse sleep quality while deployed. Less than half of these service members reported a sleep efficiency of 85% or needing less than thirty minutes to fall asleep (40% and 42%, respectively). Similarly, 72% of Soldiers and Sailors who recently returned from deployment reported sleeping six or less hours during deployment, and combat exposure was related to less sleep (Luxton et al., 2011). Deployed Sailors reported an average of 5.9 hours of sleep, with 56% meeting criteria for sleep deficiency and two-thirds receiving less than six hours of sleep on average (Taylor et al., 2014). Thus, changes in policy will likely be necessary to provide service members with an opportunity for sleep-related recovery after a traumatic experience.

Chronic Posttraumatic Nightmares

Importantly, many medical providers lack an understanding of nightmares. Youngren and colleagues (2019) found 70% of providers did not have professional experience working with nightmares, 78% were unable to accurately define nightmares,

and 75% viewed nightmares as a secondary problem. However, 72% of these providers would consider psychological treatment for idiopathic or posttraumatic nightmares.

Patients rarely report nightmares to healthcare providers. Nadorff et al. (2015) found only approximately 11% to 38% of patients with clinically significant nightmare symptoms report them to their provider, and approximately 67% believe them to be untreatable. Although patients with more severe nightmares were more likely to report their nightmares to a provider, they also were less likely to believe they were treatable (Nadorff et al., 2015). In a study of veterans receiving care through the VA, only 12.3% of residential patients receiving treatment for PTSD listed nightmares as a goal for treatment (Rosen et al., 2013). These patients also did not believe treatment would improve posttraumatic nightmares or sleep problems more generally (Rosen et al., 2013), which may have impacted their perception of it as a treatment goal. In active duty service members referred for a sleep evaluation, approximately 31% of patients had clinically significant nightmares; however, only approximately 4% were seeking evaluation for nightmare-related concerns (Creamer et al., 2018). The authors postulated this underreporting may be due to stigma or a perception that nightmares after a traumatic experience are expected or normal. Thus, provider barriers (e.g., erroneous understanding of nightmares and beliefs that nightmares are secondary problems) and patient barriers (e.g., reticence to report symptoms, stigma, and beliefs nightmares are untreatable) exist in providing patients with appropriate care. Increasing provider understanding of nightmares and their treatment may be an important first step in increasing treatment for this common symptom (i.e., 90%; Creamer et al., 2018). Additional steps should include

screening for nightmares and providing subsequent psychoeducation on treatment options to patients who screen positive.

Treating Chronic Posttraumatic Nightmares

Presently, both pharmacological and psychological treatments are often inadequate in resolving posttraumatic nightmares thus indicating a need for increased understanding into the mechanisms which initiate and perpetuate this symptom. The Departments of Veteran Affairs and Defense published clinical treatment guidelines for the treatment of PTSD (Veterans Health Administration and Department of Defense, 2017), which recommend psychological treatments, including Prolonged Exposure and Cognitive Processing Therapy, as first line treatment for PTSD. However, these evidence-based treatments for PTSD often result in refractory nightmare symptoms (e.g., Tripp et al., 2020) necessitating targeted treatments for posttraumatic nightmares. In a study of Imagery Rehearsal Therapy (IRT) in veterans, nightmares were not improved immediately following treatment, but improvements were seen at 3- and 6-month post-treatment (Lu et al., 2009). However, the authors note "significant limitations includ[ing] an uncontrolled design," thus it is unclear if these improvements were due to treatment-related or non-treatment-related factors (Lu et al., 2009, p. 239). It is suggested IRT may be more appropriate as adjunct to PTSD treatments rather than as a standalone therapy (Lu et al., 2009). Two randomized control trials of Exposure, Relaxation, and Rescripting Therapy (ERRT) have demonstrated improvements in nightmare severity and frequency that remained for 6-months post treatment (Davis et al., 2011; Davis & Wright, 2007). However, research on IRT and ERRT is limited decreasing generalizability of results and

confidence in the treatments. To our knowledge these treatments have not been compared.

At this time, only one pharmacological treatment has been implicated in the treatment of posttraumatic nightmares. A number of studies have found Prazosin, a hypertension medication, to be effective in treating posttraumatic nightmares (e.g., Kung et al., 2012; Raskind et al., 2002). However, a recent large-scale randomized control trial found no difference between Prazosin and the placebo-control condition (Raskind et al., 2018). In fact, there were no significant differences across any outcomes measured including PTSD, sleep, and clinician impression of change. This study included 13 Veteran Affairs treatment facilities and over three-hundred participants. Given the results of this study, Prazosin was downgraded to "neither recommend for or against" (Waltman et al., 2018). Thus, examination of the mechanisms related to the initiation and perpetuation of posttraumatic nightmares may provide critical insight to inform the development of better treatments.

Treatment often is considered successful if a patient reports decreased frequency and/or severity, such as in a meta-analysis by Casement and Swanson (2012) that used nightmare frequency, sleep quality, and PTSD severity as indicators of treatment success. However, we assert that rather than using frequency and severity as the primary outcome, the patient's experience should be the primary outcome measure. Phrased differently, the perceived improvement or lack thereof in regards to the impact of their posttraumatic nightmares in their daily lives should be the primary measure of treatment success. If a patient reports having fewer nightmares but still reports continued detriment to their psychological, physical, social, or occupational quality of life, has treatment truly been a

success? Quality of life has been proposed as the definitive measure of treatment outcome for other mental health disorders. For example, IsHak and colleagues (2011) stated quality of life should be the measure of treatment success for patients with major depressive disorder. Thus, treatment outcome assessment should include consideration of quality of life and the perceived effect of the posttraumatic nightmare in their life.

CULTURAL CONSIDERATIONS

As discussed previously, culture is an important component to understanding the appraisal and interpretation of the traumatic event and the nightmare. Many cultures find significant meaning and use in dreams including as new sources of knowledge (Lohmann, 2000), and in some cultures, dreams are in part responsible for the formation of one's sense of identity (Laughlin & Rock, 2014). These cultures emphasize the belief that dream content can provide knowledge that shapes the society's views about the self and the world. Dream interpretations vary across cultures (Lohmann, 2000) and require specific consideration (see "Level 3: Distant Social Contexts" above).

Religion, sex, age, and racial/ethnic backgrounds can influence one's perspective on mental health and stigma. Religious organizations may promote stigma towards mental health through actions towards members with mental health problems (e.g., counseling, sanctioning, or "disfellowship") and may "encourage" them to seek spiritual care instead of formal mental health treatment (Peteet, 2019). Peteet (2019) described one patient with posttraumatic nightmares who "was encouraged to think about her symptoms as demonic in origin and to tell negative thoughts to 'go back to the pit of hell'" (p. 846). In regards to age, adults over the age of 40 report fewer stigmatizing attitudes towards patients with generalized anxiety disorder and schizophrenia than those aged 16 to 18

(Bradbury, 2020). Additionally, females report fewer stigmatizing attitudes towards patients with generalized anxiety disorder than males (Bradbury, 2020).

Many cultures hold negative views towards mental health. In one study of mental health stigma in Egypt, people with mental health problems were viewed as a possible physical danger or otherwise harmful to others (Coker, 2005). In China, "intense level[s] of stigma" towards mental health problems exists, and mental illness is seen as reflecting poorly on the entire family, not just the individual (Hsin Yang & Pearson, 2002, p. 236). Families with children receiving mental health care in a Turkish rehabilitation center demonstrated family shame, and fathers often blamed the mother for the mental illness (as cited in Ciftci et al., 2013). In Pakistani families living in the United Kingdom, participants were unwilling to marry a person with mental illness while many were unwilling to socialize or have a close relationship with someone with a mental illness (Tabassum et al., 2000). Finally, Muslim communities demonstrate elevated social stigma and shame, which may decrease treatment seeking (Ciftci et al., 2013).

In the United States, Black/African American older adults report worse attitudes to mental health treatment and greater public and internal stigma compared to White older adults, and this internalized stigma may partially explain the relationship between race and attitudes regarding mental health treatment (Conner et al., 2009). Conversely, in a more recent study, Black/African American adults did not significantly differ from White adults on any measures of stigma in a study of adults in California (Wong et al., 2017). Wong and colleagues (2017) also found Asian-American adults reported more self-stigma than White adults. Likewise, Latinx adults interviewed in English were more likely to endorse self-stigma and a likelihood of concealing mental health problems from

colleagues compared to White adults. However, Latinx adults interviewed in Spanish were more like to believe the public to be supportive of people with mental health problems and were the least likely to hide mental health problems from their colleagues compared to any group.

The way that one is raised and culturally influenced to interpret both dreams/nightmares and mental health more generally can affect one's appraisal of their mental health symptoms (e.g., posttraumatic nightmares). We propose appraisal is a moderator to the deleterious effects of a traumatic event and posttraumatic nightmares. Namely, positive appraisals, such as "nightmares are an opportunity for me to heal" or "nightmares are a sign that I am getting better," may decrease affect distress related to the trauma and nightmare experience, thereby decreasing the posttraumatic nightmare. Negative appraisals or avoidance, however, are likely to lead to continued posttraumatic nightmares. These appraisals also may be influenced by perceived stigma of nightmares due to their relationship to PTSD (Creamer et al., 2018). Consideration of a patient's culture is important to understanding their appraisal and may provide an opportunity for culturally-based interventions and reduction of stigma. Specifically, helping a patient to reframe the posttraumatic nightmare from a sign of weakness or "brokenness" to a sign of or opportunity for healing may provide symptom relief and decrease the stigma of posttraumatic nightmares. Acceptance and commitment therapy is proposed to aid patients in reconceptualizing both the stressor and their response to it (Butts & Gutierrez, 2018).

Military Culture

The military is a distinct culture requiring special consideration, and stigma regarding mental health symptoms is commonly experienced among service members in the United States. A meta-analysis of military stigma literature found the three most frequently endorsed statements were, in order, concerns about receiving different treatment from unit leadership, that they would be seen as weak, and their unit members would have less confidence in them (Sharp et al., 2015). Additionally, using weighted prevalence, approximately one-third endorsed concerns about career impact (Sharp et al., 2015). In a RAND study of Operation Iraqi Freedom and Operation Enduring Freedom service members, nearly 44% reported fears of career implications and ability to obtain a security clearance as factors that would make it difficult to get care for an emotional or personal problem (Schell & Marshall, 2008). Other reasons included concerns about their fellow service members having less confidence in them, thinking less of themselves if they were unable to address the problem on their own, belief treatment would not be confidential, and decreased respect from their commander. Nearly 8% reported their commander/supervisor had told them not to seek treatment.

Stigma surrounding mental health symptoms and nightmares may lead a patient to underreport or deny nightmares. For example, some patients may deny "nightmares" when asked but would respond in the affirmative to other descriptors such as "disturbing dreams," "distressing dreams," or "waking up from dreams that remind you of the event." It is important to remember terms such as nightmares can be stigmatizing and may require repeated query using different terms to accurately assess a patient's symptoms.

As previously discussed, military social support is distinct from civilian social support (Wilcox, 2010) and is related to fewer PTSD symptoms (Brailey et al., 2007; Han et al., 2014; Smith et al., 2013) and reduced likelihood of PTSD diagnosis (Pietrzak et al., 2010). Veterans with PTSD report fellow veterans are the largest portion of their social network and provide more instrumental support compared to relatives and more emotional support than any other source of support, including spouse, relatives and nonveteran friends (Laffaye et al., 2008). Relatedly, firefighters who report greater unit social support (i.e., coworkers and supervisors) and/or have a greater sense of perceived belonging to the group have fewer PTSD symptoms, generally, and reexperiencing symptoms, specifically (Stanley et al., 2019). Thus, when service members identify themselves as an integral part of the military system, they may be less likely to develop severe PTSD symptoms. Identity fusion may provide insight into the importance of military-related social support. Identity fusion refers to a deep sense of oneness between oneself and the group (Swann et al., 2014) and is associated with closeness and loyalty (Swann & Buhrmester, 2015). Service members often have a strong bond with one another (Fredman et al., 2015; Swann et al., 2014). In the US military, identity fusion was found to be associated with a willingness to fight and/or die for a fellow veteran (Hart & Lancaster, 2019).

At the NICoE, patients engage in a mask making experience as part of art therapy (e.g., Walker et al., 2016). Many patients depict an inability to express themselves through images, such as sealed, stitched, or locked lips (Walker et al., 2017). Additionally, many of the service members depicted themes related to patriotism and military identity and demonstrated a sense of camaraderie and community associated

with their military identity (Walker et al., 2017). Additional visual imagery incorporated into the mask suggests a feeling of disconnect to society/the country upon return from deployment. In a follow-up study, military identity imagery was associated with fewer PTSD, depression, anxiety symptoms; however, fragmented military symbols were positively associated with PTSD, depression, and anxiety symptoms (Kaimal et al., 2018).

Special Operators

The above factors may be particularly salient for military special operators. To frame this discussion, it is important to be mindful of the unique challenges and considerations faced by special operators.

> United States Army Special Operations Soldiers are exposed to intense dangers in far-forward, austere locations. They experience relentless operations tempo between one tour of duty and the next. They work in small teams and depend heavily on each other for their mutual survival. As such, it may be said that SOF Soldiers are the epitome of Soldiers exposed [to] stress and trauma, to the point that after eleven years of war, the continual presence of both has been normalized. This acclimatization requires continual recognizance of trauma's magnitude and after-effects (Hing et al., 2012, p. 23).

Due to the nature of their role, special operators may experience more traumatic events or concussive events than service members who are not special operators, which is an important consideration for understanding mental health trajectory.

Importantly, the military is considered a high-risk organization that is associated with both threatening and acute stressful situations (Delahaij & Van Dam, 2017), and

special operators are frequently exposed to these situations (Hing et al., 2012). Despite the deleterious effects of high stress on performance (Kavanagh, 2005), service members are expected to perform at high levels. One's perceived ability to cope in these stressful situations (i.e., coping self-efficacy), including both addressing the stressor and regulating their emotions, affects one's appraisal of the situation (Folkman et al., 1986). Service members with low coping self-efficacy are more likely to appraise the situation as threatening leading to fear and anxiety (Delahaij & Van Dam, 2017). Conversely, service members with high coping self-efficacy may interpret the stressor as a challenge and are more likely to respond effectively (Delahaij & Van Dam, 2017). These appraisals not only affect a service member's ability to respond to the current stressor but also partially explain the effect of stress on mental health (Gomes et al., 2016). According to Bandura's (2001) social cognitive theory, high coping self-efficacy is related to decreased stress vulnerability and depression in response to stressful situations as well as increased resiliency to hardship. Military trainings include a focus on stress and coping to increase service members' ability to effectively respond in acute stressful situations (e.g., Robson & Manacapilli, 2014). However, these trainings and the resulting effect on appraisal may be applicable to understanding the trajectory of posttraumatic nightmares as well. As noted previously, appraisal is a key component in the proposed model. We propose that military trainings may improve one's ability to respond to stress and increase the likelihood they positively appraise their ability to respond to the stressor (e.g., posttraumatic nightmare) resulting in better outcomes and a disruption of the posttraumatic nightmare cycle.

In study one, special operators had a substantial decrease in posttraumatic nightmares in all three models. We hypothesize that specific military training for special operators, innate factors such as personality or resiliency, or unit cohesion may be responsible for these differences. Military training may improve the autonomic balance that affects sympathetic and parasympathetic tone, which may be implicated in nightmares (Simor et al., 2014). Special operators receive extensive training, which may improve autonomic balance above that seen in the general military population. Clinical observations at the NICoE support this: cerebral vasomotor reactivity and parasympathetic tone is significantly different in service members who are special operators compared to service members who are not special operators. As previously discussed, military unit support (Brailey et al., 2007; Han et al., 2014; Smith et al., 2013) and perceived belongingness (Stanley et al., 2019) are related to decreased PTSD symptomatology. As seen in the clinical work at the NICoE, special operators have a very strong sense of unit cohesion, which may help to attenuate reactions to traumatic events. This is supported by work conducted on the NICoE's art therapy program: service members who represent attachment or affiliation with a unit or the country in their art work (i.e., masks), report less PTSD symptom severity (Kaimal et al., 2018) and respond better to PTSD therapy than those who do not have strong unit connection.

Conversely, special operators may be more likely to underreport symptoms. As noted above, stigma is a significant barrier to care for service members, and this may be amplified in special operators. This may be in part due to Department of Defense policy. Department of Defense Instruction (DoDI) 6490.08 states, "The DoD shall foster a culture of support in the provision of mental health care and voluntarily sought substance

abuse education to military personnel in order to dispel the stigma of seeking mental health care and/or substance misuse education services" (Office of the Under Secretary for Personnel and Readiness, 2011, p. 2). In service of this goal, the DoDI states a command notification is not required for service members self-referring or receiving a medical referral for mental health and substance treatment. However, it makes a specific exception for command notification by healthcare providers of any special personnel (defined as "The Service member is in the Personnel Reliability Program as described in DoD Instruction 5210.42 …, or is in a position that has been preidentified by Service regulation or the command as having mission responsibilities of such potential sensitivity or urgency that normal notification standards would significantly risk mission accomplishment" (Office of the Under Secretary for Personnel and Readiness, 2011, p. 5). Thus, it is likely special operators possess greater concerns regarding career implications regarding reporting of symptoms, which can include selection for military training, security clearances, and future assignments (Hing et al., 2012). Fellow service members and family members also may be hesitant to express concern of the special operator's mental health due to similar fears that mental health stigma may result in problems related to career progression, security clearance, or future military assignments (Hing et al., 2012). Some patients may consider posttraumatic nightmares to be a normal or expected effect of a traumatic experience (Creamer et al., 2018) and thus may not report experiencing nightmares.

In a study by Hing and colleagues (2012), special operations Soldiers reported clinically significant PTSD symptoms at a rate above the estimated incidence of the general US military population. Of particular note, scores were greater after the third or

more deployment to Afghanistan. The authors suggest that training and psychological coping strategies may be protective for the first or second deployment; however, this resilience acquired through training and positive coping strategies may begin to breakdown over time, become depleted by chronic stress exposures, or be replaced by maladaptive coping strategies (Hing et al., 2012). This suggests that innate or trained strategies may initially protect against the sequelae of trauma but are not sustainable after multiple deployments. Additionally, one cannot dismiss the compounding effect of additional missions and engagements that may increase threat awareness and the stress response (Hing et al., 2012).

The overrepresentation of special operators in the present sample allows for comparison to non-special operators, such as in study one. We anticipate continued examination into differences between patients who are and are not special operators. Further research is needed to examine the role of personality factors, training, and coping mechanisms in relation to posttraumatic nightmares.

FUTURE DIRECTIONS

Future studies should seek to validate these findings in additional samples. Namely, examination of relationships in veterans, civilians, and non-treatment seeking active duty service members would increase the generalizability of the findings and thus confidence in the proposed model. Replication of imaging findings should be conducted using large ($N > 1{,}000$) datasets to allow examination of many regions to further understand the neurobiological underpinnings of posttraumatic nightmares. Replication of study three should include consideration of covariates to better elucidate the specific role of posttraumatic nightmares on suicidal ideation. Finally, future studies should

examine the temporal relationship of the proposed model through longitudinal and ecological momentary assessment methods.

Need for Improved Construct Measurement

Presently, there is not a consistently used measure of posttraumatic nightmares, which results in different operational definitions within the literature. A new and thorough measure would strengthen research of posttraumatic nightmares. Namely, a measure that builds upon existing measures and is cognizant of patients' willingness to endorse various descriptions (e.g., distressing dreams versus nightmares as discussed in the "Military Considerations" section above) would be useful to quantify the posttraumatic nightmare experience. Posttraumatic nightmares may be assessed during routine assessment of PTSD symptoms or during diagnostic interviews. These measures may include a self-assessment such as the PTSD Checklist for DSM 5 (PCL-5; Weathers, Litz, et al., 2013) or a clinician administered measure, such as the gold-standard measure of PTSD the CAPS-5 (Weathers, Blake, et al., 2013). However, a single item is insufficient to understand the complexities associated with posttraumatic nightmares. These items are also not measuring the same thing: the PCL-5 Item 2 assesses how *bothered* a patient is by disturbing dreams, and the CAPS-5 Item 2 measures the *frequency* and *severity* of unpleasant dreams.

Posttraumatic nightmares also may be assessed distinct from overall PTSD using questionnaires or diary methods (Schredl, 2002). The Pittsburgh Sleep Quality Index Addendum for PTSD (PSQI-A; Germain et al., 2005) measures the disruptive nocturnal behaviors frequently seen in patients with PTSD. The PSQI-A has four nightmare related items, which emphasizes the need to evaluate the nightmare experience for patients with

PTSD (Germain et al., 2005). The PSQI-A assesses anxiety and anger associated with the nightmare as well as identifying the time of night the nightmares occur. These items, unfortunately, do not sufficiently measure the posttraumatic nightmare experience. Further, guidance for a nightmare composite score has not been provided, necessitating the use of a single item or consideration of disruptive nocturnal behaviors more broadly.

The Trauma-Related Nightmare Survey (Cranston et al., 2017; Davis et al., 2001) was developed as part of studies examining ERRT. This measure is marketed as being specific to trauma-related nightmares; however, the instructions do not ask the patient to consider nightmares related to a traumatic nightmare and only two of the 16 questions consider trauma. Item 7 asks if nightmare onset occurred after a traumatic event, and item 13 assesses how closely the nightmare is to the traumatic event. Of note, validity for the TRNS to the Modified PTSD Symptom Scale-Self Report (Falsetti et al., 1993), a measure of PTSD, only considered nightmare frequency, number of nights, and severity rather than the complete measure (r = .54-.58; Cranston et al., 2017). This measure assesses a number of informative aspects of the nightmare experience (e.g., themes, physical response, frequency, and how long they have experienced nightmares) and is a useful step towards an improved measure specific to posttraumatic nightmares. The Fear of Sleep Inventory Short Form (FOSI-SF; Pruiksma et al., 2014) is a general measure of fear of sleep; however, Pruiksma and colleagues (2014) acknowledge its usefulness in assessing and informing treatment for patients with PTSD. The FOSI-SF is significantly correlated with the PCL and CAPS-IV (r = .61 and .57, respectively; Pruiksma et al., 2014).

The Nightmare Frequency Questionnaire (NFQ; Krakow, Melendrez, et al., 2002) is a two-item self-report questionnaire that estimates nightmare occurrence by number of nights with at least one nightmare and by number of nightmares. The Disturbing Dreams and Nightmares Severity Index (DDNSI; Krakow, Schrader, et al., 2002) is an expanded version of the NFQ. Notably, this measure does not solely assess nightmares, as many patients have difficulty distinguishing between the various terms for nightmares and bad dreams (Krakow, 2006). The Nightmare Distress Questionnaire (NDQ; Belicki, 1992) is a thirteen-item self-report measure assessing subjective distress related to nightmares. Items include fear of falling asleep, effect on quality of life, and effect on sleep. Nightmare interference with sleep, energy, and nine other areas can be measured using the Nightmare Effects Survey (NES; Krakow, Melendrez, et al., 2002). Recently, the Nightmare Disorder Inventory (NDI; Dietch et al., 2020) was developed to screen for nightmare disorder and provides a measure of symptom severity. Other, less frequently used, measures are available for assessing nightmares including the Van Dream Anxiety Scale (Ağargün et al., 1999), and the Dream Property Scale (Takeuchi et al., 2001). However, these generic measures of bad dreams and nightmares do not assess if the dream is trauma-related.

Personal Future Directions

I intend to continue interrogating and refining the proposed model. In the immediate future, this will include examining hormones associated with posttraumatic nightmares, the relationship of guilt and posttraumatic nightmares, and the association of posttraumatic nightmares and polysomnographic measures of sleep. It also is important to increase the generalizability of the present analyses. I hope to examine these relationships

in additional samples including veterans, civilians, and non-treatment seeking service members.

As my research progresses, I intend to obtain funding to further test this model through longitudinal and ecological momentary assessment methods to better understand the relationships of factors identified in the present model. This will allow elucidation of the temporal relationship in both the development and perpetuation of symptoms. Longitudinal studies can inform the development and trajectory of the model, and ecological momentary assessment methods can explicate the proposed cyclical nature of the model. This knowledge may lead to improved treatments as a result of the increased knowledge of the factors that initiate and maintain posttraumatic nightmares.

CONCLUSION

This project introduces a novel, comprehensive biopsychosocial model of chronic posttraumatic nightmares. Three studies were conducted in support of the initial testing of this model, with results largely finding support for the hypothesized relationships. Specifically, results of study one indicated patient factors (i.e., special operator status), disturbed sleep (i.e., problems falling asleep, problems staying asleep, and pain that disrupts sleep), and mental health symptoms (i.e., PTSD, anxiety, and depression) are important considerations for understanding chronic posttraumatic nightmares. Study two did not support the hypothesized structural differences in patients with posttraumatic nightmares; however, we hypothesize a functional relationship exists. Study three provided support for the need to examine posttraumatic nightmares due to the deleterious effects on a patient's well-being, namely through increasing suicidal ideation. Further study is needed to further interrogate the proposed model as well as to increase the

generalizability by examining these relationships in additional samples. The proposed project may encourage both researchers and providers to take a biopsychosocial approach to the study of posttraumatic nightmares as well as the conceptualization and treatment of patients seeking relief from posttraumatic nightmares.

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Paper 1 – Table 1. Demographic Characteristics

Measure	*Total N* = 1,550 % or M(SD)
Mean Age (Years)	38.01 (7.23)
Sex	
Male	98.2%
Female	1.8%
Race/Ethnicity	
White	76.5%
Black	3.5%
Hispanic	3.0%
Asian/Pacific Islander	2.0%
American Indian/Alaskan Native	1.4%
Unavailable	13.6%
Marital Status	
Single	11.1%
Married	78.3%
Separated	4.0%
Divorced	6.5%
Widowed	0.1%

Rank	
Enlisted	80.9%
Officer	19.0%
Unavailable	0.1%
Branch	
USA	31.4%
USN/CG	48.9%
USMC	12.6%
USAF	7.2%
Special Operations	
Yes	56.3%
No	43.7%
Military Status	
Active duty	95.5%
Reservist	1.9%
Unavailable	2.6%
Mean Time in Service	16.83 (7.16)

Paper 1 – Table 2. Final Posttraumatic Stress Symptoms Model for Odds Ratios of Posttraumatic Nightmares ($N = 902$)

Variable	OR	*SE*	*z*	*p*	95% CI	
					LL	*UL*
Posttraumatic stress symptoms	1.15	.01	130.71	**< .001**	1.12	1.18
Prazosin use	4.17	.81	3.11	.08	0.85	20.37
Pain that disrupts sleep			13.05	**< .01**		
Less than once a week	1.83	.31	3.83	.050	1.00	3.36
Once or twice a week	2.04	.29	6.14	**.01**	1.16	3.58
Three or more times a week	2.66	.27	12.97	**< .001**	1.56	4.53
Postconcussive symptoms	0.97	.01	7.86	**< .01**	0.96	0.99
Special operations status	0.62	.21	4.90	**.03**	0.41	0.95
Early awakenings			8.77	**.03**		
Less than once a week	3.10	.75	2.27	.13	0.71	13.53
Once or twice a week	2.38	.70	1.53	.22	0.60	9.42
Three or more times a week	4.07	.69	4.19	**.04**	1.06	15.57

Note. Bolded p values signify statistical significance.

Paper 1 – Table 3. Final Anxiety Model for Odds Ratios of Posttraumatic Nightmares ($N = 684$)

Variable	OR	*SE*	*z*	*p*	95% CI	
					LL	*UL*
Anxiety symptoms	1.12	.02	23.61	**< .001**	1.07	1.17
Prazosin use	7.19	.80	6.06	**.01**	1.50	34.53
Postconcussive symptoms	1.03	.01	11.36	**< .01**	1.01	1.05
Pain that disrupts sleep			18.31	**< .001**		
Less than once a week	2.00	.30	5.33	**.02**	1.11	3.59
Once or twice a week	2.57	.28	11.31	**< .01**	1.48	4.46
Three or more times a week	3.03	.27	17.27	**< .001**	1.80	5.12
Special operations status	0.54	.23	7.17	**< .01**	0.35	0.85

Note. Bolded p values signify statistical significance.

Paper 1 – Table 4. Final Depression Model for Odds Ratios of Posttraumatic Nightmares (*N* = 856)

Variable	OR	*SE*	*z*	*p*	95% CI	
					LL	*UL*
Depression symptoms	1.09	.02	12.13	**< .001**	1.04	1.14
Prazosin use	5.07	.78	4.38	**.04**	1.11	23.17
Postconcussive symptoms	1.03	.01	11.21	**< .01**	1.01	1.05
Pain that disrupts sleep			16.27	**< .01**		
Less than once a week	1.78	.28	4.30	**.04**	1.03	3.08
Once or twice a week	2.26	.26	10.25	**< .01**	1.37	3.72
Three or more times a week	2.56	.24	15.16	**< .001**	1.60	4.12
Special operations status	0.57	.20	8.32	**< .01**	0.39	0.84
Difficulty falling asleep within 30 minutes			9.69	**.02**		
Less than once a week	1.07	.28	0.06	.81	0.62	1.87
Once or twice a week	1.71	.27	3.97	**.05**	1.01	2.89
Three or more times a week	1.85	.25	5.89	**.02**	1.13	3.05

Note. Bolded p values signify statistical significance.

Study 2 – Table 1. Demographic Characteristics

Measure	Included ($N = 351$) % or M (SD)	Excluded ($N = 48$) % or M (SD)
Mean Age (Years)	40.15 (5.53)	40.81 (6.45)
Race		
White	54.1%	47.9%
Black	0.9%	2.1%
Asian/Pacific Islander	2.6%	0.0%
American Indian/Alaskan Native	2.8%	2.1%
Other	6.3%	2.1%
Unavailable	33.3%	45.8%
Marital Status		
Single	6.8%	6.3%
Married	84.6%	89.6%
Separated	4.6%	2.1%
Divorced	3.7%	2.1%
Widowed	0.3%	0.0%
Rank		
Enlisted	78.9%	70.8%
Officer	20.8%	29.2%
Unavailable	0.3%	0.0%

Branch		
US Army	27.6%	31.3%
US Navy/Coast Guard	60.1%	41.7%
US Air Force	7.7%	6.3%
US Marine Corps	4.6%	4.2%
Unavailable	0.0%	16.7%
Special Operations		
Yes	69.5%	75.0%
No	28.8%	20.8%
Unavailable	1.7%	4.2%
Mean Time in Service	19.55 (5.09)	19.39 (7.27)

Note. Patients were excluded for moderate or severe TBI. Percentages may not add up to exactly 100% due to rounding errors.

Study 2 – Table 2. Relationship of Posttraumatic Nightmares to Gray Matter Volume ($N = 351$)

Brain region	*b*	*SE*	t	*p*	95% CI	
					LL	*UL*
Subcortical gray matter volume	59.28	429.28	0.14	.89	-785.03	903.591
Left hemisphere cortical gray matter volume	0.00	0.03	0.22	.83	-0.01	0.01
Right hemisphere cortical gray matter volume	298.08	2075.38	0.14	.89	-3,783.84	4,380.00
Total cortical gray matter volume	0.00	0.00	0.19	.85	-0.01	0.01
Total gray matter volume	1,697.58	4,968.82	0.34	.73	-8,094.89	11,490.05

Note. Analyses controlled for age, sex, and history of mild TBI.

Study 2 – Table 3. Relationship of Posttraumatic Nightmares to Subcortical Surface and Cortical Thickness ($N = 351$)

Brain region	*b*	*SE*	t	*p*	95% CI *LL*	95% CI *UL*
Left amygdala	15.30	20.60	0.04	.46	-25.21	55.81
Right amygdala	-0.00	0.01	-0.34	.74	-0.01	0.01
Left hippocampus	13.56	39.04	0.35	.73	-63.22	90.35
Right hippocampus	0.00	40.65	0.00	1.00	-79.94	79.94
Left rostral medial prefrontal cortex	0.01	0.01	0.74	.46	-0.01	0.03
Right rostral medial prefrontal cortex	-0.00	0.01	-0.29	.77	-0.02	0.02
Left caudal medial prefrontal cortex	0.02	0.01	1.33	.19	-0.01	0.04
Right caudal medial prefrontal cortex	0.01	0.01	0.59	.56	-0.02	0.03
Left medial orbitofrontal cortex	1.77E-5	0.00	0.01	.99	-0.00	0.00
Right medial orbitofrontal cortex	0.00	0.00	0.09	.93	-0.00	0.00
Left rostral anterior cingulate cortex	-0.00	0.02	-0.19	.85	-0.04	0.03
Right rostral anterior cingulate cortex	-0.02	0.02	-0.88	.38	-0.06	0.02

Left caudal anterior cingulate cortex	0.00	0.02	0.47	.64	-0.03	0.05
Right caudal anterior cingulate cortex	-0.00	0.02	-0.13	.90	-0.04	0.04
Left insular cortex	-0.02	0.01	-1.46	.15	-0.04	0.01
Right insular cortex	-0.00	0.01	-0.10	.92	-0.03	0.02

Note. Analyses controlled for age, sex, and history of mild TBI.

Study 2 – Table 4. Replication of Wang et al. (2020) in Posttraumatic Nightmares ($N = 351$)

Brain region	*b*	*SE*	t	*p*	95% CI *LL*	95% CI *UL*
Left lateral orbitofrontal cortex	0.01	0.01	0.58	.56	-0.02	0.03
Right lateral orbitofrontal cortex	0.01	0.01	0.42	.67	-0.02	0.03
Left superior temporal cortex	-0.01	0.01	-0.79	.43	-0.04	0.02
Right insular cortex	-0.00	0.01	-0.10	.92	-0.03	0.02
Right lingual cortex	-0.01	0.01	-0.59	.56	-0.03	0.02
Right superior parietal cortex	-0.00	0.01	-0.50	.62	-0.02	0.01

Note. Analyses controlled for age, sex, and history of mild TBI.

Paper 3 – Table 1. Demographic Characteristics

Measure	*Total N* = 1,550 % or M (SD)
Mean Age (Years)	38.01 (7.23)
Gender	
Male	98.2%
Female	1.8%
Race/Ethnicity	
White	76.5%
Black	3.5%
Hispanic	3.0%
Asian/Pacific Islander	2.0%
American Indian/Alaskan Native	1.4%
Unavailable	13.6%
Rank	
Enlisted	80.9%
Officer	19.0%
Unavailable	0.1%
Branch	
Army	31.4%
Navy/Coast Guard	48.9%
Marine Corps	12.6%

Air Force	7.2%
Special Operations	
Yes	56.3%
No	43.7%

Paper 3 – Table 2. Odds ratios for individual sleep characteristics

Variable	*N*	*B*	*SE*	OR	95% CI	
					LL	*UL*
Arousal Index	862	0.01	0.01	1.01	0.99	1.04
Wake After Sleep Onset	977	-0.01	0.00	0.99	0.99	1.00
Sleep Latency	977	0.00	0.01	1.00	0.99	1.01
REM Latency*	977	0.00	0.00	1.00	1.00	1.01
Sleep Efficiency	977	0.02	0.01	1.02	0.99	1.04
Mean HR	977	0.02	0.01	1.02	1.00	1.04
Minimum HR	977	0.01	0.01	1.01	0.98	1.03
Maximum HR	977	0.01	0.00	1.01	1.00	1.01
Total Sleep Time	977	0.00	0.00	1.00	1.00	1.01
Supine Sleep Time	976	0.00	0.00	1.00	1.00	1.00
Stage N1 Sleep	977	-0.00	0.02	1.00	0.96	1.04
Stage N2 Sleep*	977	-0.02	0.01	0.98	0.96	1.00
Slow-wave Sleep	977	0.02	0.01	1.02	1.00	1.05
REM	977	0.02	0.02	1.02	0.98	1.05
*PSQI Total Score (Sleep Quality)***	489	0.16	0.05	1.17	1.06	1.29
*ESS (Sleepiness)**	1,188	0.05	0.02	1.05	1.01	1.09

Bad Dreams[1, 2]	1,193					
Less than once a week		0.68	0.39	1.98	0.93	4.21
*Once or twice a week***		1.48	0.35	4.39	2.23	8.65
*Three or more times a week****		2.01	0.34	7.89	4.04	15.40
Traumatic Bad Dreams[1, 2]	1,170					
A little bit		0.40	0.35	1.49	0.76	2.95
*Moderately****		1.44	0.33	4.20	2.19	8.04
*Quite a bit****		1.62	0.33	5.04	2.62	9.67
*Extremely****		2.29	0.38	9.90	4.71	20.83

Note. CI = confidence interval; *LL* = lower limit; *UL* = upper limit; OR = odds ratio; PSQI = Pittsburgh Sleep Quality Index; ESS = Epworth Sleepiness Scale.

Italics represent self-reported sleep measures. [1]Analyses controlled for use of Prazosin.

[2]Results are calculated with the lowest value as the indicator.

*$p < .05$. **$p < .01$. ***$p < .001$.

APPENDICES

APPENDIX A: STUDY SUMMARIES

Study 1 Title: The Association of Mental Health Symptoms to Posttraumatic Nightmares Among Active Duty Service Members Seeking Treatment

Authors: Maegan M. Paxton Willing,[1,2,3,4] Larissa L. Tate, [1,3,4] Thomas J. DeGraba,[1,2] David S. Riggs,[1,3] Chandler Sours Rhodes,[2] Treven C. Pickett[1,2]

Abstract: Posttraumatic nightmares (PTN) are a common experience among service members with a history of combat or mission-related trauma and are associated with decreased well-being and increased risk of developing PTSD. The present study sought to examine the potential contribution of comorbid symptoms, such as posttraumatic stress, depression, and anxiety, to the development and maintenance of PTN in an effort to inform and improve treatment outcomes. Data were collected as part of standard procedures for an intensive outpatient program for service members with history of TBI and/or psychological health conditions. Separate models were created for posttraumatic stress symptoms, depression, and anxiety inclusive of comorbid psychological symptoms, patient demographics, and military characteristics, with some variance in covariates among final models. Results demonstrated that these, and other related mental health symptoms (i.e., pain that disrupts sleep, early awakenings, sleep onset latency, postconcussive symptoms), were associated with incremental increases in odds of PTN. Findings suggest treating co-occurring symptoms may decrease the distress associated with PTN. Consideration of the association of comorbid symptoms and relevant

military characteristics (e.g., special operator status) is important for a more complete understanding of these co-occurring presentations. Future research utilizing longitudinal methods may inform the temporal aspects of these relationships.

Is study published? No

If yes, give full reference and attach publication.

If yes, was study approved by academic advisor?

If not published, what journal do you plan to submit to? *Military Behavioral Health* (in review)

Describe Student Involvement/Conceptual Leadership in Project: Mrs. Willing designed the study, cleaned and analyzed the data, interpreted the findings, and generated the manuscript under the primary guidance of Drs. Riggs and Pickett.

Proposed Timeline: Manuscript is under review.

Study 2 Title: Examination of the AMPHAC Model of Disturbing Dreams in Male Active Duty Service Members

Authors: Maegan M. Paxton Willing,[1,2,3] Rujirutana Srikanchana,[4] Treven C. Pickett,[1,4] John M. Ollinger,[4] David S. Riggs,[1,2] J. Kent Werner,[1,4] Grant H. Bonavia,[4] National Intrepid Center of Excellence Ohio State University TBI Identification Clinical Group Clinical Group,[4] Chandler Sours Rhodes[4,5]

Abstract: Posttraumatic nightmares commonly occur after a traumatic experience. Despite the significant deleterious effects on well-being and their role in posttraumatic stress disorder, posttraumatic nightmares remain understudied. The AMPHAC model (Levin & Nielsen, 2007) implicates neuroanatomical structures such as the amygdala, medial prefrontal cortex, hippocampus, and anterior cingulate cortex in the neurophysiology of disturbing dreams, though to date this model has not been validated using neuroimaging data. The present study sought to elucidate whether there are structural differences in these identified AMPHAC regions in relation to posttraumatic nightmares. Data were obtained from male active duty service members (N = 351) who had received treatment at an intensive outpatient program for traumatic brain injury (TBI) and/or psychological health conditions. Posttraumatic nightmares were not significantly related to gray matter volume or cortical thickness of any of the identified neuroanatomical regions when controlling for age and history of mild TBI. Although the present analyses do not support structural association of the AMPHAC Model to posttraumatic nightmares, we suggest that functional differences within and/or between these brain regions may be involved in posttraumatic nightmares and that future research is needed to more fully determine whether these functional differences may be associated with posttraumatic nightmares.

Is study published? No

If yes, give full reference and attach publication. N/A

If yes, was study approved by academic advisor? N/A

If not published, what journal do you plan to submit to? *Psychiatry Research: Neuroimaging*

Describe Student Involvement/Conceptual Leadership in Project: Mrs. Willing designed the study, cleaned the non-imaging data, analyzed the data, interpreted the findings, and generated the manuscript under the primary guidance of Dr. Rhodes and Mr. Srikanchana.

Proposed Timeline: Submit to PAO (USU, HJF, NICoE, and WRNMMC) in April 2021, with manuscript submission upon approval.

Study 3 Title: Understanding the Role of Sleep on Suicidal Ideation in Active Duty Service Members: Implications for Clinical Practice

Authors: Maegan M. Paxton Willing,[1,2,3,4] Treven C. Pickett,[1,2] Larissa L. Tate, [1,3,4] Chandler Sours Rhodes,[2] David S. Riggs, [1,3] Thomas J. DeGraba,[1,2]

Abstract: Suicide is a significant public health concern, particularly within the U.S. military. Sleep difficulties are hypothesized to elevate risk, yet this association is not well understood. Presently, there is some support for a positive association between subjective reports of sleep disturbances and suicidal ideation (SI); however, research regarding the relation of SI and objective measures of sleep is sparse. The present study aimed to examine the association of subjective and objectives measures of sleep on SI in a sample of active duty service members and provide recommendations to changes in clinical care. Data were obtained from the National Intrepid Center of Excellence's clinical database. Patients

(*N*=1,550) were predominantly male, Navy/Coast Guard, and enlisted rank, with a mean age of 38 years. Patients underwent a sleep study and completed a battery of measures as part of standard clinical care. SI was coded as a binary variable, and odds ratios were calculated using logistic regression. Of the 14 objective sleep indices examined, REM latency and time in sleep stage N2 were related to SI. Subjective reports, including sleep quality, sleepiness, bad dreams, and traumatic bad dreams and nightmares, were all significantly associated with increased odds of SI. Notably, subjective reports of sleep were the only measures with meaningful odds ratios, with traumatic bad dreams producing the greatest odds ratios. The present findings suggest subjective reports of sleep disturbance are important when evaluating SI in active duty service members and may represent an important point of intervention for patients experiencing SI.

Is study published? Yes, in press

If yes, give full reference and attach publication. Paxton Willing, M. M., Pickett, T. C., Tate, L. L., Sours Rhodes, C., Riggs, D. S., & DeGraba, T. J. (in press). Understanding the role of sleep on suicidal ideation in active duty service members: Implications for clinical practice. Proofs are in Appendix G.

If yes, was study approved by academic advisor? Yes

If not published, what journal do you plan to submit to? N/A

Describe Student Involvement/Conceptual Leadership in Project: Mrs. Willing designed the study, cleaned and analyzed the data, interpreted the findings, and generated the manuscript under the primary guidance of Drs. Pickett and Riggs.

Proposed Timeline: Awaiting online publication

APPENDIX B: DESCRIPTION OF IMAGING STUDIES

Article	Case	Control	Notes
Akiki et al. (2017)			69 combat-exposed US veterans with PTSD; breakdown not specified
Badura-Brack et al. (2018)	28 veterans with PTSD	16 veterans without PTSD	
Berman et al. (2018)	38 sexually assaulted women	24 non-exposed matched controls	
Crombie et al. (2021)	99 women with PTSD related to interpersonal violence	22 healthy trauma-free women without a diagnosis of PTSD	
Dahlgren et al. (2018)	12 males with PTSD	14 males without PTSD	Identical twin pairs
Fani et al. (2019)	26 traumatized women with PTSD	22 traumatized women without PTSD	
Fjell et al. (2019)			Longitudinal data: 1,299 participants with 5,116 MRIs Cross-sectional data: 21,390
Germain et al. (2013)	6 veterans with PTSD	6 veterans without PTSD	
Gong et al. (2019)	65 medication-naïve patients with chronic insomnia disorder	55 healthy controls matched for age, sex, and years of education	
Gvozdanovic et al. (2020)			74 healthy female subjects
Herringa et al. (2012)	13 combat veterans with PTSD	15 combat veterans without PTSD	All were combat-exposed
Huang et al. (2012)	10 medication-naïve primary insomnia patients	10 age- and sex-matched healthy controls	
Kasai et al. (2008)	18 combat-exposed Vietnam veterans with PTSD and 23	High- and low-risk cotwins, respectively	

	combat-exposed Vietnam veterans without PTSD		
Kroes et al. (2011)			28 participants diagnosed with PTSD
Leerssen et al. (2020)	1,053 major depressive disorder patients	2,108 healthy controls 260 clinical controls with bipolar disorder	
Liu et al. (2016)	31 subjects with insomnia symptoms	71 age- and gender-matched subjects without insomnia symptoms	
Lloyd et al. (2020)	28 military and public safety-related PTSD	18 civilian MI-exposed controls	
Logue et al. (2018)	794 PTSD patients	1,074 control subjects	358 PTSD patients and 478 control subjects came from military samples
Miedl et al. (2020)			58 healthy participants
Morey et al. (2020)	149 military veterans with PTSD	206 trauma-exposed control subjects with PTSD	
Morey et al. (2019)	794 PTSD patients	1,074 (controls not described)	
Nardo et al. (2015)	21 Developing PTSD	18 Not developing PTSD	
Neumann et al. (2020)	143 Male poor sleepers 197 Female poor sleepers	346 Male good sleepers 398 Female good sleepers	
Nofzinger et al. (2004)	7 patients with insomnia	20 healthy subjects	
O'Doherty et al. (2017)	25 adults diagnosed with PTSD	25 healthy and 25 trauma exposed age and gender matched controls	
Owens et al. (2018)			1,064 adults

Pieper et al. (2020)	29 veterans and active-duty military personnel with combat-related mTBI and comorbid PTSD	60 veterans and active-duty military personnel with combat-related mTBI only	
Rahayel et al. (2018)	41 patients with polysomnography-confirmed idiopathic rapid eye movement sleep behavior disorder	41 healthy subjects	
Stevens et al. (2017)			38 participants were recruited from the emergency department of a large level I trauma center within 24 hours of trauma.
Wang et al. (2020)	1,379 PTSD patients	2,192 controls without PTSD	
Woodward et al. (2006)	51 subjects classified as PTSD-positive (PTSD+) met criteria for current PTSD as a result of experiencing one or more military traumas.	48 subjects classified as PTSD-negative (PTSD-) had also been exposed to military operational stress but were free of diagnosable PTSD, current or lifetime, due to military or civilian trauma.	Military veterans of either the Vietnam Conflict or the Gulf War.
Xie et al. (2018)			44 survivors of a motor vehicle collision
Young et al. (2018)			142 Gulf War Veterans

Note. Descriptions are as written in the respective articles. Some studies did not provide group specific *n*s.

APPENDIX C: CORRELATION TABLE FOR STUDY 1

	Posttraumatic nightmares	PTSD	Anxiety	Depression
Posttraumatic nightmares		.72**	.48**	.51**
PTSD			.74**	.75**
Anxiety				.72**
Depression				

Note. **$p < .01$

APPENDIX D: MANUSCRIPT 1 JOURNAL SUBMISSION

Military Behavioral Health

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Author

Review

Submission Confirmation

Print

Thank you for your submission

Submitted to
Military Behavioral Health

Manuscript ID
UMBH-2021-0018

Title
The Association of Mental Health Symptoms to Posttraumatic Nightmares Among Active Duty Service Members Seeking Treatment

Authors
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Riggs, David
Sours Rhodes, Chandler
Pickett, Treven

Date Submitted
23-Mar-2021

Author Dashboard

The Association of Mental Health Symptoms to Posttraumatic Nightmares Among Active Duty Service Members Seeking Treatment

Journal:	*Military Behavioral Health*
Manuscript ID	Draft
Manuscript Type:	Original Article
Keywords:	Military, Posttraumatic nightmares, Post Traumatic Stress Disorder < Mental Health Disorders, Sleeping and Dreaming, Anxiety < Mental Health Disorders, Depression < Mental Health Behavioral Symptoms

APPENDIX E: HYPOTHESIS PLANNING FOR STUDY 2

	Nardo et al., 2015			Germain et al., 2013		Proposed Models	
	VOI	VBM	SPECT	Waking	Sleep	Levin & Nielsen, 2007	Germain et al., 2008
Amygdala	-	-		+	+	X	X
Hippocampus	-	-		+	+	X	
Medial prefrontal cortex					+	X	X
Anterior cingulate cortex	-	-	-	+	+	X	
Locus coeruleus				+	+		
Insular cortex		-	+	+	+		
Parahippocampus		-					
Striatum		-					

Dorsolateral prefrontal cortex	-	-	
Midbrain		+	
Precuneus		+	X
Orbitofrontal			X
Brainstem			X

Note. Minus sign signifies a negative relationship. Plus sign signifies a positive relationship. X = no direction specified.

APPENDIX F: PAPER 3 JOURNAL ACCEPTANCE

Date:	01/26/2021
To:	"Maegan M. M. Willing" megan.paxton.ctr@usuhs.edu;paxton.maegan@gmail.com
cc:	"Treven C. Pickett" treven.c.pickett.civ@mail.mil, "Larissa L. Tate" larissa.tate.ctr@usuhs.edu, "Chandler Sours Rhodes" chandler.s.rhodes.civ@mail.mil, "David S. Riggs" david.riggs@usuhs.edu, "Thomas J DeGraba" thomas.j.degraba.civ@mail.mil
From:	"Practice Innovations" ewilliams@apa.org
Subject:	Your Submission PRI-2021-0214

PRI-2021-0214
Understanding the Role of Sleep on Suicidal Ideation in Active Duty Service Members: Implications for Clinical Practice
Practice Innovations

Dear Mrs. Willing,

I take pleasure in confirming that, following final review, your manuscript was accepted on 01/26/2021

We are ready to move forward if you are "truly Willing" (pun intended) as demonstrated by completion of the publication forms.

APA has a number of required publication forms, regarding copyright, conflict of interest, and other matters. You will receive an email shortly from DocuSign, requesting electronic signatures for publication forms. These forms must be signed by all authors prior to your manuscript entering production. If you have questions about this process, please contact peer review coordinator, Emily Williams at ewilliams@apa.org.

Comments from the Editor and Reviewers can be found below.

Thank you for submitting your work to *Practice Innovations*.

Sincerely,

Gerry Koocher

Gerald P. Koocher, PhD, ABPP
Associate Editor
Practice Innovations

APA asks that authors please take a moment to give us your feedback on the peer review process as you experienced it, by completing a short survey, available at http://goo.gl/forms/qzKP6Zkqx9.

Comments from the Editors and Reviewers:

This manuscript was selected by the Walfish award committee, and re-reviewed by Dr. Koocher in final form for any needed corrections.
None were found.

APPENDIX G: PAPER 3 PROOFS

J_ID: ART NO: 10.1037/pri0000146 Date: 27-February-21 Page: 1 Total Pages: 11 4/Color Figure(s) FNTWOCOL

Practice Innovations

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Understanding the Role of Sleep on Suicidal Ideation in Active-Duty Service Members: Implications for Clinical Practice

AQ: au

Maegan M. Paxton Willing[1, 2, 3, 4], Treven C. Pickett[1, 2], Larissa L. Tate[1, 3, 4], Chandler Sours Rhodes[2], David S. Riggs[1, 3], and Thomas J. DeGraba[1, 2]

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Suicide is a significant public health concern, particularly within the U.S. military. Sleep difficulties are hypothesized to elevate risk, yet this association is not well understood. Presently, there is some support for a positive association between subjective reports of sleep disturbances and suicidal ideation (SI); however, research regarding the relation of SI and objective measures of sleep is sparse. The present study aimed to examine the association of subjective and objectives measures of sleep on SI in a sample of active-duty service members and provide recommendations to changes in clinical care. Data were obtained from the National Intrepid Center of Excellence's clinical database. Patients (N = 1,550) were predominantly male, Navy/Coast Guard, and enlisted rank, with a mean age of 38 years. Patients underwent a sleep study and completed a battery of measures as part of standard clinical care. SI was coded as a binary variable, and odds ratios were calculated using logistic regression. Of the 14 objective sleep indices examined, REM latency and time in sleep stage N2 were related to SI. Subjective reports, including sleep quality, sleepiness, bad dreams, and traumatic bad dreams and nightmares, were all significantly associated with increased odds of SI. Notably, subjective reports of sleep were the only measures with meaningful odds ratios, with traumatic bad dreams producing the greatest odds ratios. The present findings suggest subjective reports of sleep disturbance are important when evaluating SI in active-duty service members and may represent an important point of intervention for patients experiencing SI.

Clinical Impact Statement

The present study adds to the literature on the role of sleep, both objective and subjective, on suicidal ideation in service members. These results provide support for the need to evaluate self-reported sleep disturbances during suicide risk assessments, with a particular focus on the need to consider bad dreams and posttraumatic nightmares.

Keywords: military, suicidal ideation, sleep, nightmares, polysomnography

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The views expressed in this abstract are those of the authors and do not reflect the official policy of the Uniformed Services University, Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc., Department of Army/Navy/Air Force, Department of Defense, or U.S. Government. The identification of specific products, scientific instrumentation, or organizations is considered an integral part of the scientific endeavor and does not constitute endorsement or implied endorsement on the part of the authors, DoD, or any component agency. Additionally, the authors have no conflicts of interest to report.

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Suicide is a significantly increasing public health concern. In the United States, it is the tenth leading cause of death nationwide and occurs at a rate of 14.2 per 100,000 people (Hedegaard et al., 2020), with one person attempting suicide every 31 seconds (Center for Deployment Psychology, n.d.). Suicide is also a substantial problem facing the U.S. military, with a rate of 24.8 suicide deaths per 100,000 active-duty service members, 22.9 per 100,000 reservists, and 30.6 per 100,000 National Guardsmen (Tucker et al., 2019). This suggests a critical need to identify opportunities for intervention. It is, therefore, imperative to identify factors associated with increased risk of suicide in service members. Sleep disturbances, in particular, have been identified as one such determinant requiring further study. With the high prevalence of sleep disturbances in the U.S. military (e.g., Plumb et al., 2014), it is particularly important to increase the understanding of the role sleep plays in suicide risk among active-duty service members.

Some sleep disorders, including sleep apnea and insomnia, have been shown to be related to increased suicidal ideation and attempts. In a sample of patients who underwent a one-night polysomnography (PSG) evaluation, approximately 20% of those diagnosed with obstructive sleep apnea (OSA) reported suicidal ideation (Timkova et al., 2020). Patients with sleep apnea also have been found to have increased odds of suicidal ideation and suicidal planning, even when controlling for relevant demographics, substance use, and depression; however, they did not have increased odds of suicidal attempts (Bishop et al., 2018). In contrast, Bishop and colleagues (2020) examined suicide attempts and psychiatric diagnoses among veterans seeking care in the Department of Veterans Affairs (VA) and found sleep-related breathing disorders, such as OSA, were positively associated with suicide attempts when controlling for age, gender, utilization of sleep or mental health services, and comorbid sleep disorders. However, this association was no longer significant when further controlling for PTSD, depression, anxiety disorders, schizophrenia, bipolar disorder, and substance use disorder.

Insomnia also has been implicated in the relationship of sleep to suicide. It is important to note insomnia is both a diagnosis as well as a symptom. To highlight the differences, we will discuss the literature as it relates to both the disorder and as a self-reported symptom (below). In a large review of VA medical records, a diagnosis of insomnia was found to be associated with having attempted suicide, even when controlling for patient age, gender, sleep or mental health treatment utilization, and other sleep disorders (Bishop et al., 2020). This relationship remained significant after controlling for relevant mental health disorders and medical comorbidity. Pompili et al. (2013) examined patients who were admitted to an emergency room after seeking psychiatric care and found those with a diagnosis of insomnia were *less* likely to have attempted suicide in the last 24 hr. However, for those patients with insomnia who *had* attempted suicide within this timeframe, they were more likely to have used a violent method.

Objective Measures of Sleep

Little research has examined objective measures of sleep in relation to suicide. In a study of civilians with PTSD who were receiving an at home sleep apnea test, respiratory disturbance index (RDI), apnea-hypopnea index (AHI), and oxygen desaturation index were positively associated with suicidal ideation (Gupta & Jarosz, 2018). In this study, OSA severity was measured by RDI, thus suggesting OSA severity is associated with increased suicidal ideation. One study (Bernert, Hom et al., 2017) examined objective measures of sleep as measured by actigraphy in relation to suicidal ideation. Time of sleep onset was predictive of suicidal ideation, but not sleep onset latency (SOL), total sleep time, wake after sleep onset, sleep efficiency, or sleep offsets (i.e., time of final awakening; Bernert, Hom et al., 2017). Notably, this study included only patients with high suicide risk, and, therefore, should be replicated with patients of other suicidal risk levels.

Bernert, Luckenbaugh et al. (2017) compared patients with and without suicidal ideation on objective sleep measures (e.g., sleep efficiency (*SE*), REM (REM) latency, wake after sleep onset (WASO), total sleep time (TST), percent of time spent in REM, and time spent in non-rapid eye movement (NREM) Stages 1–4) during an electroencephalograph (EEG) sleep study. Patients with suicidal ideation had less

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J_ID: ART NO: 10.1037/pri0000146 Date: 27-February-21 Page: 3 Total Pages: 11 4/Color Figure(s) FNTWOCOL

NREM Stage IV sleep and lower *SE* but greater WASO when controlling for depressive symptoms and a diagnosis of bipolar disorder or major depressive disorder (Bernert, Luckenbaugh et al., 2017). This study employed a sample of treatment-seeking patients with treatment-resistant depression, underscoring the need for replication in additional populations.

Subjective Sleep Reports

Subjective sleep reports have been associated with increased suicidal ideation (e.g., Bernert et al., 2014; Tae et al., 2019). In a study of treatment-seeking patients with depression, subjective reports of sleep quality as measured by the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) were positively associated with suicidal ideation (Tae et al., 2019). This study further identified that each of the seven components of the PSQI (i.e., sleep quality, sleep latency, time asleep, sleep efficiency, sleep disturbances, use of sleep medication, and impact on daytime functioning) were positively correlated with suicidal ideation. Additionally, results demonstrated coughing or snoring loudly, as reported on the PSQI, to be associated with greater suicidal ideation, when controlling for age, depression symptoms, and marital status. Sleep quality also has been found to predict suicide risk at 10-year follow up in older adults (Bernert et al., 2014). In a study of Afghanistan and Iraq era veterans receiving care in the VA, subjectively reported poor sleep quality was related to suicidal ideation, but self-reported sleep duration was not (Swinkels et al., 2013). However, a separate study found self-reported short sleep duration was associated with suicide risk in a study of veterans recently home from deployment (Luxton et al., 2011).

Self-reported insomnia symptoms also have been shown to be related to suicidal ideation. In patients with a history of suicidal ideation, plan, or attempt, prior levels of insomnia symptoms were positively associated with subsequent increases in suicidal ideation (Zuromski et al., 2017). In undergraduates with high suicide risk, subjective reports of insomnia and nightmares were each predictive of increased suicidal ideation (Bernert, Hom et al., 2017). Sleep quality also has been found to be longitudinally associated with a greater risk of death by suicide, which remained when controlling for depressive symptoms (Bernert et al., 2014).

A number of studies have examined the role of bad dreams and/or nightmares in suicidal ideation (e.g., Bishop et al., 2018; Sandman et al., 2017; Tae et al., 2019). It is important to examine both idiopathic (without known origin) and traumatic (related to a traumatic event) bad dreams and nightmares, as there may be a differential effect on suicidal ideation. Idiopathic bad dreams were positively associated with suicidal ideation in patients with depression when controlling for age, depression symptoms, and marital status (Tae et al., 2019). Posttraumatic nightmares have been associated with increased suicidal ideation in a study of civilians with PTSD receiving an in-home diagnostic test for OSA (Gupta & Jarosz, 2018). Additionally, in an examination of data from VA patients, nightmare disorder and suspected posttraumatic nightmares also were found to be associated with a suicide attempt when controlling for patient age, gender, sleep or mental health treatment utilization, and sleep disorders; however, this relationship did not remain when controlling for mental health diagnoses including PTSD, depression, anxiety disorders, schizophrenia, bipolar disorder, and substance use disorder (Bishop et al., 2020). This study classified patients as having nightmares if they had a nightmare disorder diagnosis or a PTSD diagnosis and also had been prescribed prazosin (Bishop et al., 2020); a commonly used medication for the treatment of posttraumatic nightmares (Taylor et al., 2008). This operational definition likely omitted a number of other patients who experienced nightmares and, thus, supports future studies that incorporate patient reports rather than relying solely on diagnoses documented in medical records.

To date, research has focused on the role of subjective sleep reports (e.g., sleep quality; Tae et al., 2019) and common sleep disorders (e.g., insomnia and sleep apnea; Bishop et al., 2018; Timkova et al., 2020) on increased suicidal ideation, but has largely neglected consideration of objective measures of sleep. Additionally, much of the extant research has been conducted in civilian samples and, thus, requires replication in military samples to increase the generalizability of results. The present study, therefore, aims to examine the association of various sleep indices, both subjective and objective, in relation to suicidal ideation among active-duty military personnel in order to provide empirically informed recommendations for clinical practice.

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J_ID: ART NO: 10.1037/pri0000146 Date: 27-February-21 Page: 4 Total Pages: 11 4/Color Figure(s) FNTWOCOL

Method

Participants

Patients included in the present study were active-duty service members enrolled in a four-week interdisciplinary intensive outpatient program (IOP) at the National Intrepid Center of Excellence (NICoE), Walter Reed National Military Medical Center (WRNMMC), Bethesda, Maryland, for treatment of unresolved persisting neurobehavioral symptoms related to traumatic brain injury (e.g., cognitive, pain, or sleep problems) and comorbid psychological health problems. Service members from all branches of the military including the National Guard were eligible for referral to the program by a provider at their duty station. Inclusion criteria for the four-week IOP included being active-duty, sustained exposure to forces or event that provisionally resulted in a TBI, available to attend the four-week care program in-person, able to participate in a structured discharge plan upon return to their duty station, not pose a risk to self or others, not be at risk of alcohol or narcotic withdrawal, not require monitoring or nursing care beyond what can be provided in an outpatient facility, and not have any legal issues pending. If prior psychiatric or inpatient care for substance use had been previously required, treatment must have been completed at least 30 days before their referral to NICoE. Please see DeGraba et al. (2020) for a description of the methods and outcomes of the IOP treatment program.

All patients included in the study were enrolled in the program between March 2012 and January 2019. Service members engaged in a standardized assessment from providers in up to 17 colocated disciplines to develop a comprehensive initial characterization of each patient's clinical neurological and behavioral health status at the start of the program. Patients had an average age of 38.01 years, were approximately 98% male, and approximately 77% white (see T1 Table 1 for complete demographic breakdown). In regards to military characteristics, approximately 80% were enlisted, 49% were United States Navy or Coast Guard, and 56% were special operators. There was one patient who was a member of the Coast Guard and one patient who was a cadet. To prevent patient identification, these patients were collapsed into the Navy branch and officer rank, respectively.

Table 1
Demographic Characteristics

Measure	Total $N = 1{,}550$ % or M (SD)
Mean Age (Years)	38.01 (7.23)
Gender	
Male	98.2%
Female	1.8%
Race/Ethnicity	
White	76.5%
Black	3.5%
Hispanic	3.0%
Asian/Pacific Islander	2.0%
American Indian/Alaskan Native	1.4%
Unavailable	13.6%
Rank	
Enlisted	80.9%
Officer	19.0%
Unavailable	0.1%
Branch	
Army	31.4%
Navy/Coast Guard	48.9%
Marine Corps	12.6%
Air Force	7.2%
Special Operations	
Yes	56.3%
No	43.7%

Procedure

All service members signed informed consent through IRB-approved protocols at WRNMMC that allowed for standard of care clinical data to be prospectively collected, and also available for retrospective analysis. Demographic data were collected from intake questionnaires, and baseline behavioral health assessments on the first day of admission included self-report scales of PTSD Checklist Military Version (PCL-M), Generalized Anxiety Disorder-7 (GAD-7), and the Patient Health Questionnaire (PHQ-9) for posttraumatic stress, anxiety, and depression, respectively. Behavioral health diagnoses were confirmed through in-depth in-person evaluation by the team's psychiatrist. Further, in the first week of the program all service members underwent a comprehensive consultation by a sleep neurologist was obtained and included a thorough sleep history, polysomnography, and a five-day actigraphy recording to characterize any sleep disturbance. In all, over 105 patient-

ID: navin.prajapati Time: 23:55 I Path: //mumnasprod/home$/45417$/AP-PRIJ210003

J_ID: ART NO: 10.1037/pri0000146 Date: 27-February-21 Page: 5 Total Pages: 11 4/Color Figure(s) FNTWOCOL

provider encounters occurs in the evaluation and treatment of the patients in the four-week IOP including blood work, neuroimaging, electrophysiological and physiological assessments, vision and hearing assessments. All information is captured and stored in "The National Intrepid Center of Excellence (NICoE) Clinical Research Database to study the Natural History of Traumatic Brain Injury and Psychological Health Outcomes in Military Personnel" protocol, from which the present data were obtained during the patient's first week at NICoE.

The present study was conducted at NICoE in accordance with all Department of Defense; Departments of the Army, Navy, and Air Force; and federal laws, regulations, and standards after review and approval by the Institutional Review Board at Walter Reed National Military Medical Center, Bethesda, Maryland. All data for analysis were de-identified and analyzed in batch to assure patient confidentiality.

Measures

Polysomnography

Polysomnography continually records neurophysiologic, cardiopulmonary, and other physiological measures typically over an entire night to identify abnormalities of sleep, wakefulness, sleep-wake transition, and organ functioning during sleep such as apneas (Jafari & Mohsenin, 2010). These readings produce measures of time spent in sleep stages, sleep latency, respiratory functioning, and heart rate, among others, and were used as measures of objective sleep functioning in the present study.

Pittsburgh Sleep Quality Index (PSQI)

The PSQI comprehensively examines sleep over a one-month period (Buysse et al., 1989). This 10-item self-report measure evaluates self-reported sleep efficiency and sleep quality. The PSQI is made up of seven components that are combined into a global score of sleep quality, with higher scores indicating lower sleep quality. This measure demonstrates good psychometric properties (Backhaus et al., 2002). Additionally, the PSQI assesses frequency of problems sleeping caused by bad dreams, which was used in the present study as a measure of idiopathic bad dreams and nightmares.

Epworth Sleepiness Scale

The Epworth Sleepiness Scale is an eight-item self-report questionnaire designed to measure a patient's general daytime sleepiness (Johns, 1991). Items assess how likely the patient is to fall asleep in a number of contexts including sitting and talking to someone or as a passenger in a vehicle. This scale has demonstrated a high-level of reliability (Johns, 1992).

PTSD Checklist-Military (PCL-M)

This 17-item self-report assessment is a common measure of PTSD symptoms and has demonstrated adequate psychometric properties (Weathers et al., 1993). The military version of the PCL assesses PTSD symptoms specifically related to a military experience. For the present study, posttraumatic bad dreams and nightmares were measured using item two of the PCL-*M* ("Repeated, disturbing dreams of a stressful experience from the past;" Weathers et al., 1993). This approach is consistent with previous studies (e.g., Greenbaum et al., 2017; Pigeon et al., 2013).

Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 (Kroenke & Spitzer, 2002) is a nine-item depression measure that has been found to have excellent reliability and strong validity (Kroenke et al., 2001). Item nine (i.e., "thoughts that you would be better off dead or of hurting yourself in some way") of the PHQ-9 was used as a binary measure of suicidal ideation (Kroenke & Spitzer, 2002; p. 6). This use is consistent with past literature and has been found to be related to increased suicide risk in veterans (Louzon et al., 2016).

Data Analysis

All analyses were conducted using IBM SPSS 25.0. T-tests or appropriate nonparametric tests were used to compare demographics of patients with and without suicidal ideation. Odds of suicidal ideation were obtained via logistic regression. To assess the relationship of traumatic bad dreams to suicidal ideation, the lowest item rating on the PCL-*M* ("Not during the past month") was used as the referent group; each of the other levels of response to this item was compared to this response. For traumatic bad dreams, patients who reported being "not at all" bothered by bad dreams

ID: navin.prajapati Time: 23:55 I Path: //mumnasprod/home$/45417$/AP-PRIJ210003

J_ID: ART NO: 10.1037/pri0000146 Date: 27-February-21 Page: 6 Total Pages: 11 4/Color Figure(s) FNTWOCOL

related to their traumatic event were the referent group. Analyses of bad dreams or nightmares controlled for the use of prazosin, an alpha-1 receptor antagonist associated with improvement of posttraumatic nightmares (George et al., 2016). Complete data were not available for all patients due to the nature of the clinical database, which precluded running analyses to control for all relevant covariates. Therefore, analyses were conducted on individual items to preserve power and prevent overmatching and multicollinearity. Furthermore, this approach allowed individual symptoms to be analyzed in an effort to understand the role of each sleep symptom within the context of the many other factors that may contribute to suicidal ideation in service members.

Results

Among the objective measures of sleep examined, two were significant at $p < .05$ (see Table 2). REM latency was associated with increased odds of suicidal ideation (*OR* = 1.00, 95% CI: 1.00, 1.01). Time in Stage N2 Sleep was related to decreased odds of suicidal ideation (*OR* = .98, 95% CI: .96, 1.00). Nonsignificant objective measures are described in Table 2. The association of subjective sleep measures to suicidal ideation also was examined with all showing a significant association to suicidal ideation. For every one unit increase in sleep quality (PSQI), the odds of suicidal ideation increase by 1.17 (95% CI: 1.06, 1.29). The odds of suicidal ideation increased by 1.05 (95% CI: 1.01. 1.09) for every unit of increase in sleepiness (ESS).

Patients who reported bad dreams "once or twice per week" on the PSQI had increased odds of 4.39 (95% CI: 2.23, 8.65) for suicidal ideation compared to patients who did not report bad dreams in the last month. For patients reporting bad dreams "three or more times per week," odds of suicidal ideation increased by 7.89 (95% CI: 4.04, 15.40) compared to the referent group. By comparison patients

Table 2
Odds Ratios for Individual Sleep Characteristics

Variable	*N*	*B*	*SE*	*OR*	95% CI *LL*	95% CI *UL*
Arousal Index	862	0.01	0.01	1.01	0.99	1.04
Wake After Sleep Onset	977	−0.01	0.00	0.99	0.99	1.00
Sleep Latency	977	0.00	0.01	1.00	0.99	1.01
REM Latency*	977	0.00	0.00	1.00	1.00	1.01
Sleep Efficiency	977	0.02	0.01	1.02	0.99	1.04
Mean HR	977	0.02	0.01	1.02	1.00	1.04
Minimum HR	977	0.01	0.01	1.01	0.98	1.03
Maximum HR	977	0.01	0.00	1.01	1.00	1.01
Total Sleep Time	977	0.00	0.00	1.00	1.00	1.01
Supine Sleep Time	976	0.00	0.00	1.00	1.00	1.00
Stage N1 Sleep	977	−0.00	0.02	1.00	0.96	1.04
Stage N2 Sleep*	977	−0.02	0.01	0.98	0.96	1.00
Slow-wave Sleep	977	0.02	0.01	1.02	1.00	1.05
REM	977	0.02	0.02	1.02	0.98	1.05
*PSQI Total Score (Sleep Quality)***	489	0.16	0.05	1.17	1.06	1.29
*ESS (Sleepiness)**	1,188	0.05	0.02	1.05	1.01	1.09
Bad Dreams[1, 2]	1,193					
Less than once a week		0.68	0.39	1.98	0.93	4.21
*Once or twice a week****		1.48	0.35	4.39	2.23	8.65
*Three or more times a week****		2.01	0.34	7.89	4.04	15.40
Traumatic Bad Dreams[1, 2]	1,170					
A little bit		0.40	0.35	1.49	0.76	2.95
*Moderately****		1.44	0.33	4.20	2.19	8.04
*Quite a bit****		1.62	0.33	5.04	2.62	9.67
*Extremely****		2.29	0.38	9.90	4.71	20.83

Note. CI = confidence interval; *LL* = lower limit; *UL* = upper limit; *OR* = odds ratio; PSQI = Pittsburgh Sleep Quality Index; ESS = Epworth Sleepiness Scale. Italics represent self-reported sleep measures.
[1] Analyses controlled for use of Prazosin. [2] Results are calculated with the lowest value as the indicator.
* $p < .05$. ** $p < .01$. *** $p < .001$.

ID: navin.prajapati Time: 23:55 I Path: //mumnasprod/home$/45417$/AP-PRIJ210003

J_ID: ART NO: 10.1037/pri0000146 Date: 27-February-21 Page: 7 Total Pages: 11 4/Color Figure(s) FNTWOCOL

reporting bad dreams "less than once a week" were no more likely to report suicidal ideation that were those in the referent group (*OR* = 1.98, 95% CI: .93, 4.21). The use of prazosin was controlled for in all of these analyses.

Patients who reported being "moderately bothered" by traumatic bad dreams had an increased odds of 4.20 (95% CI: 2.19, 8.04) compared to the referent group. Patients who reported being bothered "quite a bit" by traumatic bad dreams had an increased odds of suicidal ideation compared to patients who were "not at all" bothered by bad dreams of their trauma (*OR* = 5.04, 95% CI: 2.62, 9.67). For patients reporting being "extremely bothered" by traumatic bad dreams, the odds of suicidal ideation increased by 9.90 (95% CI: 4.71, 20.83) compared to the referent group. However, patients who reported being bothered by bad dreams or nightmares of their traumatic event "a little bit" did not differ significantly from the referent group (*OR* = 1.49, 95% CI: .76, 2.95). Again, each analysis controlled for the use of prazosin.

Discussion

The present results add to the nascent body of research examining objectively measured sleep quality as it relates to suicidal ideation (Bernert, Hom et al., 2017; Bernert, Luckenbaugh et al., 2017; Gupta & Jarosz, 2018). To our knowledge, this was the first study to find REM latency and time spent in Stage N2 to be significantly related to suicidal ideation. However, these relations were small suggesting these factors do not play a meaningful role in suicidal ideation. Further, there was no evidence of a relationship between objectively measured sleep indices previous identified as suicide correlates in the literature. Variables including respiratory disturbance index, apnea-hypopnea index, oxygen desaturation index, wake after sleep onset, time spent in Stage IV sleep, and sleep efficiency did not significantly differ between patients with and without suicidal ideation. Further, although Bishop et al. (2020) identified a relationship between sleep-related breathing disorders, including OSA, and suicide attempts, the apnea-hypopnea index, a measure of OSA severity (Caples et al., 2005), used in the present study was not significant. Notably, patients in the NICoE IOP have reported anecdotally that they sleep better during their sleep studies than on a typical night in their own bed. Therefore, it is possible that results obtained during the polysomnography may not accurately reflect an average night's sleep.

Consistent with the extant literature (e.g., Bernert et al., 2014; Tae et al., 2019), all subjective sleep reports in the present study were significantly associated with suicidal ideation. These measures also were the only ones to produce meaningful odds ratios. Additional research is needed to better understand their possible role in suicidal ideation.

Bad dreams or nightmares, and specifically posttraumatic bad dreams and nightmares, were associated with large increases in odds of suicidal ideation. This may be explained in part by emotion regulation, as Ward-Ciesielski and colleagues (2018) found emotion regulation mediated the relationship of nightmares to both suicide risk and suicide attempts. However, these results were demonstrated in a sample recruited from Amazon's Mechanical Turk (MTurk), an online crowdsourcing website, and may not be generalizable to treatment-seeking or military samples such as in the present study. Self-reported sleep quality also showed increased odds of suicidal ideation. This may be explained by thwarted belongingness, or feelings of social disconnect, which has been found to mediate of the relationship of insomnia symptoms to suicidal ideation (Chu et al., 2017).

This study was strengthened by the use of a large dataset of patients with diverse military characteristics. However, demographic characteristics, such as race and gender, as well as the treatment-seeking characteristics of the sample were rather homogenous. Therefore, these results may not be generalizable to all patients and require replication in additional samples. The use of clinical data provide an understanding of these important relationships in a naturalistic setting and are more applicable to patients seeking care. However, the use of clinical data resulted in some variables not being available for all patients, as some measures were changed or updated over the course of nearly ten years of data collection. Thus, due to differences in available data, as well as issues with multicollinearity, the present study was unable to conduct analyses that controlled for possible covariates such as comorbid symptoms.

To our knowledge, this is the first study to examine objective measures of sleep in relation to suicidal ideation in active duty service members. The present study also replicated and expanded previous findings regarding the role of subjective sleep reports found in nonmilitary samples (e.g., Bernert, Hom et al., 2017; Gupta & Jarosz, 2018; Tae et al.,

ID: navin.prajapati Time: 23:55 I Path: //mumnasprod/home$/45417$/AP-PRIJ210003

J_ID: ART NO: 10.1037/pri0000146 Date: 27-February-21 Page: 8 Total Pages: 11 4/Color Figure(s) FNTWOCOL

2019; Zuromski et al., 2017). The replication of these earlier findings strengthens the confidence in results of the present study. Future studies should examine the temporal relationship of nightmares and suicidal thoughts utilizing longitudinal or ecological momentary assessment methods.

Clinical Implications and Conclusion

These results also highlight the importance of the *subjective* view of sleep. A sleep study or period of monitoring via actigraphy may not be necessary to understand the impact of poor sleep on suicidal ideation; rather, it is the patient's subjective experience that appears critical to the evaluation of suicidal risk. Notably, in the present study bad dreams or nightmares, both idiopathic and traumatic, were related to a substantial increase in odds of suicidal ideation, suggesting these factors may be an important inclusion for a comprehensive risk assessment. These results also may provide a secondary avenue for reduction of suicidal risk through sleep targeted treatments. The Departments of Defense and VA recommend Brief Behavioral Therapy for Insomnia (BBTI) and strongly recommend Cognitive Behavioral Therapy for Insomnia (CBT-I) for treatment and management of insomnia (Management of Chronic Insomnia Disorder & Obstructive Sleep Apnea Work Group, 2019). Additionally, they suggest the use of *short-term* pharmacotherapy. Incorporating sleep treatments in conjunction with treatment for suicidal ideation may aid in further reducing suicidal risk.

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The impact of military factors on sleep should be considered when working to improve sleep for these patients in order to mitigate suicidal risk, particularly military-specific environmental and occupational ones. These can include, but are not limited to, characteristics related to sleeping in barracks or sleeping in a deployed environment where sleep is frequently disturbed, impacted by the warzone, and affected by missing a familiar bed partner. Shift work and working in environments that may negatively affect sleep, such as being stationed on a submarine, ship, or as part of an air crew, should be considered and may require tailored interventions.

In conclusion, subjective reports of sleep disturbances were found to be associated with increased odds of suicidal ideation and may provide a critical area for therapeutic intervention for patients with suicidal ideation. As suicide is a current public health crisis facing the U.S. military and nation as a whole, it is important that providers consider all possible avenues to mitigate suicidal risk. Therefore, as an adjunct to a provider's standard procedures when conducting a risk assessment, providers should evaluate subjective sleep symptoms, particularly bad dreams and nightmares, in combination with comorbid conditions. In addition to being a provisionally important indicator for suicidal ideation, subjective sleep assessments also may serve as markers for efficacy of treatment. Clinic leaders and administrators may consider requiring regular screening for sleep disturbances and their inclusion in all suicide risk assessments. Though requiring replication, the present results suggest bad dreams and nightmares, particularly trauma-related ones, hold promise as a possible point of intervention to help reduce suicidal ideation in active-duty service members.

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ID: navin.prajapati Time: 23:55 I Path: //mumnasprod/home$/45417$/AP-PRIJ210003

APPENDIX H: PTSD CHECKLIST – MILITARY VERSION

PTSD CheckList – Military Version (PCL-M)

Patient's Name: _____ **Date:** _____

SSN:_____ **Service:**_____**Rank:**_____

Instruction to patient: **Below is a list of problems and complaints that veterans sometimes have in response to stressful military experiences. Please read each one carefully, put an "X" in the box to indicate how much you have been bothered by that problem *in the last month*.**

		Frequency:				
No.	**Problem or Complaint:**	**Not at all (1)**	**A little bit (2)**	**Moderately (3)**	**Quite a bit (4)**	**Extremely (5)**
1.	Repeated, disturbing *memories, thoughts,* or *images* of a stressful military experience?					
2.	Repeated, disturbing *dreams* of a stressful military experience?					
3.	Suddenly *acting* or *feeling* as if a stressful military experience *were happening again* (as if you were reliving it)?					
4.	Feeling very upset when something reminded you of a stressful military experience?					
5.	Having *physical reactions* (e.g., heart pounding, trouble breathing, or sweating) when *something reminded* you of a stressful military experience?					
6.	Avoid *thinking about* or *talking* about a stressful military experience or avoid *having feelings* related to it?					
7.	Avoid *activities* or *talking about* a stressful military experience or avoid *having feelings* related to it?					
8.	Trouble *remembering important parts* of a stressful military experience?					
9.	Loss of *interest* in things that you used to enjoy?					
10.	Feeling *distant* or *cut off* from other people?					
11.	Feeling *emotionally numb* or being unable to have loving feelings for those close to you?					
12.	Feeling as if your *future* will somehow be *cut short*?					
13.	Trouble *falling* or *staying* asleep?					
14.	Feeling *irritable* or having *angry outbursts*?					
15.	Having *difficulty* concentrating?					
16.	Being "*super alert*" or watchful on guard?					
17.	Feeling *jumpy* or easily startled?					

PCL-M for DSM-IV (11/1/94)

Weathers, F.W., Huska, J.A., Keane, T.M. PCL-M for DSM-IV. Boston; National Center for PTSD – Behavioral Science Division, 1991.

APPENDIX I: PTSD CHECKLIST – CIVILIAN VERSION

PTSD CheckList – Civilian Version (PCL-C)

Client's Name: _____

Instruction to patient: Below is a list of problems and complaints that veterans sometimes have in response to stressful life experiences. Please read each one carefully, put an "X" in the box to indicate how much you have been bothered by that problem *in the last month*.

No.	Response	Not at all (1)	A little bit (2)	Moderately (3)	Quite a bit (4)	Extremely (5)
1.	Repeated, disturbing *memories, thoughts, or images* of a stressful experience from the past?					
2.	Repeated, disturbing *dreams* of a stressful experience from the past?					
3.	Suddenly *acting* or *feeling* as if a stressful experience *were happening* again (as if you were reliving it)?					
4.	Feeling *very upset* when *something reminded* you of a stressful experience from the past?					
5.	Having *physical reactions* (e.g., heart pounding, trouble breathing, or sweating) when *something reminded* you of a stressful experience from the past?					
6.	Avoid *thinking about* or *talking about* a stressful experience from the past or avoid *having feelings* related to it?					
7.	Avoid *activities* or *situations* because they *remind you* of a stressful experience from the past?					
8.	Trouble *remembering important parts* of a stressful experience from the past?					
9.	Loss of *interest in things that you used to enjoy?*					
10.	Feeling *distant* or *cut* off from other people?					
11.	Feeling *emotionally numb* or being unable to have loving feelings for those close to you?					
12.	Feeling as if your *future* will somehow be *cut short*?					
13.	Trouble *falling* or *staying asleep*?					
14.	Feeling *irritable* or having *angry outbursts*?					
15.	Having *difficulty concentrating*?					
16.	Being *"super alert"* or watchful on guard?					
17.	Feeling *jumpy* or easily startled?					

PCL-M for DSM-IV (11/1/94) Weathers, Litz, Huska, & Keane National Center for PTSD - Behavioral Science Division

APPENDIX J: PATIENT HEALTH QUESTIONNAIRE – 9 (PHQ-9)

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
☐	☐	☐	☐

APPENDIX K: GENERALIZED ANXIETY DISORDER SCREENER (GAD-7)

Generalized Anxiety Disorder Screener (GAD-7)

Over the *last 2 weeks*, how often have you been bothered by the following problems?	Not at all	Several Days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritated	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3
	Add columns			
	Total Score			
8. 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

When did the symptoms begin? _____

APPENDIX L: PITTSBURGH SLEEP QUALITY INDEX (PSQI)

Name:_____ Date: _____

Pittsburgh Sleep Quality Index (PSQI)

Instructions: The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. **Please answer all questions.**

1. During the past month, what time have you usually gone to bed at night? _____
2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night? _____
3. During the past month, what time have you usually gotten up in the morning? _____
4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.) _____

5. During the past month, how often have you had trouble sleeping because you…	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. Cannot get to sleep within 30 minutes				
b. Wake up in the middle of the night or early morning				
c. Have to get up to use the bathroom				
d. Cannot breathe comfortably				
e. Cough or snore loudly				
f. Feel too cold				
g. Feel too hot				
h. Have bad dreams				
i. Have pain				
j. Other reason(s), please describe:				
6. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?				
	No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem
8. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?				
	Very good	Fairly good	Fairly bad	Very bad
9. During the past month, how would you rate your sleep quality overall?				

	No bed partner or room mate	Partner/room mate in other room	Partner in same room but not same bed	Partner in same bed
10. Do you have a bed partner or room mate?				
	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
If you have a room mate or bed partner, ask him/her how often in the past month you have had:				
a. Loud snoring				
b. Long pauses between breaths while asleep				
c. Legs twitching or jerking while you sleep				
d. Episodes of disorientation or confusion during sleep				
e. Other restlessness while you sleep, please describe:				

APPENDIX M: EPWORTH SLEEPINESS SCALE (ESS)

Epworth Sleepiness Scale[11]

How likely are you to nod off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times.

Even if you haven't done some of these things recently, try to work out how they would have affected you. It is important that you answer each question as best you can.

Use the following scale to choose the most appropriate number for each situation.

	Would never nod off 0	Slight chance of nodding off 1	Moderate chance of nodding off 2	High chance of nodding off 3
Sitting and reading				
Watching TV				
Sitting, inactive, in a public place (e.g., in a meeting, theater, or dinner event)				
As a passenger in a car for an hour or more without stopping for a break				
Lying down to rest when circumstances permit				
Sitting and talking to someone				
Sitting quietly after a meal without alcohol				
In a car, while stopped for a few minutes in traffic or at a light				

Add up your points to get your total score. A score of 10 or greater raises concern: you may need to get more sleep, improve your sleep practices, or seek medical attention to determine why you are sleepy.

APPENDIX N: NEUROBEHAVIORAL SYMPTOM INVENTORY (NSI)

Neurobehavioral Symptom Inventory (NSI)

Please rate the following symptoms with regard to how much they have disturbed you IN THE LAST 2 Weeks.
The purpose of this inventory is to track symptoms over time. Please do not attempt to score.

0 = None – Rarely if ever present; not a problem at all

1 = Mild – Occasionally present, but it does not disrupt my activities; I can usually continue what I'm doing; doesn't really concern me.

2 = Moderate – Often present, occasionally disrupts my activities; I can usually continue what I'm doing with some effort; I feel somewhat concerned.

3 = Severe – Frequently present and disrupts activities; I can only do things that are fairly simple or take little effort; I feel I need help.

4 = Very Severe – Almost always present and I have been unable to perform at work, school or home due to this problem; I probably cannot function without help.

Symptoms	**0**	**1**	**2**	**3**	**4**
Feeling Dizzy	O	O	O	O	O
Loss of balance	O	O	O	O	O
Poor coordination, clumsy	O	O	O	O	O
Headaches	O	O	O	O	O
Nausea	O	O	O	O	O
Vision problems, blurring, trouble seeing	O	O	O	O	O
Sensitivity to light	O	O	O	O	O
Hearing difficulty	O	O	O	O	O
Sensitivity to noise	O	O	O	O	O
Numbness or tingling on parts of my body	O	O	O	O	O
Change in taste and/or smell	O	O	O	O	O
Loss of appetite or increased appetite	O	O	O	O	O
Poor concentration, can't pay attention, easily distracted	O	O	O	O	O
Forgetfulness, can't remember things	O	O	O	O	O
Difficulty making decisions	O	O	O	O	O
Slowed thinking, difficulty getting organized, can't finish things	O	O	O	O	O
Fatigue, loss of energy, getting tired easily	O	O	O	O	O
Difficulty falling or staying asleep	O	O	O	O	O
Feeling anxious or tense	O	O	O	O	O
Feeling depressed or sad	O	O	O	O	O
Irritability, easily annoyed	O	O	O	O	O
Poor frustration tolerance, feeling easily overwhelmed by things	O	O	O	O	O

Date:

Name:

Medical Record #:

Used with permission: Cicerone,KD: J Head Tr Rehabil 1995;10(3):1-17

APPENDIX O: OHIO STATE UNIVERSITY TBI IDENTIFICATION METHOD

Name: _____ Current Age: _____ Interviewer Initials: _____ Date: _____

Ohio State University TBI Identification Method — Interview Form

Step 1

Ask questions 1-5 below. Record the cause of each reported injury and any details provided spontaneously in the chart at the bottom of this page. You do not need to ask further about loss of consciousness or other injury details during this step.

I am going to ask you about injuries to your head or neck that you may have had anytime in your life.

1. In your lifetime, have you ever been hospitalized or treated in an emergency room following an injury to your head or neck? Think about any childhood injuries you remember or were told about.
   ☐ No ☐ Yes—Record cause in chart
2. In your lifetime, have you ever injured your head or neck in a car accident or from crashing some other moving vehicle like a bicycle, motorcycle or ATV?
   ☐ No ☐ Yes—Record cause in chart
3. In your lifetime, have you ever injured your head or neck in a fall or from being hit by something (for example, falling from a bike or horse, rollerblading, falling on ice, being hit by a rock)? Have you ever injured your head or neck playing sports or on the playground?
   ☐ No ☐ Yes—Record cause in chart
4. In your lifetime, have you ever injured your head or neck in a fight, from being hit by someone, or from being shaken violently? Have you ever been shot in the head?
   ☐ No ☐ Yes—Record cause in chart
5. In your lifetime, have you ever been nearby when an explosion or a blast occurred? If you served in the military, think about any combat- or training-related incidents.
   ☐ No ☐ Yes—Record cause in chart

Interviewer instruction:
If the answers to any of the above questions are "yes," go to Step 2. If the answers to all of the above questions are "no," then proceed to Step 3.

Step 2

Interviewer instruction: If the answer is "yes" to any of the questions in Step 1 ask the following additional questions about each reported injury and add details to the chart below.

Were you knocked out or did you lose consciousness (LOC)?

If yes, how long?

If no, were you dazed or did you have a gap in your memory from the injury?

How old were you?

Step 3

Interviewer instruction: Ask the following questions to help identify a history that may include multiple mild TBIs and complete the chart below.

Have you ever had a period of time in which you experienced multiple, repeated impacts to your head (e.g. history of abuse, contact sports, military duty)?

If yes, what was the typical or usual effect-–were you knocked out (Loss of Consciousness - LOC)?

If no, were you dazed or did you have a gap in your memory from the injury?

What was the most severe effect from one of the times you had an impact to the head?

How old were you when these repeated injuries began? Ended?

Step 1	Step 2						
	Loss of consciousness (LOC)/knocked out				Dazed/Mem Gap		Age
Cause	No LOC	< 30 min	30 min-24 hrs	> 24 hrs	Yes	No	

If more injuries with LOC: How many?_____ Longest knocked out?_____ How many ≥ 30 mins.?_____ Youngest age? _____

Step 3	Typical Effect		Most Severe Effect				Age	
Cause of repeated injury	Dazed/ memory gap, no LOC	LOC	Dazed/ memory gap, no LOC	LOC < 30 min	LOC 30 min - 24 hrs.	LOC > 24 hrs.	Began	Ended

Adapted with permission from the Ohio State University TBI Identification Method (Corrigan, J.D., Bogner, J.A. (2007). Initial reliability and validity of the OSU TBI Identification Method. J Head Trauma Rehabil, 22(6):318-329.

APPENDIX P: SATISFACTION WITH LIFE SCALE

Satisfaction with Life Scale

Scale:

Instructions: Below are five statements that you may agree or disagree with. Using the 1 - 7 scale below, indicate your agreement with each item by placing the appropriate number on the line preceding that item. Please be open and honest in your responding.

- 7 - Strongly agree
- 6 - Agree
- 5 - Slightly agree
- 4 - Neither agree nor disagree
- 3 - Slightly disagree
- 2 - Disagree
- 1 - Strongly disagree

____ In most ways my life is close to my ideal.

____ The conditions of my life are excellent.

____ I am satisfied with my life.

____ So far I have gotten the important things I want in life.

____ If I could live my life over, I would change almost nothing.

Scoring:

Though scoring should be kept continuous (sum up scores on each item), here are some cut-offs to be used as benchmarks.

- 31 - 35 Extremely satisfied
- 26 - 30 Satisfied
- 21 - 25 Slightly satisfied
- 20 Neutral
- 15 - 19 Slightly dissatisfied
- 10 - 14 Dissatisfied
- 5 - 9 Extremely dissatisfied