ROLE OF SLEEP IN EXPOSURE THERAPY FOR POSTTRAUMATIC STRESS DISORDER IN OEF/OIF COMBAT VETERANS

by

FRANKLIN MESA
M.S. University of Central Florida, 2013
B.S. University of Maryland, College Park, 2009

A dissertation submitted in partial fulfillment of the requirements
for the degree of Doctor of Philosophy
in the Department of Psychology
in the College of Sciences
at the University of Central Florida
Orlando, Florida

Summer Term
2016

Major Professor: Deborah C. Beidel

ABSTRACT

Exposure therapy is theorized to reduce posttraumatic stress disorder (PTSD) symptomatology by promoting habituation/extinction of fear responses to trauma-related cues. Empirical evidence indicates that emotional memory, including habituation/extinction learning, is enhanced by sleep. However, service members with combat-related PTSD often report disturbed sleep. In this study, quality of sleep and indicators of extinction learning were examined in veterans of recent wars who had completed an exposure-based PTSD intervention. Fifty-five participants were categorized into two groups based on self-reported quality of sleep: low sleep disruption severity (LSDS; N = 29) and high sleep disruption severity (HSDS; N = 26). Participants in the LSDS group exhibited faster habituation to their traumatic memories and reported less PTSD symptomatology during and following treatment relative to participants in the HSDS group. These findings indicate that individuals with combat-related PTSD reporting less disturbed sleep experience greater extinction learning during exposure therapy. Thus, incorporating interventions that target PTSD-related sleep disturbances may be one way to maximize exposure therapy outcomes in service members with PTSD.

To Yolanda Mesa, my mother, whose faith, love, and resilience inspired me to reach farther and higher, and to Marybelle Mesa, my wife, for her support and love, and above all else, her patience.

TABLE OF CONTENTS

LIST OF TABLES

CHAPTER 1: INTRODUCTION

In March of 2014, the United States Department of Veterans Affairs (VA) reported that more than 1.05 million veterans of Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF) and Operation New Dawn (OND) have sought medical or psychiatric services at a VA facility (VA, 2014). More than 56% of these service members received at least one psychiatric diagnosis, a proportion surpassed only by diagnoses of musculoskeletal and connective tissue diseases. The most frequently diagnosed psychiatric disorder is posttraumatic stress disorder (PTSD). PTSD is conceptualized as a constellation of psychological symptoms developing after a traumatic experience in which an individual is exposed to actual or threatened death, serious injury or sexual violence (APA, 2013). The prolonged use of ground combat and occupation in the recent US military engagements has exposed a large proportion of service members to a variety of extremely stressful and threatening situations, including receiving gunfire, handling other service members killed in action, witnessing the detonation of improvised explosive devices or killing enemy combatants (Hoge et al., 2004; Kline et al., 2010). Thus, military personnel deployed to combat zones are clearly at an increased risk to develop PTSD.

The symptoms of the disorder begin after a traumatic experience and are categorized into four clusters: intrusion (e.g., trauma-related nightmares and flashbacks); avoidance (e.g., avoidance of trauma-related thoughts or feelings or external reminders); negative alterations in cognitions and mood (e.g., significantly decreased interest in activities and feelings of detachment from others); and alterations in arousal (e.g., hypervigilance and sleep disturbance; APA, 2013). Although presently conceptualized as a symptom of PTSD, sleep disturbances have

received increased attention as a potential core feature of the disorder (Babson & Feldner, 2010; Spoormaker & Montgomery, 2008).

Many individuals report acute sleep disturbances after a traumatic event (Babson & Feldner, 2010), a response that perhaps is a normal reaction to significant stress (Bonanno, 2004; Pillar, Malhotra & Lavie, 2000). Among survivors of a natural disaster, sleep disturbance was the most frequently endorsed symptom, as 63% and 46% reported difficulty sleeping at 3- and 8 weeks posttrauma, respectively (Kato, Asukai, Miyake, Minakawa & Nisiyama, 1996). Similarly, 70% of survivors of the 1995 bombing of US federal offices reported sleep disturbances, with more than half endorsing trauma-related nightmares six months after the trauma (North et al., 1999). Additionally, empirical evidence suggests that sleep disturbances begin soon after a trauma and may be precursors of the later onset of PTSD. In these studies, self-reported insomnia at one month posttrauma predicted a diagnosis of PTSD 12 months later (Koren, Amon, Lavie & Klein, 2002) and trauma-related nightmares soon after a trauma were related to significantly increased PTSD severity 6 weeks later (Mellman, David, Bustamante, Torres & Fins, 2001). Furthermore, Luxton and colleagues (2011) found that service members with combat experiences (not necessarily defined as traumatic events) were more likely than service members without such experiences to report shortened sleep durations (i.e., less than 6 hours). In turn, reduced sleep duration was related to an increased the risk of screening positive for PTSD.

Rates of sleep disturbances are predictably elevated among individuals diagnosed with PTSD, as the common occurrence of insomnia and nightmares may interrupt sleep and create anticipatory anxiety about sleep periods (Harvey et al., 2003). Accordingly, combat veterans

with PTSD frequently report multiple sleep difficulties, including initial, middle and late insomnia, nightmares (with combat and non-combat themes), startle awakenings and violent movement/thrashing in bed (Mellman, Kulick-Bell, Ashlock & Nolan, 1995; Neylan et al., 1998). However, although subjective reports of sleep disturbance are consistent in patients with PTSD, objective examinations of sleep have produced mixed outcomes and do not always coincide with the subjective reports (Harvey et al., 2003). Using polysomnography, prior studies have found significantly reduced sleep efficiency (Mellman et al., 1995; Mellman, Nolan, Hebding, Kulick-Bell & Dominguez, 1997) and more frequent awakenings (Mellman et al., 1995; Mellman, David, Kulick-Bell, Hebding & Nolan, 1995) in individuals with PTSD, indicating that more time was spent awake during sleep periods relative to controls. Other studies have failed to find these effects using actigraphy (Dagan, Zinger, & Lavie, 1997) or polysomnography (Engdahl, Eberly, Hurwitz, Mahowald, & Blake, 2000; Hurwitz, Mahowald, Kuskowski, & Engdahl, 1998), instead reporting that civilians and combat veterans with PTSD may overestimate their sleep latency and underestimate their total sleep duration. Nevertheless, a meta-analysis of polysomnographic examinations of sleep in patients with PTSD revealed greater rapid eye movement (REM) density (i.e., greater frequency of eye movements per unit of time), reduced slow wave sleep (stages 3 and 4 of non-REM (NREM)), and greater stage 1 sleep relative to individuals without PTSD (Kobayashi, Boarts & Delahanty, 2007). REM sleep is characterized by paradoxical general paralysis of the body accompanied by rapid eye movements and the peak of brain activity during sleep. Most dreams occur during REM stages, which become progressively longer and consume a larger proportion of the sleep cycle later in the sleep period. In contrast, NREM sleep consists of four stages (stages 1 through 4) wherein sleep

progressively deepens from stage 1 to stage 4 (Shneerson, 2000). Thus, the meta-analytic findings support the occurrence of the nightmares during REM stages and increased light, non-restorative sleep among individuals with PTSD.

Sleep disturbances experienced with PTSD contribute significantly to daytime impairment and may contribute to the maintenance of the disorder (Belleville, Guay & Marchand, 2009; Maher, Rego & Asnis, 2006; Rothbaum & Mellman, 2001; Spoormaker & Montgomery, 2008). In addition to impaired work and social functioning, deficits in cognitive functioning may occur as well. For example, a considerable volume of empirical evidence indicates that sleep has a significant effect on memory consolidation (*for review see* Diekelman, Wilhelm & Born, 2009). As defined by Diekelmann and Born (2010), consolidation is the process whereby new memories encoded during wake periods become stable representations and are integrated into the network of preexisting long-term memories. The consolidation of memory and learning are enhanced by subsequent sleep, including emotional memories and learning. This effect seems to be mediated largely by the amygdala and its projections to other areas of the brain involved in memory consolidation, such as the hippocampus (McGaugh, 2004; Phelps & LeDoux, 2005). Amygdala activity is heightened during REM sleep (Maquet et al., 1996; Nofzinger, 2005), which is the specific stage of sleep often found to enhance emotional memory consolidation (Diekelman et al., 2009). Furthermore, greater emotional memory consolidation is associated with enhanced activity in hippocampal and medial prefrontal cortical (mPFC) regions (Sterpenich et al., 2007), indicating that amygdala activity during REM may enhance connectivity between the hippocampus and mPFC (Diekelman et al., 2009). These brain regions

are implicated in functional neuroanatomical examinations of PTSD (Liberzon & Sripada, 2007) as well as fear conditioning and extinction (Moustafa et al., 2013).

To date, exposure-based interventions have demonstrated the greatest efficacy in reducing combat-related PTSD symptomology (Foa, Hembree, & Rothbaum, 2007; Frueh, Turner & Beidel, 1995; Goodson et al., 2011; Institute of Medicine, 2007). Based on an extinction paradigm, exposure therapy for PTSD is intended to produce habituation, or reduced physiological, behavioral and/or cognitive conditioned (learned) fear responses, to trauma-related cues. This is accomplished through controlled, systematic and repeated contact with feared, trauma-related cues in the absence of actual threat for an extended duration of time (Rothbaum & Schwartz, 2002). This process, called extinction learning, is theorized to weaken the fear-based associations and stimulate the formation of new inhibitory associations that compete with the prior associations (McNally, 2007).

Emerging evidence supports the notion that the enhancing effects of sleep on emotional memory may bolster the learning processes targeted by exposure therapy (Harvey et al., 2014). In an examination of habituation/extinction, Pace-Schott and colleagues (2011) repeatedly presented negatively-valenced or neutral images during two sessions. The sessions were separated by a 2.5 hour period during which participants either slept for 120 minutes or remained awake. Participants who slept demonstrated greater between-session sympathetic habituation (i.e., significantly fewer skin conductance responses in session two relative to session one) to repeated images. However, habituation was not observed in heart rate or subjective ratings of emotional valence and arousal. In another study, Pace-Schott and colleagues (2009) evaluated the effect of sleep on habituation/extinction learning *retention*. The authors implemented a

classical conditioning paradigm wherein two stimuli were paired with a mild shock. Subsequently, one conditioned stimulus was extinguished by repeated presentations without a shock. Following the extinction trials, participants either completed a full night of sleep or remained awake for 12 hours. The stimuli were then presented again. Significantly fewer skin conductance responses to the unextinguished stimulus were observed in the sleep group, demonstrating generalization of extinction of the extinction process. Moreover, although the sleep group exhibited less sympathetic activation to the extinguished stimulus (d = .31), the result was not statistically significant.

More recent investigations have examined the effect of sleep on extinction learning in exposure-based paradigms. While measuring physiological responses, Pace-Schott and colleagues (2012) repeatedly exposed individuals with spider phobia to a spider stimulus. After a delay consisting of a full night of sleep or a 12-hour wake period, participants were repeatedly presented the prior stimulus again followed by repeated presentations of a novel spider stimulus. When presented with the previous spider the second time, distress ratings and skin conductance responses *increased* in the group that remained awake (wake group). Additionally, the wake group demonstrated *sensitization*, as evidenced by an increased distress and sympathetic response when they were later shown the novel spider. In contrast, relative to their initial responses to the first spider, the sleep group exhibited reduced physiological reactivity to the novel spider. Thus, while the wake group failed to retain extinction learning and developed sensitization of the fear response, the sleep group demonstrated greater generalization of extinction learning. These findings support the beneficial effects of sleep on exposure therapy.

Approaching a more traditional exposure therapy procedure, Kleim and colleagues (2013) examined the effect of sleep on extinction learning among individuals diagnosed with spider phobia. Participants completed a single, 45-minute session of virtual reality (VR) exposure followed by a 90-minute sleep or wake period. While the groups did not differ when assessed immediately after the 90-minute period, the sleep group reported significantly reduced distress ratings and negative spider-related cognitions relative to the wake group 1 week later.

Collectively, these studies support the enhancing effects of sleep on exposure-based extinction learning. They also point to one reason why the efficacy of exposure-based therapy for PTSD may be attenuated in combat veterans. Specifically, if one of the cardinal complaints of PTSD is sleep disturbance, then one might expect less consolidation of learning (and therefore poorer outcome) in patients with primary sleep complaints. Presently, the effect of sleep on habituation and extinction learning in a population where sleep disturbance is a primary complaint (e.g., combat-related PTSD) is unknown. As a next step in understanding the role of sleep in the treatment of PTSD, this study examined the relationship between self-reported quality of sleep and extinction learning during an intensive exposure-based intervention in military personnel with combat-related PTSD. The following hypotheses were evaluated:

1) Participants with less self-reported sleep disruption will exhibit significantly greater reductions in peak ratings of distress across exposure sessions.
2) Participants with less self-reported sleep disruption will exhibit significantly greater reductions in baseline ratings of distress across exposure sessions.
3) Participants with less self-reported sleep disruption will achieve overall habituation in fewer sessions.

4) Participants with less self-reported sleep disruption will report fewer symptoms of PTSD following treatment.

CHAPTER 2: METHOD

Data were collected from OEF/OIF military personnel who participated in a Department of Defense-funded clinical trial of a 3-week intensive behavioral intervention for combat-related PTSD, described below, between the dates of May, 2011 and December, 2014. Recruitment strategies for the trial included advertising through various forms of media (e.g., web, radio and local news broadcasts), clinician and case manager referral, and military and community-based events. All participants included in the present study met DSM-IV-TR (APA, 2000) diagnostic criteria for PTSD. Veterans who evidenced primary psychosis, substance dependence, medical conditions that precluded participation in exposure therapy (e.g., cardiac conditions) or suicidality during the intake assessment were excluded from the trial and referred to appropriate service providers. Most participants were prescribed psychiatric medications. Participants were asked to not change current dosages. Medication usage was recorded weekly and any changes were noted. Only one participant included in the present study reported a change in medication during the trial.

The data in this study were from 55 OEF/OIF service members with combat-related PTSD who completed the 3-week program. They were categorized into two groups based on quality of sleep using a procedure described below. Sample demographics and characteristics by group may be found in Table 1.

Treatment

Trauma Management Therapy (TMT; Frueh, Turner, Beidel, Mirabella & Jones, 1996; Turner, Beidel & Frueh, 2005) is a comprehensive behavioral intervention for PTSD consisting

of individual, VR-assisted exposure therapy and by group-based social skills training, anger management and brief behavioral activation for depression. The intervention has demonstrated efficacy in improving combat-related PTSD in Vietnam War veterans (Beidel, Frueh, Uhde, Wong & Mentrikoski, 2011; Frueh et al., 1996). Data for this study were drawn from participants who completed a 3-week long adaptation of TMT in which individual VR-assisted exposure therapy was delivered in the morning and group therapy in the afternoon on each weekday.

During the first individual session of TMT, clinicians gathered additional information about the combat trauma to compose imaginal exposure scenes. Various visual and auditory VR stimuli, as well as olfactory cues, were tested for similarity with the patient's experience and were included during exposure therapy when appropriate. Furthermore, participants were oriented to the 9-point subjective units of distress scale (SUDS) and instructed to report ratings of distress due only to the imaginal scene. Imaginal exposure therapy began in the second session. Exposure sessions typically continued until within-session habituation was achieved (i.e., at least 50% reduction in peak SUDS or return to baseline SUDS) or 90 minutes of exposure had elapsed. Some patients progressed to in vivo exposure therapy after habituating to their imaginal scene. However, for the purposes of this investigation, data to examine extinction learning were drawn only from VR-assisted imaginal exposure sessions. All participants also received group therapy each day.

Measures

Clinician-Administered PTSD Scale (CAPS)

The CAPS (Blake et al., 1995) is a semi-structured interview to assess for DSM-IV-TR criteria of PTSD. Symptoms are rated by frequency and severity from 0 (not present) to 4 (extremely frequent/severe), the sum of which produces the total score. Subjective distress and social and occupational functioning are also evaluated. The CAPS has demonstrated acceptable psychometric properties and diagnostic utility (Weathers, Keane & Davidson, 2001). The interviews were completed at pretreatment and 1-week posttreatment by licensed clinical psychologists, post-doctoral fellows, and doctoral students trained previously by a licensed clinical psychologist familiar with the CAPS. Twenty percent of CAPS interviews were randomly selected for review by a second rater for interrater reliability purposes. Analyses revealed excellent consistency for CAPS total scores (*ICC* = .995) and PTSD diagnosis (*k* = 1.00).

PTSD Checklist – Military Version (PCL-M).

The PCL-M (Weathers, Litz, Herman, Huska, & Keane, 1993) is a 17-item self-report measure of PTSD symptoms related to traumatic military experiences. Although the measure is typically used to assess past month symptoms on a 5-point Likert scale ranging from 1 (not at all) to 5 (extremely), participants in this study evaluated the severity of *past-week* symptomatology. The measure was administered at the beginning of each week of the protocol (e.g., pretreatment/week 1, week 2, and week 3) and during the posttreatment assessment 1 week after the completion of treatment. The PCL-M is widely used with military samples and has

demonstrated excellent reliability and convergent validity with other measures of PTSD (Blanchard, Jones-Alexander, Buckley, & Forneris, 1996; Wilkins, Lang, & Norman, 2011).

Pittsburgh Sleep Quality Index Addendum for PTSD (PSQI-A)

The PSQI-A (Germain, Hall, Krakow, Shear & Buysse, 2005) is a self-report measure of past month disruptive nocturnal behaviors (e.g., nightmares or hot flashes during sleep) related to PTSD. The measure consists of 7 items rated from 0 (not during the past month) to 3 (three or more times a week) and produces a total score ranging from 0 to 21. Prior investigations have demonstrated that a total score ≥ 4 on the PSQI-A reliably indicates a diagnosis of PTSD (Germain et al., 2005; Insana, Hall, Buysse & Germain, 2013). The PSQI-A was administered during the pretreatment and posttreatment assessments.

Subjective Units of Distress (SUDS)

SUDS during exposure sessions were rated on a 9-point scale ranging from 0 (no anxiety) to 8 (extreme anxiety). Clinicians obtained a baseline SUDS prior to initiating exposure therapy. Afterward, SUDS were obtained every 5 to 10 minutes until the end of the session.

Procedure

Participants were classified into two groups based on quality of sleep during treatment: low sleep disruption severity (LSDS) and high sleep disruption severity (HSDS). A median split of the posttreatment PSQI-A determined group assignment, as the posttreatment measure included the treatment period (i.e., "in the last month") in its targeted timeframe. Thus, given the median score of 10, thirty participants were labeled LSDS (PSQI-A ≤ 10) and 26 participants

were labeled HSDS (PSQI-A > 10). Table 2 contains descriptive statistics of the PSQI-A completed at posttreatment.

Extinction learning variables were extracted from the SUDS ratings gathered during imaginal exposure sessions. Expectedly, the number of sessions completed varied across participants. Therefore, sessions were aggregated into three periods (Early, Mid, and Late sessions). Each participant's sessions were grouped such that each period contained as close to an equal number of sessions as possible. For instance, ten sessions of data were divided into four Early, three Mid, and three Late sessions. *Baseline* SUDS level prior to scene initiation and *peak* SUDS level after scene initiation were extracted for each session and averaged by period, resulting in three peak and baseline SUDS means for each participant. Additionally, we examined habituation rate, defined as the number of imaginal exposures completed until peak SUDS rating across sessions decreased by 50%.

Data Preparation and Statistical Analysis

Prior to performing statistical analyses, the data set was surveyed for completeness. One week 3 and one posttreatment PCL-M were not present. These missing values were replaced by the scores from the participants' preceding PCL-M assessments. Additionally, one participant did not complete the post-treatment CAPS and was not included in the CAPS analyses. Subsequently, the variables of interest were examined for normality and univariate outliers within each group. All variables were reasonably normally distributed and did not have outliers, with the exception of Late Baseline SUDS which contained one outlier in the LSDS group. The

outlier was dropped from the group and all further analyses. Examination of Mahalanobis distances did not indicate any multivariate outliers.

Group differences in peak and baseline SUDS across exposure sessions were examined with 2 (group) by 3 (time) mixed factorial ANOVAs. Change in PCL-M total score was assessed with a 2 (group) by 4 (time) mixed factorial ANOVA. Similarly, change in CAPS total score was examined with a 2 (group) by 2 (time) mixed factorial ANOVA. In instances where the assumption of sphericity was violated, the appropriate correction was applied to the significance test (i.e., Greenhouse-Geiser if $\varepsilon < .75$ and Huynh-Feldt if $\varepsilon > .75$). Analyses that resulted in significant main effects or group by time interactions were followed by post-hoc comparisons. Finally, an independent groups t-test was conducted to evaluate mean overall extinction rate. Descriptive statistics and between-group significance testing of habituation measures and symptomatology are contained in Table 3.

CHAPTER 3: RESULTS

Habituation Measures

Peak SUDS level

Analysis of peak SUDS level revealed a significant main effect of time, $F(1.642, 85.77) = 182.197$, $p < .001$, $\eta_p^2 = .778$, but not group, $F(1, 52) = 2.880$, $p < .096$, $\eta_p^2 = .052$. Additionally, a significant group by time interaction was observed, $F(1.642, 85.77) = 4.611$, $p = .018$, $\eta_p^2 = .081$. Post-hoc examination of the simple effects indicated that while there were no group differences in peak SUDS level during Early ($p = .446$) or Mid ($p = .528$) sessions, participants in the LSDS group reported lower peak SUDS level during Late sessions relative to participants in the HSDS group ($F(1,52) = 6.221$, $p = .016$, $\eta_p^2 = .107$).

Baseline SUDS Level

With respect to baseline SUDS level, only a significant main effect of time was indicated, $F(1.744, 90.685) = 82.389$, $p < .001$, $\eta_p^2 = .613$. There was no effect of group, $F(1, 52) = .039$, $p = .844$, $\eta_p^2 = .001$. Similarly, the group by time interaction was not significant, $F(1.744, 90.685) = 1.632$, $p = .204$, $\eta_p^2 = .030$.

Habituation Rate

Participants with LSDS achieved overall habituation to their primary imaginal scene in fewer sessions than participants with HSDS, adjusted $t(41.703) = -2.149$, $p = .037$.

PTSD Symptomatology

PCL-M

The mixed factorial ANOVA for the PCL-M revealed significant main effects for time, $F(2.754, 143.201) = 78.782$, $p < .001$, $\eta_p^2 = .602$, and group, $F(1, 52) = 10.672$, $p = .002$, $\eta_p^2 = .170$, as well as a significant group by time interaction, $F(2.754, 143.201) = 8.338$, $p < .001$, $\eta_p^2 = .138$. Further evaluation of the PCL-M means indicated that there were no group differences in self-reported PTSD symptomatology at pretreatment/week 1 ($p = .157$) or week 2 ($p = .089$). However, service members in the LSDS group endorsed significantly less PTSD symptom severity than service members in the HSDS group at week 3, $F(1, 52) = 4.718$, $p = .034$, $\eta_p^2 = .083$, and posttreatment, $F(1, 52) = 27.477$, $p < .001$, $\eta_p^2 = .346$. This result was unchanged when the analysis was repeated with the sleep item removed from the PCL-M total scores for each participant.

Additionally, all within-group pairwise comparisons in the LSDS group indicated significant reductions in symptomatology over time (all ps $\leq .001$). However, although the HSDS group evidenced significantly reduced PCL-M total from pretreatment/week 1 to week 2 and week 2 to week 3 ($p < .001$ and $p = .005$, respectively), the PCL-M *increased* significantly from week 3 to posttreatment ($p = .025$) in this group. At posttreatment, the HSDS group's mean PCL-M was not significantly different ($p = .264$) from the group mean at week 2.

CAPS

For the CAPS, significant main effects for time, $F(1, 50) = 298.077$, $p < .001$, $\eta_p^2 = .856$, and group, $F(1, 50) = 13.259$, $p = .001$, $\eta_p^2 = .210$, and a significant interaction, $F(1, 50) = 6.383$, $p = .015$, $\eta_p^2 = .113$, were found. Post-hoc analyses revealed a significant group difference in

posttreatment CAPS total, $F(1, 50) = 13.925$, $p < .001$, $\eta_p^2 = .218$, as the LSDS group exhibited less clinician-rated PTSD symptomatology than the HSDS group. There was no pretreatment group difference in CAPS total ($p = .172$).

Additional Findings

Habituation Achieved

To further examine extinction learning, the proportion of participants in each group that achieved the criterion for habituation (e.g., a 50% reduction in peak SUDS rating across exposure sessions) was evaluated. Seventy-six percent of participants in the LSDS group achieved habituation to their primary imaginal scene relative to 52% of HSDS participants. This disparity approached statistical significance, $\chi^2(1, 54) = 3.352$, $p = .067$.

Sleep Medication

Sleep medication usage was examined to assess potential contributions to the findings. Twenty LSDS (68.9%) and 17 HSDS (68%) participants reported using prescribed and/or over the counter sleep medications. A chi-squared test indicated that there was not a different rate of usage between groups, $\chi^2(1, 54) = .006$, $p = .939$. Additionally, after splitting the sample by sleep medication use (use or no use), the means of the variables of interest did not appear to differ significantly.

CHAPTER 4: DISCUSSION

Growing empirical evidence supports the enhancing effects of sleep on extinction learning. However, prior studies utilized conditioning and extinction learning paradigms and had not examined this effect in (a) a clinical sample characterized by disturbed sleep or (b) in the context of complex treatment provision (exposure therapy) rather than a basic learning paradigm. In this investigation, indicators of extinction learning were examined in veterans with combat-related PTSD who participated in an intensive, exposure-based treatment protocol and were categorized into two groups by severity of sleep disturbances. Relative to participants with HSDS, participants with LSDS exhibited greater extinction following VR-enhanced imaginal exposure therapy. Specifically, veterans with LSDS habituated to the memories of their traumatic event in fewer treatment sessions as indicated by significantly lower peak SUDS ratings during latter exposure sessions. These findings are consistent with outcomes of individuals with spider phobia who reported decreased subjective distress (Kleim et al., 2013) and decreased sympathetic reactivity (Pace-Schott et al., 2012) to spider stimuli following a single session of exposure therapy and a subsequent sleep period.

In addition to decreases in peak distress, baseline SUDS level decreased across imaginal exposure sessions, a finding also reported for patients with flight phobia treated with VR exposure therapy (Maltby, Kirsch, Mayers, & Allen, 2002). Baseline distress consists largely of anticipatory anxiety, an anxious response to impending threatening or feared stimuli. Many of the brain structures and regions implicated in processing present feared stimuli are also active during anticipatory anxiety (Etkin & Wager, 2007). Therefore, reductions in baseline distress would be expected to mirror those in peak distress level, as they did in this investigation.

However, contrary to our hypothesis, LSDS participants did not report lower baseline distress than HSDS participants. PTSD is differentiated from other anxious conditions in that the feared stimuli are not environmentally based (and therefore capable of being avoided outside of exposure therapy sessions). In PTSD, the "feared stimuli" are ever-present in the form of traumatic memories. Thus, in this diagnostic group, baseline SUDS ratings may be more representative of general arousal (or hyperarousal) levels, rather than anticipatory anxiety, and may be less relevant as a metric of differential treatment outcome.

The LSDS and HSDS groups exhibited a similar pattern of decreasing self-reported PTSD symptomatology from pretreatment through 1 week of treatment. After completing 2 weeks of treatment, the LSDS group reported significantly less symptom severity than the HSDS group. This trend was magnified at posttreatment (conducted one week after the last treatment session) when LSDS patients reported further decreases in self-reported PTSD symptomatology while HSDS patients reported a significant increase in symptomatology. Newly-formed memories, such as those formed by habituation and extinction learning, are strengthened over time through sleep-driven consolidation and reconsolidation (Inda, Muravieva, & Alberini, 2011; Pace-Schott, Germain, & Milad, 2015a; Stickgold & Walker, 2007). Thus, the inhibitory associations formulated through exposure therapy appeared be strengthened by overall better sleep quality in the LSDS group. However, the newly-formed inhibitory associations were less robust in the HSDS group as measured by peak SUDS ratings and rate of habituation. In turn, the fearful traumatic memories may have regained primacy, contributing to recovery of fear as indicated by increased self-reported PTSD symptomatology and attenuated reductions in clinician-rated symptomatology at posttreatment.

Some researchers have expressed skepticism about the role of between-session habituation in exposure therapy outcomes, highlighting to inconsistent findings linking between-session habituation and outcome measures (Craske et al., 2008). However, a recent study found that responder status and change in PTSD symptomatology were related to decreasing between-session SUDS level (Sripada & Rauch, 2015). Similarly, our findings suggest that between-session habituation is an important indicator of better exposure therapy outcome in combat-related PTSD. The LSDS group achieved between-session habituation to their imaginal scene sooner and more often, suggesting faster learning and/or faster memory consolidation. They also reported less PTSD symptomatology at posttreatment than the HSDS group.

Although this investigation contributes unique data to the empirical literature, the following limitations should be considered. The primary limitation was the reliance on a retrospective self-report measure to assess quality of sleep. Participants completed the measure during the posttreatment assessment and their assessment of sleep quality may have been influenced by their response to treatment. However, perusal of the pretreatment PSQI-A indicated that quality of sleep within in each group was similar in the month prior to initiating TMT. Emerging empirical evidence suggests a reciprocal relationship between quality of sleep and consolidation of extinction memory (Pace-Schott, Germain, & Milad, 2015b; Sturm, Czisch, & Spoormaker, 2013). However, the interplay among quality of sleep, habituation, and symptomatology throughout treatment could not be carefully examined with a measure of past month sleep. Future research may further elucidate the role of sleep in exposure therapy for PTSD by incorporating repeated polysomnography assessments throughout the course of exposure. Specifically, future studies should aim to identify the dynamics of the sleep cycle as it

relates to PTSD symptomatology during treatment. Additionally, PTSD symptomatology was only assessed through 1 week posttreatment in this study. Longitudinal examinations are needed to determine the duration or resilience of sleep-enhanced extinction learning from exposure therapy for combat-related PTSD. Reducing the chronicity and relapse of PTSD in military personnel would obviously increase long-term relief from this debilitating condition.

Identifying methods for improving sleep in PTSD samples appears to be imperative to improving exposure therapy outcomes for this group. In this study, approximately 68% of participants were prescribed sleep medications, yet most still met the PSQI-A cutoff for significant PTSD-related sleep disturbances. An alternative (or adjunct) to medication may include supplementing exposure-based interventions with behavioral strategies that target sleep disruption. For instance, imagery rehearsal (IR) therapies and cognitive-behavioral therapy for insomnia (CBT-I) have demonstrated some promise in improving posttraumatic sleep difficulties (Nappi, Drummond, & Hall, 2012). At the core of the multiple iterations of IR therapy is sleep education and creating a novel narrative of a nightmare (i.e., rescripting; Krakow & Zadra, 2006) that is rehearsed daily. Some IR therapies also include elements of exposure (e.g., Exposure, Relaxation, and Rescripting Therapy; Davis, 2009; Imagery Rehearsal and Exposure Therapy; Long et al., 2011) and/or CBT-I (Ulmer, Edinger, & Calhoun, 2011). CBT-I consists of sleep hygiene, stimulus control, and sleep restriction. Although there are preliminary data supporting IR and CBT-I for PTSD-related sleep difficulties, few of these data are derived from randomized controlled trials. Moreover, delivery of the interventions has not been standardized across studies (Casement & Swanson, 2012; Nappi et al., 2012). The next step in identifying an efficacious and efficient sleep supplement to exposure therapy for combat-related PTSD may be a randomized

controlled trial comparing IR and CBT-I alone and exposure therapy supplemented by either intervention. Researchers should also strive to identify whether particular sleep symptom profiles in PTSD are more responsive to one sleep intervention than the other, given the considerable variability in quality of sleep among veterans with the disorder (Straus, Drummond, Nappi, Jenkins, & Norman, 2015).

To our knowledge, this is the first study to examine the impact of quality of sleep on habituation/extinction learning during a multi-session, exposure-based intervention for combat-related PTSD. Collectively, the results of this investigation begin to elucidate the role of sleep during exposure-based interventions for PTSD. Specifically, we found that veterans with combat-related PTSD reporting less disturbed sleep appear to experience greater extinction learning and less symptomatology over the course of VR-enhanced imaginal exposure therapy. Sleep may be an important target in future exposure-based interventions to maximize outcome.

APPENDIX A: TABLES

Table 1Sample Demographics and Characteristics

	Low Sleep Disturbance (N = 30)	High Sleep Disturbance (N = 25)
Age M (SD)	36.63 (10.04)	36.96 (8.57)
Sex		
Male	27	24
Female	3	1
Race		
Caucasian	18	20
African American	6	2
Hispanic	5	1
Asian/Pacific Islander	0	1
Multiracial	1	1
Military Branch/Service		
Army	23	17
Navy	1	1
Marine Corp	3	5
Air Force	3	2
Service Status		
Active Duty	5	11
Discharged	25	14
SC Disability	19	13
TBI History	14	10

SC Disability: Service-connected disability through Veterans Administration; TBI: Traumatic brain injury

Table 2 PSQI-A Descriptive Statistics

	All N = 54	LSDS N = 30	HSDS N = 25
Statistic			
Mean	9.49	6.20	13.44
Standard dev.	4.55	2.92	2.55
Median	10.00	7.00	13.00

PSQI-A: Pittsburgh Sleep Quality Index – Addendum for PTSD

Table 3 Means, Standard Deviations, and Between-group Comparisons of Symptomatology and Habituation Measures

Variable	LSDS (N = 29)	HSDS (N = 25)	*p*	η_p^2	*d*
PCL-M					
Pre/Week 1	62.86 (9.86)	66.52 (8.66)	.157	.038	
Week 2	49.76 (13.43)	55.76 (11.79)	.089	.054	
Week 3	41.31 (13.04)	48.96 (12.74)	.034	.083	
Post	35.45 (11.77)	53.08 (12.94)	<.001	.346	
CAPS					
Pre	93.81 (14.72)	99.00 (16.71)	.172	.037	
Post	31.18 (16.71)	52.36 (23.83)	<.001	.218	
Peak SUDS					
Early	7.08 (0.81)	7.22 (0.56)	.446	.011	
Mid	5.94 (1.21)	6.14 (1.07)	.528	.008	
Late	3.90 (1.41)	4.85 (1.35)	.016	.107	
Baseline SUDS*					
Early	4.25 (1.51)	4.23 (1.64)			
Mid	3.21 (1.42)	3.06 (1.38)			
Late	2.14 (0.91)	2.51 (1.39)			
Habituation Rate	8.65 (2.30)	10.36 (3.34)	.032		.596

*Post-hoc analyses were not performed for Baseline SUDS. PCL: PTSD Checklist – Military Version; CAPS: Clinician-Administered PTSD Scale; SUDS: Subjective Units of Distress Scale.

APPENDIX B: IRB APPROVAL LETTER

University of Central Florida Institutional Review Board
Office of Research & Commercialization
12201 Research Parkway, Suite 501
Orlando, Florida 32826-3246
Telephone: 407-823-2901 or 407-882-2276
www.research.ucf.edu/compliance/irb.html

Approval of Human Research

From: **UCF Institutional Review Board #1**
FWA00000351, IRB00001138

To: **Deborah Casamassa Beidel**

Date: **September 18, 2014**

Dear Researcher:

On 9/18/2014 the IRB approved the following human participant research until 8/26/2015 inclusive:

Type of Review:	Submission Response for IRB Continuing Review Application Form
Project Title:	Trauma Management Therapy for OEF and OIF Combat Veterans
Investigator:	Deborah Casamassa Beidel
IRB Number:	SBE-10-07066
Funding Agency:	DOD/Army
Grant Title:	
Research ID:	1048785

The scientific merit of the research was considered during the IRB review. The Continuing Review Application must be submitted 30days prior to the expiration date for studies that were previously expedited, and 60 days prior to the expiration date for research that was previously reviewed at a convened meeting. Do not make changes to the study (i.e., protocol, methodology, consent form, personnel, site, etc.) before obtaining IRB approval. A Modification Form **cannot** be used to extend the approval period of a study. All forms may be completed and submitted online at https://iris.research.ucf.edu .

If continuing review approval is not granted before the expiration date of 8/26/2015, approval of this research expires on that date. When you have completed your research, please submit a Study Closure request in iRIS so that IRB records will be accurate.

Use of the approved, stamped consent document(s) is required. The new form supersedes all previous versions, which are now invalid for further use. Only approved investigators (or other approved key study personnel) may solicit consent for research participation. Participants or their representatives must receive a signed and dated copy of the consent form(s).

All data, including signed consent forms if applicable, must be retained and secured per protocol for a minimum of five years (six if HIPAA applies) past the completion of this research. Any links to the identification of participants should be maintained and secured per protocol. Additional requirements may be imposed by your funding agency, your department, or other entities. Access to data is limited to authorized individuals listed as key study personnel.

In the conduct of this research, you are responsible to follow the requirements of the Investigator Manual.

On behalf of Sophia Dziegielewski, Ph.D., L.C.S.W., UCF IRB Chair, this letter is signed by:

Signature applied by Patria Davis on 09/18/2014 04:54:52 PM EDT

IRB Coordinator

REFERENCES

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders, fourth edition, text revision*. Washington, DC: American Psychiatric Association.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders, fifth edition*. Washington, DC: American Psychiatric Association.

Babson, K. A., & Feldner, M. T. (2010). Temporal relations between sleep problems and both traumatic event exposure and PTSD: A critical review of the empirical literature. *Journal of Anxiety Disorders, 24*(1), 1-15. doi:10.1016/j.janxdis.2009.08.002

Beidel, D. C., Frueh, B. C., Uhde, T. W., Wong, N., & Mentrikoski, J. M. (2011). Multicomponent behavioral treatment for chronic combat-related posttraumatic stress disorder: A randomized controlled trial. *Journal of Anxiety Disorders, 25*(2), 224-231. doi: 10.1016/j.janxdis.2010.09.006

Belleville, G., Guay, S., & Marchand, A. (2009). Impact of sleep disturbances on PTSD symptoms and perceived health. *Journal of Nervous and Mental Disease, 197*(2), 126-162. doi: 10.1097/NMD.0b013e3181961d8e

Blake, D., Weathers, F. W., Nagy, L. M., Kaloupek, D. G., Gusman, F. D., Charney, D. S., et al. (1995). The development of a clinician-administered PTSD scale. *Journal of Traumatic Stress, 8*(1), 75-90. doi: 10.1002/jts.2490080106

Blanchard, E. B., Jones-Alexander, J., Buckley, T. C., & Forneris, C. A. (1996). Psychometric properties of the PTSD checklist (PCL). *Behaviour Research and Therapy, 34*(8), 669-673. doi: 10.1016/0005-7967(96)00033-2

Bonanno, G. A. (2004). Loss, trauma, and human resilience: Have we underestimated the human capacity to thrive after extremely aversive events? *American Psychology, 59*(1), 20-28. doi: 10.1037/0003-066X.59.1.20

Casement, M. D., & Swanson, L. M. (2012). A meta-analysis of imagery rehearsal for post-trauma nightmares: Effects on nightmare frequency, sleep quality, and posttraumatic stress. *Clinical Psychology Review, 32*, 566-574. doi:10.1016/j.cpr.2012.06.002

Dagan, Y., Zinger, Y., & Lavie, P. (1997). Actigraphic sleep monitoring in posttraumatic stress disorder (PTSD) patients. *Journal of Psychosomatic Research, 42*, 577–581. doi: 10.1016/S0022-3999(97)00013-5

Davis, J. L. (2009). *Treating post-trauma nightmares: A cognitive behavioral approach*. New York, NY: Springer.

Department of Veterans Affairs. (2014). *Analysis of VA Health Care Utilization among Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) Veterans*. Retrieved from http://www.publichealth.va.gov/docs/epidemiology/healthcare-utilization-report-fy2014-qtr2.pdf.

Diekelmann, S., & Born, J. (2010). The memory function of sleep. *Nature Reviews Neuroscience, 11*, 114-126. doi:10.1038/nrn2762

Diekelmann, S., Wilhelm, I., & Born, J. (2009). The whats and whens of sleep-dependent memory consolidation. *Sleep Medicine Reviews, 13*, 309-321. doi:10.1016/j.smrv.2008.08.002

Engdahl, B. E., Eberly, R. E., Hurwitz, T. D., Mahowald, M. W., & Blake, J. (2000). Sleep in a community sample of elderly war veterans with and without posttraumatic stress disorder. *Biological Psychiatry, 47*, 520–525. doi: 10.1016/S0006-3223(99)00201-2

Etkin, A., & Wager, T. D. (2007). Functional neuroimaging of anxiety: A meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. *American Journal of Psychiatry, 164*(10), 1476-1488. doi:10.1176/appi.ajp.2007.07030504

Foa, E. B., Hembree, E. A., & Rothbaum, B. O. (2007). *Prolonged exposure therapy for PTSD: Emotional processing of traumatic experiences therapist guide*. New York, NY: Oxford University Press.

Frueh, B., Turner, S. M., & Beidel, D. C. (1995). Exposure therapy for combat-related PTSD: A critical review. *Clinical Psychology Review, 15*(8), 799-817. doi: 10.1016/0272-7358(95)00049-6

Frueh, B., Turner, S. M., Beidel, D. C., Mirabella, R. F., & Jones, W. J. (1996). Trauma Management Therapy: A preliminary evaluation of a multicomponent behavioral treatment for chronic combat-related PTSD. *Behaviour Research and Therapy, 34*(7), 533-543. doi: 10.1016/0005-7967(96)00020-4

Germain, A., Hall, M., Krakow, B., Shear, M. K., & Buysse, D. J. (2005). A brief sleep scale for posttraumatic stress disorder: Pittsburgh Sleep Quality Index Addendum for PTSD. *Journal of Anxiety Disorders, 19*, 233-244. doi:10.1016/j.janxdis.2004.02.001

Goodson, J., Helstrom, A., Halpern, J. M., Ferenschak, M. P., Gillihan, S. J., & Powers, M. B. (2011). The treatment of posttraumatic stress disorder in U.S. combat veterans: A meta-

analytic review. *Psychological Reports, 109*(2), 573-599. doi: 10.2466/02.09.15.16.PR0.109.5.573-599

Harvey, A. G., Jones, C., & Schmidt, D. A. (2003). Sleep and posttraumatic stress disorder: A review. *Clinical Psychology Review, 23*, 377-407. doi: 10.1016/S0272-7358(03)00032-1

Harvey, A. G., Lee, J., Williams, J., Hollon, S. D., Walker, M. P., Thompson, M. A., et al., (2014). Improving outcome of psychosocial treatments by enhancing memory and learning. *Perspectives on Psychological Science, 9*(2), 161-179. doi: 10.1177/1745691614521781

Hoge, C. W., Castro, C. A., Messer, S. C., McGurk, D., Cotting, D. I., & Koffman, R. L. (2004). Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *The New England Journal of Medicine, 351*(1), 13-22. doi: 10.1056/NEJMoa040603

Hurwitz, T. D., Mahowald, M. W., Kuskowski, M., & Engdahl, B. E. (1998). Polysomnographic sleep is not clinically impaired in Vietnam combat veterans with chronic posttraumatic stress disorder. *Biological Psychiatry, 44*, 1066–1073. doi: 10.1016/S0006-3223(98)00089-4

Inda, M. C., Muravieva, E. V., & Alberini, C. M. (2011). Memory retrieval and the passage of time: From reconsolidation and strengthening to extinction. *The Journal of Neuroscience, 31*(5), 1635-1643. doi:10.1523/JNEUROSCI.4736-10.2011

Insana, S. P., Hall, M., Buysse, D. J., & Germain, A. (2013). Validation of the Pittsburgh Sleep Quality Index Addendum for Posttraumatic Stress Disorder (PSQI-A) in male military veterans. *Journal of Traumatic Stress, 26*(2), 192-200. doi:10.1002/jts.21793

Institute of Medicine and National Research Council. (2007). *Treatment of posttraumatic stress disorder: An assessment of the evidence.* Washington, D.C.: The National Academies Press.

Kato, H., Asukai, N., Miyake, Y., Minakawa, K., & Nishiyama, S. (1996). Post-traumatic symptoms among younger and elderly evacuees in the early stages following the 1995 Hanshin-Awaji earthquake in Japan. *Acta Psychiatrica Scandinavica, 93,* 477-481. doi: 10.1111/j.1600-0447.1996.tb10680.x

Kobayashi, I., Boarts, J. M., & Delahanty, D. L. (2007). Polysomnographically measured sleep abnormalities in PTSD: A meta-analytic review. *Psychophysiology, 44,* 660-669. doi: 10.1111/j.1469-8986.2007.537.x

Kleim, B., Wilhelm, F. H., Temp, L., Margraf, J., Wiederhold, B. K., & Rasch, B. (2013). Sleep enhances exposure therapy. *Psychological Medicine, 44*(7), 1511-1519. doi: 10.1017/S0033291713001748

Kline, A., Falca-Dodson, M., Sussner, B., Ciccone, D. S., Chandler, H., Callahan, L., & Losonczy, M. (2010). Effects of repeated deployment to Iraq and Afghanistan on the health of New Jersey Army National Guard troops: Implications for military readiness. *American Journal of Public Health, 100*(2), 276-283. doi: 10.2105/AJPH.2009.162925

Koren, D., Arnon, I., Lavie, P. & Klein, E. (2002). Sleep complaints as early predictors of posttraumatic stress disorder: A 1-year prospective study of injured survivors of motor vehicle accidents. *American Journal of Psychiatry, 159,* 855-857. doi:10.1176/appi.ajp.159.5.855

Krakow, B., & Zadra, A. (2006). Clinical management of chronic nightmares: Imagery rehearsal

therapy. *Behavioral Sleep Medicine, 4*(1), 45-70. doi: 10.1207/s15402010bsm0401_4

Liberzon, I., & Sripada, C. S. (2007). The functional neuroanatomy of PTSD: A critical review. *Progress in Brain Research, 167*, 151-169.

Long, M. E., Hammons, M. E., Davis, J. L., Frueh, B. C., Khan, M. M., Elhai, J. D., & Teng, E. J. (2011). Imagery rescripting and exposure group treatment of posttraumatic nightmares in veterans with PTSD. *Journal of Anxiety Disorders, 25*, 531-535. doi:10.1016/j.janxdis.2010.12.007

Luxton, D. D., Greenburg, D., Ryan, J., Niven, A., Wheeler, G., & Mysliwiec, V. (2011). Prevalence and impact of short sleep duration in redeployed OIF soldiers. *Sleep, 34*(9), 1189-1195. doi: 10.5665/sleep.1236

Maher, M. J., Rego, S. A., & Asnis, G. M. (2006). Sleep disturbances in patients with post-traumatic stress disorder: Epidemiology, impact and approaches to management. *CNS Drugs, 20*(7), 567-590. doi: 10.2165/00023210-200620070-00003

Maltby, N., Kirsch, I., Mayers, M., & Allen, G. J. (2002). Virtual reality exposure therapy for the treatment of fear of flying: A controlled investigation. *Journal of Clinical and Consulting Psychology, 70*(5), 1112-1118. doi: 10.1037//0022-006X.70.5.1112

Maquet, P., Peters, J., Aerts, J., Delfiore, G., Degueldre, C., Luxen, A., et al. (1996). Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. *Nature, 383*(6596), 163-166. doi: 10.1038/383163a0

McGaugh, J. L. (2004). The amygdala modulates the consolidation of memories of emotionally arousing experiences. *Annual Review of Neuroscience, 27*, 1-28. doi: 10.1146/annurev.neuro.27.070203.144157

McNally, R. J. (2007). Mechanisms of exposure therapy: How neuroscience can improve psychological treatments for anxiety disorders. *Clinical Psychology Review, 27,* 750-759. doi: 10.1016/j.cpr.2007.01.003

Mellman, T. A., David, D., Bustamante, V., Torres, J. & Fins, A. (2001). Dreams in the acute aftermath of traum a and their relationship to PTSD. *Journal of Traumatic Stress, 14*(1), 241-247. doi: 10.1023/A:1007812321136

Mellman, T. A., David, D., Kulick-Bell, R., Hebding, J., & Nolan, B. (1995). Sleep disturbance and its relationship to psychiatric morbidity after Hurricane Andrew. A*merican Journal of Psychiatry, 152,* 1659-1663.

Mellman, T. A., Kulick-Bell, R., Ashlock, L. E., & Nolan, B. (1995) . Sleep events among veterans with combat-related posttraumatic stress disorder. *American Journal of Psychaitry, 152*, 110-115.

Mellman, T. A., Nolan, B., Hebding, J., Kulick-Bell, R., & Dominguez, R. (1997). A polysomnographic comparison of veterans with combat-related PTSD, depressed men, and non-ill controls. *Sleep, 20,* 46-51.

Moustafa, A. A., Gilbertson, M. W., Orr, S. P., Herzallah, M. M., Servatius, R. J., & Myers, C. E. (2013). A model of amygdala-hippocampal-prefrontal interaction in fear conditioning and extinction in animals. *Brain and Cognition, 81,* 29-43. doi: 10.1016/j.bandc.2012.10.005

Nappi, C. M., Drummond, S. P. A., Hall, J. M. H. (2012). Treatming nightmares and insomnia in posttraumatic stress disorder: A review of current evidence. *Neuropharmacology, 62,* 576-585. doi:10.1016/j.neuropharm.2011.02.029

Neylan, T. C., Marmar, C. R., Metzler, T. J., Weiss, D. S., Zatzick, D. F., Delucchi, K. L., et al. (1998). Sleep disturbances in the Vietnam generation: Findings from a nationally representative sample of maleVietnam veterans. *American Journal of Psychiatric, 155*, 929-933.

North, C. S., Nixon, S. J., Shariat, S., Mallonee, S., McMillen J. C., Spitznagel, E. L., et al. (1999). Psychiatric disorders among survivors of the Oklahoma City Bombing. *The Journal of the American Medical Association,* 282, 755-762. doi:10.1001/jama.282.8.755

Nozfinger, E. A. (2005). Functional neuroimaging of sleep. *Seminars in Neurology, 25*(1), 9-18. doi: 10.1055/s-2005-867070

Pace-Schott, E. F., Germain, A., & Milad, M. R. (2015a). Effects of sleep on memory for conditioned fear and fear extinction. *Psychological Bulletin,* Advance online publication. http://dx.doi.org/10.1037/bul0000014

Pace-Schott, E. F., Germain, A., & Milad, M. R. (2015b). Sleep and REM sleep disturbance in the pathophysiology of PTSD: The role of extinction memory. *Biology of Mood & Anxiety Disorders, 5*(3). doi: 10.1186/s13587-015-0018-9

Pace-Schott, E. F., Milad, M. R., Orr, S. P., Rauch, S. L., Stickgold, R., & Pitman, R. K. (2009). Sleep promotes generalization of extinction of conditioned fear. *Sleep, 32,* 19–26.

Pace-Schott, E. F., Shepherd, E., Spencer, R. M., Marcello, M., Tucker, M., Propper, R. E., et al. (2011). Napping promotes inter-session habituation to emotional stimuli. *Neurobiology of Learning and Memory, 95,* 24–36. doi: 10.1016/j.nlm.2010.10.006

Pace-Schott, E. F., Verga, P. W., Bennett, T. S., & Spencer, R. M. (2012). Sleep promoted consolidation and generalizaton of extinction learning in simulated exposure therapy for

spider fear. *Journal of Psychiatric Research, 46,* 1036–1044. doi: 10.1016/j.jpsychires.2012.04.015

Phelps, E. A., & LeDoux, J. E. (2005). Contributions of the amygdala to emotion processing: From animal models to human behavior. *Neuron, 48,* 175-187. doi: 10.1016/j.neuron.2005.09.025

Pillar, G., Malhotra, A., & Lavie, P. (2000). Post-traumatic stress disorder and sleep—what a nightmare! *Sleep Medicine Reviews, 4*(2), 183-200. doi:10.1053/smrv.1999.0095

Rothbaum, B. O., & Mellman, T. A. (2001). Dreams and exposure therapy in PTSD. *Journal of Traumatic Stress, 14*(3), 481-490. doi: 10.1023/A:1011104521887

Rothbaum, B. O., & Schwartz, A. C. (2002). Exposure therapy for posttraumatic stress disorder. *American Journal of Psychotherapy, 56*(1), 59-75.

Shneerson, J. M. (2000). *Handbook of sleep medicine*. Oxford: Blackwell.

Spoormaker, V. I., & Montgomery, P. (2008). Disturbed sleep in post-traumatic stress disorder: Secondary symptom or core feature? *Sleep Medicine Reviews, 12,* 169-184. doi:10.1016/j.smrv.2007.08.008

Sripada, R. K., & Rauch, S. A. M. (2015). Between-session and within-session habituation in Prolonged Exposure Therapy for posttraumatic stress disorder: A hierarchical linear modeling approach. *Journal of Anxiety Disorders, 30,* 81-87. http://dx.doi.org/10.1016/j.janxdis.2015.01.002

Sterpenich, V., Albouy, G., Boly, M., Vandewalle, G., Darsaud, A., Balteau, E., et al. (2007). Sleep-related hippocampo-cortical interplay during emotional memory recollection. *PLoS Biology, 5*(11): e282. doi: 10.1371/journal.pbio.0050282

Stickgold, R., & Walker, M. P. (2007). Sleep-dependent memory consolidation and reconsolidation. *Sleep Medicine, 8*(4), 331-343. doi:10.1016/j.sleep.2007.03.011

Straus, L. D., Drummond, S. P. A., Nappi, C. M., Jenkins, M. M., &Norman, S. B. (2015). Sleep variability in military-related PTSD: A comparison to primary insomnia and healthy controls. *Journal of Traumatic Stress, 28*, 8-16. doi: 10.1002/jts.21982

Sturm, A., Czisch, M., & Spoormaker, V. I. (2013). Effects of unconditioned stimulus intensity and fear extinction on subsequent sleep architecture in an afternoon nap. *Journal of Sleep Research, 22*, 648-655. doi: 10.1111/jsr.12074

Turner, S. M., Beidel, D. C., & Frueh, B. C. (2005). Multicomponent behavioral treatment for chronic combat-related posttraumatic stress disorder: Trauma Management Therapy. *Behavior Modification, 29*(1), 39-69. doi: 10.1177/0145445504270872

Ulmer, C. S., Edinger, J. D., & Calhoun, P. S. (2011). A multi-component cognitive-behavioral intervention for sleep disturbance in veterans with PTSD: A pilot study. *Journal of Clinical Sleep Medicine, 7*(1), 57-68.

Weathers, F. W., Keane, T. M., & Davidson, J. T. (2001). Clinician-Administered PTSD Scale: A review of the first ten years of research. *Depression and Anxiety, 13*(3), 132-156. doi: 10.1002/da.1029

Weathers, F. W., Litz. B. T., Herman, D. S., Huska. J. A., & Keane,T. M. (1993, November). *The PTSD Checklist (PCL): Reliability, validity, and diagnostic utility.* Paper presented at the 9th annual meeting of the ISTSS, San Antonio, TX.

Wilkins, K. C., Lang, A. J., & Norman, S. B. (2011). Synthesis of the psychometric properties of the PTSD checklist (PCL) military, civilian, and specific versions. *Depression and Anxiety, 28*(7), 596-606. doi: 10.1002/da.20837