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(802) 296-5132
FAX (802) 296-5135
Email: ncptsd@va.gov

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PTSD and Sleep

Philip Gehrman, PhD
University of Pennsylvania, Department of Psychiatry

Gerlinde Harb, PhD
Estadt Psychological Services and
Corporal Michael J. Crescenz VA Medical Center

Richard Ross, MD, PhD
Department of Veterans Affairs Medical Center and
University of Pennsylvania, Department of Psychiatry

Introduction

PTSD is unique among mental health disorders in that sleep problems represent two of the diagnostic criteria of the fifth edition of the American Psychiatric Association's (APA) *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*); recurrent nightmares are part of the intrusion cluster of symptoms, and insomnia is a component of the arousal cluster. While these sleep problems are symptoms of PTSD, the evidence suggests that they tend to become independent problems over time, warranting sleep-focused assessment and treatment. Further, it has been argued that the sleep disturbance plays a critical role in the maintenance of PTSD and is a hallmark of the disorder (Ross, Ball, Sullivan, & Caroff, 1989). Fortunately, efficacious treatment options, both medications and forms of cognitive-behavioral therapy, exist.

Prevalence and Consequences of Sleep Problems

Insomnia is one of the most common symptoms of PTSD, and has been reported to occur in 90-100% of Vietnam era Veterans with the disorder (McLay, Klam, & Volkert, 2010; Neylan et al., 1998). In the Millennium Cohort Study, an ongoing epidemiologic cohort study of military health, 92% of active duty personnel with PTSD, compared to 28% of those without PTSD, reported clinically significant insomnia (Seelig et al., 2010). As these studies indicate, insomnia is the norm for Veterans with PTSD.

A smaller number of studies have examined the prevalence of chronic nightmares in Veterans with PTSD. In the National Vietnam Veterans Readjustment Study, 52% of combat Veterans with PTSD reported a significant nightmare problem (Neylan et al., 1998). In a general community sample, nightmares were endorsed by 71% of individuals with PTSD (Leskin, Woodward, Young, & Sheikh, 2002). Posttraumatic nightmares are independently associated with daytime distress and impaired functioning over and above the impact of overall PTSD severity (Levin & Nielsen, 2007; Littlewood, Gooding, Panagioti, & Kyle, 2016).

Insomnia and recurrent nightmares are traditionally thought of as symptoms of PTSD, but this view has changed over time due to several converging lines of evidence. First, individuals with insomnia prior to trauma exposure are more likely to develop PTSD following the exposure, indicating that disturbed sleep increases vulnerability to PTSD (Gehrman et al., 2013). Second, insomnia occurring in the acute aftermath of a traumatic event is a significant risk factor for the later development of PTSD (Mellman, Bustamante, Fins, Pigeon, & Nolan, 2002), suggesting that early sleep disturbance precedes the development of the full disorder. Third, recent studies are finding that insomnia and recurrent nightmares are independently associated with a number of negative sequelae, including suicidal ideation and behavior, over and above the effects of PTSD and depression (Betts, Williams, Najman, & Alati, 2013). Finally, studies also indicate that insomnia often persists following trauma-focused treatments such as Prolonged Exposure (PE) or Cognitive Processing Therapy (CPT; Gutner, Casement, Stavitsky Gilbert, & Resick, 2013; Pruiksma et al., 2016). Even when trauma-focused therapy is associated with statistically

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Authors' Addresses: **Philip Gehrman, PhD** is affiliated with the Department of Psychiatry, University of Pennsylvania, 3535 Market Street, Suite 670, Philadelphia, PA 19104 and the Corporal Michael J. Crescenz VA Medical Center, University and Woodland Avenues, Philadelphia, PA 19104. **Gerlinde Harb, PhD** is affiliated with the Estadt Psychological Services, 2101 Pine Street 2nd Floor, Philadelphia, PA 19103 and the Corporal Michael J. Crescenz VA Medical Center, University and Woodland Avenues, Philadelphia, PA 19104. **Richard Ross, MD, PhD** is affiliated with the Department of Veterans Affairs Medical Center (116 MHC) University and Woodland Avenues, Philadelphia, PA 19104 and the Department of Psychiatry, University of Pennsylvania, 3535 Market Street, Suite 670, Philadelphia, PA 19104. Email Addresses: gehrman@exchange.upenn.edu and ross_r@mail.trc.upenn.edu.

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significant improvements in sleep, effect sizes are small and not clinically significant. Like insomnia, nightmares frequently do not improve with trauma-focused treatment although the degree of improvement is larger than for insomnia (Belleville, Guay, & Marchand, 2011). If the sleep disturbance were purely a symptom of PTSD it should resolve following successful treatment of the overall disorder. Insomnia and, to a lesser extent, nightmares are now thought of as comorbid problems that develop a degree of independence over time and warrant targeted treatment (see below).

It is important to be aware that insomnia and recurrent nightmares are often not the only sleep disorders that individuals with PTSD experience. There is growing evidence that this population also suffers from obstructive sleep apnea (OSA), a sleep-related breathing disorder, more often than the general population (Jaoude, Vermont, Porhomayon, & El-Solh, 2015) although not all studies have found an association with PTSD (Mysliwiec et al., 2015). OSA involves repetitive blockage of the airway that leads to fragmented sleep and reduced flow of oxygen to the brain. Given the impact of OSA on sleep, it is not surprising that studies are finding that treatment of comorbid apnea can improve not only sleep symptoms, but overall PTSD severity as well (Tamanna, Parker, Lyons, & Ullah, 2014). The primary treatment for OSA is continuous positive airway pressure (CPAP), in which a mask is worn at night that delivers pressurized air to keep the airway open. In some studies, patients with PTSD have lower adherence to CPAP (Collen, Lettieri, & Hoffman, 2012). A small body of evidence is beginning to show that parasomnias other than nightmares, such as sleep walking and rapid eye movement (REM) behavior disorder, are also more common in patients with PTSD, but it is not clear to what extent these represent comorbid disorders or are directly caused by trauma-related mechanisms (Mysliwiec et al., 2014). What is clear is that screening for sleep disorders beyond insomnia and recurrent nightmares needs to be routinely incorporated in the clinical assessment of PTSD.

Treatment of Sleep Problems in PTSD

Two primary approaches to treating sleep problems exist in PTSD, pharmacotherapy, and psychotherapy. Each has demonstrated efficacy when compared to placebo or control conditions, but little is known about the efficacy of using both approaches concurrently. The preferred treatment approach for insomnia, when available, is cognitive behavioral therapy.

Pharmacotherapy

One approach to the treatment of insomnia in the context of PTSD is the use of hypnotic medications and other medications with sedative side effects. However, there are very few clinical trials examining the efficacy of these medications in individuals with PTSD. Of note, some medications used to treat PTSD can cause or exacerbate insomnia (e.g., selective serotonin reuptake inhibitors [SSRIs]). In terms of nightmares, the main option available is prazosin, an alpha-adrenergic receptor antagonist that has been used for the treatment of hypertension. Prazosin has been found to be effective for reducing nightmares and improving sleep in Veterans with PTSD in multiple trials (Khachatryan, Groll, Booij, Sepehry, & Schütz, 2016; Petrakis et al., 2016; Raskind et al., 2007; Raskind et al., 2013). However, the rigorous, recently completed large US Department of Veterans Affairs (VA) multisite VA Cooperative Study found no advantage of prazosin compared to placebo in reducing the nightmare disturbance and improving sleep (VA Office of Research and Development, 2016). Evidence also exists that shows patients frequently discontinue prazosin use prematurely (Alexander, Lund, Bernardy, Christopher, & Friedman, 2015). Raskind et al. (2016) have suggested that higher standing blood pressure, an indicator of noradrenergic stimulation of alpha-1 adrenoceptors, may be a useful biomarker for identifying a subgroup of individuals with combat-related PTSD likely to benefit from prazosin. Of note, prazosin is not sedating so it does not shorten sleep onset latency although it does promote REM sleep continuity. The antihistaminergic drug hydroxyzine was found to decrease nightmares and improve sleep in one placebo-controlled trial (Ahmadpanah et al., 2014). Hertzberg, Feldman, Beckham, and Davidson (1996) provided some evidence for the usefulness of trazodone in treating PTSD, including the sleep disturbance, but there has been no large randomized controlled trial (RCT). Although no benzodiazepine has been studied in such a trial, the non-benzodiazepine drug eszopiclone, which acts at the benzodiazepine receptor, showed efficacy for treating PTSD and the associated sleep disturbance in a small RCT (Pollack et al., 2011). Regarding the atypical antipsychotic drugs, adjunctive risperidone had modest efficacy in improving sleep quality in Veterans with PTSD (Krystal et al., 2016) and, in a RCT, quetiapine monotherapy was shown to reduce symptoms of military-related PTSD, with an unclear effect on sleep quality specifically (Villarreal et al., 2016).

Cognitive Behavioral Treatments

The preferred treatment approach for insomnia is cognitive behavioral treatment for insomnia (CBT-I), a series of strategies focused on stimulus control, sleep restriction, de-arousal techniques, sleep hygiene, and cognitive restructuring. Treatment length is typically 6 sessions but ranges from 4-8 sessions for most patients. CBT-I has demonstrated efficacy in patients with primary insomnia in many randomized trials and several meta-analyses. CBT-I has demonstrated sustained improvement in insomnia symptoms on follow-up assessments ranging from 1 to 3 years. The durability of treatment effects is a clear advantage over long-term pharmacotherapy, as are the lower risk of side effects and the absence of drug interactions. A recent randomized trial in Veterans with PTSD found that CBT-I led to greater improvements in sleep and reductions in disruptive sleep-related behaviors than placebo, demonstrating the efficacy of CBT-I in this population (Ho, Chan, & Tang, 2016; Talbot, Hairston, Eidelman, Gruber, & Harvey, 2009). CBT-I may also be a good first step prior to beginning trauma-focused therapy (Baddeley & Gros, 2013).

A psychotherapeutic (CBT) approach to treating nightmares is imagery rehearsal therapy (IR), which is also referred to as nightmare re-scripting because it entails choosing a recurrent nightmare and finding a way to change (i.e., re-script) the content in a way that makes it less intense or distressing. There are several trials of IR with positive outcomes in civilian populations (e.g. Krakow et al., 2001) but a large, randomized trial in Vietnam Veterans with PTSD failed to demonstrate clear efficacy (Cook et al., 2010). Recent systematic reviews found that most of the clinical trials to date were of mixed scientific rigor (Casement & Swanson, 2012; Harb et al., 2013). Additional studies are needed before conclusions can be made regarding the efficacy of this treatment approach in Veteran and non-Veteran populations, as well as comparing IR to prazosin (Seda, Sanchez-Ortuno, Welsh, Halbower, & Edinger, 2015).

Group Treatment

Both CBT-I and IR can be delivered individually as well as in a group format; also, CBT-I or components of CBT-I can be added to IR. A typical group consists of 6-8 individuals and meets weekly for ~6

weeks (longer if CBT-I and IR are both delivered) for 90 minutes per visit. The material is the same as in the individual treatments, with the added element of hearing the experiences of other Veterans with PTSD. A pilot study of combined CBT-I and IR delivered in a group format found significant improvements in both insomnia and nightmares (Swanson, Favorite, Horin, & Arnedt, 2009), although most of the improvement in nightmares occurred prior to the introduction of IR content. This suggests that, at least for some individuals, CBT-I alone can lead to improvements in nightmares.

Summary

In summary, sleep problems are highly prevalent in Veterans with PTSD. Beyond being a symptom of PTSD, the sleep problems usually evolve into independent disorders that are also associated with significant distress and impairment, including an increased risk for suicidality. Treatment options include both pharmacologic and cognitive behavioral approaches, and both have demonstrated efficacy for insomnia and recurrent nightmares, although the results for nightmares are more mixed. Sleep-focused assessment and treatment should be established as standard care for Veterans with PTSD.

FEATURED ARTICLES

Belleville, G., Guay, S., & Marchand, A. (2011). **Persistence of sleep disturbances following cognitive-behavior therapy for posttraumatic stress disorder.** *Journal of Psychosomatic Research, 70*, 318-327. doi:10.1016/j.jpsychores.2010.09.022 *Objectives:* The objectives of the present study were (1) to assess the impact of cognitive-behavior therapy (CBT) for posttraumatic stress disorder (PTSD) on associated sleep disturbances and (2) to explore the correlates of persistent sleep difficulties in terms of anxiety and depression symptoms and perceived health. *Method:* Fifty-five individuals with PTSD were administered a series of assessments designed to evaluate sleep, PTSD symptoms, symptoms of anxiety and depression, and perceived health before and after individual CBT for PTSD and at 6-month follow-up. *Results:* Significant improvements were observed on sleep quality, sleep onset latency, sleep efficiency, and sleep disturbances. These changes were not fully maintained after 6 months, and 70% of people who reported baseline sleep difficulties (Pittsburgh Sleep Quality Index >5) still reported significant problems with sleep after treatment. Persistent sleep difficulties were associated with more severe posttraumatic, anxious, and depressive symptoms as well as poorer health. *Conclusion:* Although CBT for PTSD had a favorable impact on sleep, the majority of participants suffered from residual sleep difficulties. Individuals with persistent sleep difficulties posttreatment may experience more residual posttraumatic, depression, and anxiety symptoms and poorer mental and physical health than those who do not report sleep problems posttreatment. Further research in this area will allow clinicians to treat sleep problems in these individuals more effectively.

Betts, K. S., Williams, G. M., Najman, J. M., & Alati, R. (2013). **The role of sleep disturbance in the relationship between post-traumatic stress disorder and suicidal ideation.** *Journal of Anxiety Disorders, 27*, 735-741. doi:10.1016/j.janxdis.2013.09.011 We tested if the risk of suicidal ideation in individuals with PTSD symptoms was dependent on comorbid sleep disturbance. Our cross-sectional sample included

FEATURED ARTICLES *continued*

2465 participants with complete data from the 21 year follow-up of the Mater University Study of Pregnancy (MUSP), a birth cohort study of young Australians. Using structural equation modelling with indirect pathways we found that 12 month PTSD symptoms did not directly predict suicidal ideation at 21 when adjusting for major depression symptoms, polyvictimization and gender. However, PTSD symptoms had an indirect effect on suicidal ideation via past-month sleep disturbance. Our results suggest that increased suicidal ideation in those with PTSD may result from the fact that PTSD sufferers often exhibit other comorbid psychiatric conditions which are themselves known to predict suicidal behaviours. Sleep disturbance may be targeted in those who experience PTSD to help prevent suicidal ideation.

Cook, J. M., Harb, G. C., Gehrman, P. R., Cary, M. S., Gamble, G. M., Forbes, D., & Ross, R. J. (2010). **Imagery rehearsal for posttraumatic nightmares: A randomized controlled trial.** *Journal of Traumatic Stress, 23*, 553-563. doi:10.1002/jts.20569 One hundred twenty-four male Vietnam War veterans with chronic, severe posttraumatic stress disorder (PTSD) were randomly assigned to imagery rehearsal (n = 61) or a credible active comparison condition (n = 63) for the treatment of combat-related nightmares. There was pre-post change in overall sleep quality and PTSD symptoms for both groups, but not in nightmare frequency. Intent-to-treat analyses showed that veterans who received imagery rehearsal had not improved significantly more than veterans in the comparison condition for the primary outcomes (nightmare frequency and sleep quality), or for a number of secondary outcomes, including PTSD. Six sessions of imagery rehearsal delivered in group format did not produce substantive improvement in Vietnam War veterans with chronic, severe PTSD. Possible explanations for findings are discussed.

Gehrman, P., Seelig, A. D., Jacobson, I. G., Boyko, E. J., Hooper, T. I., Gackstetter, G. D., . . . Smith, T. C. (2013). **Predeployment sleep duration and insomnia symptoms as risk factors for new-onset mental health disorders following military deployment.** *Sleep, 36*, 1009-1018. doi:10.5665/sleep.2798 *Study Objectives:* To evaluate predeployment sleep duration and insomnia symptoms in relation to the development of mental health symptoms. *Design:* Longitudinal cohort study. *Setting:* The Millennium Cohort Study survey is administered via a secure website or US mail. *Participants:* Data were from 15,204 participants who completed their first deployment between the submissions of 2 consecutive Millennium Cohort questionnaires (2001-2008). *Interventions:* N/A. *Measurements and Results:* Using self-reported data from the Millennium Cohort Study we evaluated the association of predeployment sleep duration and insomnia symptoms on the development of new-onset mental disorders among deployers. Multivariable logistic regression was used to estimate the odds of developing posttraumatic stress disorder (PTSD), depression, and anxiety, while adjusting for relevant covariates including combat-related trauma. The study outcomes were assessed using validated instruments, including the PTSD checklist-civilian version, and the PRIME-MD Patient Health Questionnaire. We identified 522 people with new-onset PTSD, 151 with anxiety, and 303 with depression following deployment. In adjusted models, combat-related trauma and predeployment insomnia symptoms were significantly associated with higher odds of developing posttraumatic stress disorder, depression, and anxiety postdeployment. *Conclusions:* Sleep characteristics, especially insomnia symptoms, are related to the development of mental disorders following military deployments.

Assessment of insomnia symptoms predeployment may help to better identify those at highest risk for subsequent adverse mental health outcomes.

Harb, G. C., Phelps, A. J., Forbes, D., Ross, R. J., Gehrman, P. R., & Cook, J. M. (2013). **A critical review of the evidence base of imagery rehearsal for posttraumatic nightmares: Pointing the way for future research.** *Journal of Traumatic Stress, 26*, 570-579. doi:10.1002/jts.21854 In this article, the authors provide information on key characteristics of imagery rehearsal treatment protocols and examine the quality of reporting of randomized controlled and uncontrolled trials of imagery rehearsal for treating posttraumatic nightmares. Using a reliable and valid scale, two independent psychologists rated 16 trials. Most reports provided insufficient information on a range of variables including the definition of treatment delivery (e.g., therapist supervision, treatment fidelity), description of the participant sample, data analysis (e.g., determination of sample size), and treatment assignment (e.g., randomization procedures). Low methodological quality and poor reporting can lead to inflation of estimates of treatment effects and inadequately substantiated conclusions, such as inflated effect sizes in meta-analytic studies. Numerous imagery rehearsal protocols exist, but in some cases are given different names and tested in pilot studies, slowing progression in the field. Randomized controlled trials of imagery rehearsal with credible comparison conditions, examination of predictors of dropout and outcome, as well as dismantling studies of imagery rehearsal treatment components are needed.

Hertzberg, M. A., Feldman, M. E., Beckham, J. C., & Davidson, J. R. T. (1996). **Trial of trazodone for posttraumatic stress disorder using a multiple baseline group design.** *Journal of Clinical Psychopharmacology, 16*, 294-298. Six patients with combat-related posttraumatic stress disorder (PTSD) entered a multiple-baseline trial of trazodone, beginning with 50 mg/day and increasing to 400 mg/day until response was maximal. Total Clinician-Administered PTSD Scale scores decreased from a mean of 92 at baseline to 79 at end point, and self-reported PTSD symptoms as measured by the Davidson Trauma Scale paralleled these results (mean of 102 at baseline to 88 at end point). Based on clinician global improvement scores, four patients were rated as much improved and two were rated to be minimally improved. Improvement in social and occupational functioning, and depression was minimal. Available follow-up scores for PTSD symptoms indicated that gains were maintained. Sleep was the first symptom to improve at 2 to 3 months. No dropouts during the treatment period occurred, and reported side effects were quite low. These preliminary data suggest that trazodone may be effective in reducing the three primary clusters of symptoms of PTSD. These findings should be confirmed by using a larger sample in a double-blind, placebo-controlled study.

Jaoude, P., Vermont, L. N., Porhomayon, J., & El-Solh, A. A. (2015). **Sleep-disordered breathing in patients with post-traumatic stress disorder.** *Annals of the American Thoracic Society, 12*, 259-268. doi:10.1513/AnnalsATS.201407-299FR Post-traumatic stress disorder (PTSD) and sleep-disordered breathing (SDB) are shared by many patients. They both affect sleep and the quality of life of affected subjects. A critical review of the literature supports an association between the two disorders in both combat-related and non–combat-related PTSD. The exact mechanism linking PTSD and SDB is not fully understood. A complex interplay between sleep fragmentation and neuroendocrine pathways is suggested. The overlap of symptoms between PTSD and SDB raises diagnostic challenges that may require a novel approach in the methods used to diagnose the coexisting disorders. Similar therapeutic challenges face patients and providers when treating concomitant PTSD and SDB. Although continuous positive airway pressure therapy imparts a mitigating effect on PTSD symptomatology, lack of both acceptance and adherence are common. Future research should focus on ways to improve adherence to continuous positive airway pressure therapy and on the use of alternative therapeutic methods for treating SDB in patients with PTSD.

Krakow, B., Hollifield, M., Johnston, L., Koss, M., Schrader, R., Warner, T. D., . . . Prince, H. (2001). **Imagery rehearsal therapy for chronic nightmares in sexual assault survivors with posttraumatic stress disorder: A randomized controlled trial.** *Journal of the American Medical Association, 286*, 537-545. doi:10.1001/jama.286.5.537 *Context:* Chronic nightmares occur frequently in patients with posttraumatic stress disorder (PTSD) but are not usually a primary target of treatment. *Objective:* To determine if treating chronic nightmares with imagery rehearsal therapy (IRT) reduces the frequency of disturbing dreams, improves sleep quality, and decreases PTSD symptom severity. *Design, Setting, and Participants:* Randomized controlled trial conducted from 1995 to 1999 among 168 women in New Mexico; 95% had moderate-to-severe PTSD, 97% had experienced rape or other sexual assault, 77% reported life-threatening sexual assault, and 58% reported repeated exposure to sexual abuse in childhood or adolescence. *Intervention:* Participants were randomized to receive treatment (n = 88) or to the wait-list control group (n = 80). The treatment group received IRT in 3 sessions; controls received no additional intervention, but continued any ongoing treatment. *Main Outcome Measures:* Scores on the Nightmare Frequency Questionnaire (NFQ), Pittsburgh Sleep Quality Index (PSQI), PTSD Symptom Scale (PSS), and Clinician-Administered PTSD Scale (CAPS) at 3- and 6-month follow-up. *Results:* A total of 114 participants completed follow-up at 3 and/or 6 months. Comparing baseline to follow-up (n = 97-114), treatment significantly reduced nights per week with nightmares (Cohen d = 1.24; P<.001) and number of nightmares per week (Cohen d = 0.85; P<.001) on the NFQ and improved sleep (on the PSQI, Cohen d = 0.67; P<.001) and PTSD symptoms (on the PSS, Cohen d = 1.00; P<.001 and on the CAPS, Cohen d = 1.53; P<.001). Control participants showed small, nonsignificant improvements for the same measures (mean Cohen d = 0.21). In a 3-point analysis (n = 66-77), improvements occurred in the treatment group at 3-month follow-up (treatment vs control group, Cohen d = 1.15 vs 0.07 for nights per week with nightmares; 0.95 vs –0.06 for nightmares per week; 0.77 vs 0.31 on the PSQI, and 1.06 vs 0.31 on the PSS) and were sustained without further intervention or contact between 3 and 6 months. An intent-to-treat analysis (n = 168) confirmed significant differences between treatment and control groups for nightmares, sleep, and PTSD (all P<.02) with moderate effect sizes for treatment (mean Cohen d = 0.60) and small effect sizes for controls (mean Cohen d = 0.14). Posttraumatic stress symptoms decreased by at least 1 level of clinical severity in 65% of the treatment group compared with symptoms worsening or not changing in 69% of controls (χ^2_1 = 12.80; P<.001). *Conclusions:* Imagery rehearsal therapy is a brief, well-tolerated treatment that appears to decrease chronic nightmares, improve sleep quality, and decrease PTSD symptom severity.

Leskin, G. A., Woodward, S. H., Young, H. E., & Sheikh, J. I. (2002). **Effects of comorbid diagnoses on sleep disturbance in PTSD.** *Journal of Psychiatric Research, 36*, 449-452. doi:10.1016/S0022-3956(02)00025-0 *Objective:* Patients with post-traumatic stress disorder (PTSD) are frequently diagnosed with other psychiatric comorbid conditions. This study tested the hypothesis that PTSD patients suffer a greater proportion of sleep problems according to comorbid diagnoses. *Method:* National Comorbidity Survey (NCS) data from 591 individuals diagnosed with PTSD were analyzed. Revised versions of the Diagnostic Interview Schedule and Composite International Diagnostic Interview were administered to a representative sample of males and females. Groups consisted of patients diagnosed with lifetime PTSD and with current comorbid panic disorder, major depressive disorder, generalized anxiety disorder, and alcohol dependence. *Results:* Patients diagnosed with PTSD/panic disorder reported a significantly greater proportion of nightmare complaints (96%) and insomnia (100%) compared with the other comorbid groups. *Conclusions:* A greater proportion of PTSD patients with comorbid panic disorder complain of sleep-related problems than other comorbid groups. This effect appears unique to panic, rather than other general anxiety disorder or depression. Prospective sleep studies are needed to differentiate the role of sleep in PTSD and PD, as well as to examine the role of psychiatric comorbidity in worsening sleep in PTSD patients.

Levin, R., & Nielsen, T. A. (2007). **Disturbed dreaming, posttraumatic stress disorder, and affect distress: A review and neurocognitive model.** *Psychological Bulletin, 133*, 482-528. doi:10.1037/0033-2909.133.3.482 Nightmares are common, occurring weekly in 4%-10% of the population, and are associated with female gender, younger age, increased stress, psychopathology, and dispositional traits. Nightmare pathogenesis remains unexplained, as do differences between nontraumatic and posttraumatic nightmares (for those with or without posttraumatic stress disorder) and relations with waking functioning. No models adequately explain nightmares nor have they been reconciled with recent developments in cognitive neuroscience, fear acquisition, and emotional memory. The authors review the recent literature and propose a conceptual framework for understanding a spectrum of dysphoric dreaming. Central to this is the notion that variations in nightmare prevalence, frequency, severity, and psychopathological comorbidity reflect the influence of both *affect load*, a consequence of daily variations in emotional pressure, and *affect distress*, a disposition to experience events with distressing, highly reactive emotions. In a cross-state, multilevel model of dream function and nightmare production, the authors integrate findings on emotional memory structures and the brain correlates of emotion.

Mellman, T. A., Bustamante, V., Fins, A. I., Pigeon, W. R., & Nolan, B. (2002). **REM sleep and the early development of posttraumatic stress disorder.** *American Journal of Psychiatry, 159*, 1696-1701. doi:10.1176/appi.ajp.159.10.1696 *Objective:* The potential for chronicity and treatment resistance once posttraumatic stress disorder (PTSD) has become established has stimulated interest in understanding the early pathogenesis of the disorder. Arousal regulation and memory consolidation appear to be important in determining the development of PTSD; both are functions of sleep. Sleep findings from patients with chronic PTSD are complex and somewhat contradictory, and data from the acute phase are quite limited. The aim of the present study was to obtain polysomnographic recordings during an acute period after life-threatening experiences and injury and to relate measures of sleep duration and maintenance and the timing, intensity, and continuity of REM sleep to the early development of PTSD. *Method:* Twenty-one injured subjects meeting study criteria received at least one polysomnographic recording close to the time of medical/surgical stabilization and within a month of injury. PTSD symptoms were assessed concurrently and 6 weeks later. Sleep measures were compared among injured subjects with and without significant PTSD symptoms at follow-up and 10 noninjured comparison subjects and were also correlated with PTSD severity. *Results:* There was more wake time after the onset of sleep in injured, trauma-exposed patients than in noninjured comparison subjects. Development of PTSD symptoms was associated with shorter average duration of REM sleep before a stage change and more periods of REM sleep. *Conclusions:* The development of PTSD symptoms after traumatic injury is associated with a more fragmented pattern of REM sleep.

Neylan, T. C., Marmar, C. R., Metzler, T. J., Weiss, D. S., Zatzick, D. F., Delucchi, K. L., . . . Schoenfeld, F. B. (1998). **Sleep disturbances in the Vietnam generation: Findings from a nationally representative sample of male Vietnam veterans.** *American Journal of Psychiatry, 155*, 929-933. doi:10.1176/ajp.155.7.929 *Objective:* This study analyzed questionnaire items that address complaints about sleep from the National Vietnam Veterans Readjustment Study, a nationally representative sample of the 3.1 million men and women who served in Vietnam. This study compared the frequency of nightmares and difficulties with sleep onset and sleep maintenance in male Vietnam theater veterans with male Vietnam era veteran and male civilian comparison subjects. It focused on the role of combat exposure, nonsleep posttraumatic stress disorder (PTSD) symptoms, comorbid psychiatric and medical disorder, and substance abuse in accounting for different domains of sleep disturbance. *Method:* The authors undertook an archival analysis of the National Vietnam Veterans Readjustment Study database using correlations and linear statistical models. *Results:* Frequent nightmares were found exclusively in subjects diagnosed with current PTSD at the time of the survey (15.0%). In the sample of veterans who served in Vietnam (N=1,167), combat exposure was strongly correlated with frequency of nightmares, moderately correlated with sleep onset insomnia, and weakly correlated with disrupted sleep maintenance. A hierarchical multiple regression analysis showed that in Vietnam theater veterans, 57% of the variance in the frequency of nightmares was accounted for by war zone exposure and non-sleep-related PTSD symptoms. Alcohol abuse, chronic medical illnesses, panic disorder, major depression, and mania did not predict the frequency of nightmares after control for nonsleep PTSD symptoms. *Conclusions:* Frequent nightmares appear to be virtually specific for PTSD. The nightmare is the domain of sleep disturbance most related to exposure to war zone traumatic stress.

Pollack, M. H., Hoge, E. A., Worthington, J. J., Moshier, S. J., Wechsler, R. S., Brandes, M., & Simon, N. M. (2011). **Eszopiclone for the treatment of posttraumatic stress disorder and associated insomnia: A randomized, double-blind, placebo-controlled trial.** *Journal of Clinical Psychiatry, 72*, 892-897. doi:10.4088/JCP.09m05607gry *Objective:* The development of novel strategies for the treatment of posttraumatic stress disorder (PTSD) represents a critical public health need. We present the first prospective, randomized, double-blind, placebo-controlled trial of a non-benzodiazepine hypnotic agent for the treatment of PTSD and associated insomnia.

Method: Twenty-four patients with PTSD by DSM-IV criteria and sleep disturbance were treated in a randomized, double-blind, placebo-controlled crossover study of 3 weeks of eszopiclone 3 mg at bedtime compared to placebo. The primary outcome measures were changes in scores on the Short PTSD Rating Interview (SPRINT) and the Pittsburgh Sleep Quality Index (PSQI). The data were collected from April 2006 to June 2008. *Results:* Three weeks of eszopiclone pharmacotherapy was associated with significantly greater improvement than placebo on PTSD symptom measures including the SPRINT (*P* = .032) and the Clinician-Administered PTSD Scale (*P* = .003), as well as on measures of sleep including the PSQI (*P* = .011) and sleep latency (*P* = .044). Greater improvement with eszopiclone on PTSD measures was present even when specific sleep-related items were excluded. Adverse events were consistent with the known profile of the drug. *Conclusions:* This study provides initial evidence that pharmacotherapy with eszopiclone may be associated with short-term improvement in overall PTSD severity as well as associated sleep disturbance. Longer, more definitive study of eszopiclone in PTSD is warranted.

Pruiksma, K. E., Taylor, D. J., Wachen, J. S., Mintz, J., Young-McCaughan, S., Peterson, A. L., . . . Resick, P. A. (2016). **Residual sleep disturbances following PTSD treatment in active duty military personnel.** *Psychological Trauma: Theory, Research, Practice, and Policy, 8*, 697-701. doi:10.1037/tra0000150 *Objective:* Sleep disturbances, including nightmares and insomnia, are frequently reported symptoms of posttraumatic stress disorder (PTSD). Insomnia is one of the most common symptoms to persist after evidence-based PTSD treatment. The purpose of this study was to examine the prevalence of sleep disturbances in a sample of active duty military personnel before and after receiving therapy for PTSD in a clinical trial and to explore the associations of insomnia and nightmares with PTSD diagnosis after treatment. *Method:* Sleep parameters were evaluated with the PTSD Checklist in 108 active duty U.S. Army soldiers who had completed at least one deployment in support of the wars in Iraq and Afghanistan and who participated in a randomized clinical trial comparing Group Cognitive Processing Therapy–Cognitive Only Version with Group Present-Centered Therapy. *Results:* Insomnia was the most frequently reported symptom before and after treatment, with 92% reporting insomnia at baseline and 74%–80% reporting insomnia at follow-up. Nightmares were reported by 69% at baseline and by 49%–55% at follow-up. Among participants who no longer met criteria for PTSD following treatment, 57% continued to report insomnia, but only 13% continued to report nightmares. At baseline, 54% were taking sleep medications, but sleep medication use did not affect the overall results. *Conclusions:* Insomnia was found to be one of the most prevalent and persistent problems among service members receiving PTSD treatment. Nightmares were relatively more positively responsive to treatment. For some service members with PTSD, the addition of specific treatments targeting insomnia and/or nightmares may be indicated.

Raskind, M. A., Peskind, E. R., Hoff, D. J., Hart, K. L., Holmes, H. A., Warren, D., . . . McFall, M. E. (2007). **A parallel group placebo controlled study of prazosin for trauma nightmares and sleep disturbance in combat veterans with post traumatic stress disorder.** *Biological Psychiatry, 61*, 928-934. doi:10.1016/j.biopsych.2006.06.032 *Background:* Excessive brain responsiveness to norepinephrine appears to contribute to post-traumatic stress disorder (PTSD), particularly at night. Prazosin, a brain active alpha-1 adrenergic receptor antagonist, significantly reduced trauma nightmares and sleep disturbance in 10 Vietnam War combat veterans in a previous placebo-controlled crossover study. The current parallel group trial in a larger sample of veterans evaluated prazosin effects on trauma nightmares, sleep quality, global clinical status, dream characteristics, and comorbid depression. *Methods:* Forty veterans (mean age 56 ± 9) with chronic PTSD and distressing trauma nightmares and sleep disturbance were randomized to evening prazosin (13.3 ± 3 mg/day) or placebo for 8 weeks. *Results:* In the evaluable sample (n = 34), primary outcome measures demonstrated that prazosin was significantly superior to placebo for reducing trauma nightmares and improving sleep quality and global clinical status with large effect sizes. Prazosin shifted dream characteristics from those typical of trauma-related nightmares toward those typical of normal dreams. Blood pressure changes from baseline to end study did not differ significantly between prazosin and placebo. *Conclusions:* Prazosin is an effective and well-tolerated treatment for trauma nightmares, sleep disturbance and global clinical status in veterans with chronic PTSD.

Raskind, M. A., Peterson, K., Williams, T., Hoff, D. J., Hart, K., Holmes, H., . . . Peskind, E. R. (2013). **A trial of prazosin for combat trauma PTSD with nightmares in active-duty soldiers returned from Iraq and Afghanistan.** *American Journal of Psychiatry, 170*, 1003-1010. doi:10.1176/appi.ajp.2013.12081133 *Objective:* The authors conducted a 15-week randomized controlled trial of the alpha-1 adrenoreceptor antagonist prazosin for combat trauma nightmares, sleep quality, global function, and overall symptoms in active-duty soldiers with posttraumatic stress disorder (PTSD) returned from combat deployments to Iraq and Afghanistan. *Method:* Sixty-seven soldiers were randomly assigned to treatment with prazosin or placebo for 15 weeks. Drug was titrated based on nightmare response over 6 weeks to a possible maximum dose of 5 mg midmorning and 20 mg at bedtime for men and 2 mg midmorning and 10 mg at bedtime for women. Mean achieved bedtime doses were 15.6 mg of prazosin (SD=6.0) and 18.8 mg of placebo (SD=3.3) for men and 7.0 mg of prazosin (SD=3.5) and 10.0 mg of placebo (SD=0.0) for women. Mean achieved midmorning doses were 4.0 mg of prazosin (SD=1.4) and 4.8 mg of placebo (SD=0.8) for men and 1.7 mg of prazosin (SD=0.5) and 2.0 mg of placebo (SD=0.0) mg for women. Primary outcome measures were the nightmare item of the Clinician-Administered PTSD Scale (CAPS), the Pittsburgh Sleep Quality Index, and the change item of the Clinical Global Impressions Scale anchored to functioning. Secondary outcome measures were the 17-item CAPS, the Hamilton Depression Rating Scale, the Patient Health Questionnaire–9, and the Quality of Life Index. Maintenance psychotropic medications and supportive psychotherapy were held constant. *Results:* Prazosin was effective for trauma nightmares, sleep quality, global function, CAPS score, and the CAPS hyperarousal symptom cluster. Prazosin was well tolerated, and blood pressure changes did not differ between groups. *Conclusions:* Prazosin is effective for combat-related PTSD with trauma nightmares in active-duty soldiers, and benefits are clinically meaningful. Substantial residual symptoms suggest that studies combining prazosin with effective psychotherapies might demonstrate further benefit.

Ross, R. J., Ball, W. A., Sullivan, K. A., & Caroff, S. N. (1989). **Sleep disturbance as the hallmark of posttraumatic stress disorder.** *American Journal of Psychiatry, 146*, 697-707. doi:10.1176/ajp.146.6.697

FEATURED ARTICLES *continued*

The reexperiencing of a traumatic event in the form of repetitive dreams, memories, or flashbacks is one of the cardinal manifestations of posttraumatic stress disorder (PTSD). The dream disturbance associated with PTSD may be relatively specific for this disorder, and dysfunctional REM sleep mechanisms may be involved in the pathogenesis of the posttraumatic anxiety dream. Furthermore, the results of neurophysiological studies in animals suggest that CNS processes generating REM sleep may participate in the control of the classical startle response, which may be akin to the startle behavior commonly described in PTSD patients. Speculating that PTSD may be fundamentally a disorder of REM sleep mechanisms, the authors suggest several strategies for future research.

Seelig, A. D., Jacobson, I. G., Smith, B., Hooper, T. I., Boyko, E. J., Gackstetter, G. D., . . . Smith, T. C. (2010). **Sleep patterns before, during, and after deployment to Iraq and Afghanistan.** *Sleep, 33*, 1615-1622. *Study Objectives:* To determine the associations between deployment in support of the wars in Iraq and Afghanistan and sleep quantity and quality. *Design:* Longitudinal cohort study *Setting:* The Millennium Cohort Study survey is administered via a secure website or US mail. *Participants:* Data were from 41,225 Millennium Cohort members who completed baseline (2001-2003) and follow-up (2004-2006) surveys. Participants were placed into 1 of 3 exposure groups based on their deployment status at follow-up: nondeployed, survey completed during deployment, or survey completed postdeployment. *Interventions:* N/A. *Measurements And Results:* Study outcomes were self-reported sleep duration and trouble sleeping, defined as having trouble falling asleep or staying asleep. Adjusted mean sleep duration was significantly shorter among those in the deployed and postdeployment groups compared with those who did not deploy. Additionally, male gender and greater stress were significantly associated with shorter sleep duration. Personnel who completed their survey during deployment or postdeployment were significantly more likely to have trouble sleeping than those who had not deployed. Lower self-reported general health, female gender, and reporting of mental health symptoms at baseline were also significantly associated with increased odds of trouble sleeping. *Conclusions:* Deployment significantly influenced sleep quality and quantity in this population though effect size was mediated with statistical modeling that included mental health symptoms. Personnel reporting combat exposures or mental health symptoms had increased odds of trouble sleeping. These findings merit further research to increase understanding of temporal relationships between sleep and mental health outcomes occurring during and after deployment.

Swanson, L. M., Favorite, T. K., Horin, E., & Arnedt, J. T. (2009). **A combined group treatment for nightmares and insomnia in combat veterans: A pilot study.** *Journal of Traumatic Stress, 22*, 639-642. doi:10.1002/jts.20468 Insomnia and nightmares are hallmarks of posttraumatic stress disorder (PTSD). Sleep disturbances in PTSD negatively impact clinical course and functioning. In this open clinical trial, the preliminary effects of a combined treatment for insomnia and nightmares in combat veterans with PTSD were assessed. Ten combat veterans participated in a 10-session group treatment combining cognitive–behavioral therapy for insomnia with exposure, rescripting, and relaxation therapy. Participants maintained daily sleep and dream diaries and completed self-report measures of sleep quality and PTSD symptoms pre- and posttreatment. Participants reported improvements in sleep and nightmares following treatment. Future research using controlled designs to evaluate this treatment is warranted.

FEATURED ARTICLES *continued*

Talbot, L. S., Hairston, I. S., Eidelman, P., Gruber, J., & Harvey, A. G. (2009). **The effect of mood on sleep onset latency and REM sleep in interepisode bipolar disorder.** *Journal of Abnormal Psychology, 118*, 448-458. doi:10.1037/a0016605 The present study investigates whether interepisode mood regulation impairment contributes to disturbances in sleep onset latency (SOL) and rapid eye movement (REM) sleep. Individuals with interepisode bipolar disorder (n = 28) and healthy controls (n = 28) slept in the laboratory for 2 baseline nights, a happy mood induction night, and a sad mood induction night. There was a significant interaction whereby on the happy mood induction night the bipolar group exhibited significantly longer SOL than did the control group, while there was no difference on the baseline nights. In addition, control participants exhibited shorter SOL on the happy mood induction night compared to the baseline nights, a finding that was not observed in the bipolar group. On the sad mood induction night, participants in both groups had shorter SOL and increased REM density when compared to the baseline nights. Bipolar participants exhibited heightened REM density compared to control participants on both nights. These results raise the possibility that regulation of positive stimuli may be a contributor to difficulties with SOL, while hyperactivity may be characteristic of REM sleep.

Villarreal, G., Hamner, M. B., Cañive, J. M., Robert, S., Calais, L. A., Durklaski, V., . . . Qualls, C. (2016). **Efficacy of quetiapine monotherapy in posttraumatic stress disorder: A randomized, placebo-controlled trial.** *American Journal of Psychiatry, 173*, 1205-1212. doi:10.1176/appi.ajp.2016.15070967 *Objective:* This was a 12-week randomized, placebo-controlled trial to assess the efficacy of quetiapine monotherapy in the treatment of posttraumatic stress disorder (PTSD). *Method:* Eighty patients were randomly assigned to treatment with either quetiapine or placebo. The primary outcome measure was the Clinician-Administered PTSD Scale (CAPS). Secondary efficacy measures included the CAPS subscales, the Davidson Trauma Scale, the Positive and Negative Syndrome Scale (PANSS), the Clinical Global Impressions (CGI) scales for severity of Illness and improvement, the Hamilton Depression Rating Scale (HAM-D), and the Hamilton Anxiety Rating Scale (HAM-A). Safety measurements included adverse events, vital signs, the Abnormal Involuntary Movement Scale, the Barnes Akathisia Scale, the Simpson-Angus Scale, and the Arizona Sexual Experiences Scale. *Results:* After a 1-week placebo run-in, quetiapine was started at a daily dosage of 25 mg and increased to a maximum of 800 mg; the average was 258 mg (range, 50–800 mg). Reductions in CAPS total, re-experiencing, and hyperarousal scores were significantly greater for the quetiapine group than for the placebo group. Greater improvements were also observed for quetiapine in scores on the Davidson Trauma Scale, CGI severity and improvement ratings, PANSS positive symptom and general psychopathology subscales, HAM-A, and HAM-D than for placebo. Adverse events were generally mild and expected based on prior studies of quetiapine in this and other patient population. There were no differences in safety measures between groups. *Conclusion:* Quetiapine monotherapy was efficacious in the treatment of PTSD. These findings suggest quetiapine as a single agent is effective in treating military PTSD.

ADDITIONAL CITATIONS

Ahmadpanah, M., Sabzeiee, P., Hosseini, S. M., Torabian, S., Haghighi, M., Jahangard, L., . . . Brand, S. (2014). **Comparing the effect of prazosin and hydroxyzine on sleep quality in patients suffering from posttraumatic stress disorder.** *Neuropsychobiology, 69*, 235-242. doi:10.1159/000362243 Given the evidence for heightened

central nervous system adrenergic activity in PTSD, the alpha-1 adrenergic receptor antagonist prazosin has been introduced as a treatment for PTSD sleep disturbances. There also is evidence for the efficacy of the histamine-1 receptor antagonist hydroxyzine in managing disturbed sleep and stress in PTSD. In this randomized, placebo-controlled trial of prazosin and hydroxyzine in PTSD, the authors reported that both improved sleep and reduced nightmares; improvement was greater with prazosin.

Alexander, B., Lund, B. C., Bernardy, N. C., Christopher, M. L. D., & Friedman, M. J. (2015). **Early discontinuation and suboptimal dosing of prazosin: A potential missed opportunity for veterans with posttraumatic stress disorder.** *Journal of Clinical Psychiatry, 76*, e639-644. doi:10.4088/JCP.14m09057 VA/Department of Defense Guidelines recommend prazosin as pharmacotherapy for the sleep and nightmare disturbances in PTSD. Using administrative data from fiscal year 2010, the authors investigated a large cohort of Veterans with PTSD who were prescribed prazosin and determined the duration of use and dosing patterns. Less than 40% were still taking the drug one year after treatment was initiated, and less than 20% received the minimum recommended dose. Factors underlying these prescribing patterns should be elucidated in order to develop strategies for reducing barriers to optimal treatment.

Baddeley, J. L., & Gros, D. F. (2013). **Cognitive behavioral therapy for insomnia as a preparatory treatment for exposure therapy for posttraumatic stress disorder.** *American Journal of Psychotherapy, 67*, 203-214. This case study examined the effects of sequencing CBT-I and exposure therapy for treatment of insomnia and PTSD. CBT-I was used as a first-step treatment followed by exposure therapy. The authors suggest that CBT-I may be a good way to start treatment for patients with these commonly co-occurring disorders rather than beginning with trauma-focused therapy and that improving sleep may lead to better outcomes in PTSD treatment.

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 This meta-analysis was aimed at evaluating the efficacy of IR as an intervention for nightmares, overall sleep quality, and PTSD symptoms. The authors conclude that IR does improve sleep and reduce PTSD symptoms across a diverse range of studies. The methodological quality of the studies in this meta-analysis represents an important caveat for the interpretation of its findings: only five of the 13 studies were RCTs, only one study compared IR to an active treatment control condition, and most studies (*n*=8) lacked a wait-list control condition.

Collen, J. F., Lettieri, C. J., & Hoffman, M. (2012). **The impact of posttraumatic stress disorder on CPAP adherence in patients with obstructive sleep apnea.** *Journal of Clinical Sleep Medicine, 8*, 667-672. doi:10.5664/jcsm.2260 Previous studies have examined how OSA may impact PTSD, but few have looked in the other direction to see if PTSD impacts OSA and its treatment. In this study, rates of adherence to CPAP treatment were examined in active duty military personnel with OSA. PTSD was associated with lower rates of adherence (61.4% of nights) compared to those without PTSD (76.8% of nights). Given that treatment of OSA may improve symptoms of PTSD, this highlights the need for concurrent treatment of both disorders.

Gutner, C. A., Casement, M. D., Stavitsky Gilbert, K., & Resick, P. A. (2013). **Change in sleep symptoms across cognitive processing therapy and prolonged exposure: A longitudinal perspective.** *Behaviour Research and Therapy, 51*, 817-822. doi:10.1016/j.brat.2013.09.008 This study examined changes in sleep symptomatology following CPT, PE, or minimal attention for PTSD. While some improvement was present, neither evidence-based PTSD treatment resulted in the remission of the PTSD-related sleep disturbance, with women remaining symptomatic after treatments. The authors concluded that sleep-specific treatments are warranted to eliminate sleep symptomatology and suggest that sleep treatment before or after PTSD treatment may enhance treatment gains in these trauma-focused treatments.

Ho, F. Y-Y., Chan, C. S., & Tang, K. N-S. (2016). **Cognitive-behavioral therapy for sleep disturbances in treating posttraumatic stress disorder symptoms: A meta-analysis of randomized controlled trials.** *Clinical Psychology Review, 43*, 90-102. doi:10.1016/j.cpr.2015.09.005 This meta-analysis examined the efficacy of sleep-focused CBT in ameliorating PTSD symptoms, sleep symptoms and depression. Of 11 RCTs examined, eight used a sleep- focused CBT alone, including CBT-I (2 studies), Exposure Rescripting and Relaxation Therapy (2 studies), IR (1 study), mind–body bridging (MBB; 1 study), and behavioral sleep intervention (BSI; 1 study); three RCTs used a combination of CBT-I plus IR. CBT for sleep disturbances was found to be efficacious for the daytime PTSD symptoms and depressive symptoms, as well as sleep quality and continuity. Depressive symptoms also responded to sleep-focused CBT, with small to medium effect sizes. The authors conclude that treatments that target sleep disturbances appear effective in mitigating symptoms of PTSD and major depressive disorder, in addition to sleep itself.

Khachatryan, D., Groll, D., Booij, L., Sepehry, A. A., & Schütz, C. G. (2016). **Prazosin for treating sleep disturbances in adults with posttraumatic stress disorder: A systematic review and meta-analysis of randomized controlled trials.** *General Hospital Psychiatry, 39*, 46-52. doi:10.1016/j.genhosppsych.2015.10.007 Consistent with the evidence for central noradrenergic hyperactivity in PTSD, the alpha-1 adrenoceptor antagonist prazosin has been found effective for treating PTSD sleep disturbances in several RCTs. In this meta-analysis of six RCTs, Khachatryan et al. reported that prazosin was significantly more effective than placebo in reducing PTSD symptoms overall and sleep disturbances in particular.

Krystal, J. H., Pietrzak, R. H., Rosenheck, R. A., Cramer, J. A., Vessicchio, J., Jones, K. M., . . . Krystal, A. D. (2016). **Sleep disturbance in chronic military-related PTSD: Clinical impact and response to adjunctive risperidone in the Veterans Affairs Cooperative Study #504.** *Journal of Clinical Psychiatry, 77*, 483-491. doi:10.4088/JCP.14m09585 This study was a secondary analysis of a 24-week RCT of adjunctive risperidone in Veterans with chronic military-related PTSD only partially responsive to antidepressants and other standard pharmacotherapies. Krystal et al. reported that 88% of patients had clinically significant sleep disturbances that were correlated with PTSD severity and reduced quality of life. Adjunctive risperidone produced significant, but only modest, improvements in sleep quality, which were correlated with small reductions in PTSD severity and improvements in quality of life.

ADDITIONAL CITATIONS *continued*

Littlewood, D. L., Gooding, P. A., Panagioti, M., & Kyle, S. D. (2016). **Nightmares and suicide in posttraumatic stress disorder: The mediating role of defeat, entrapment, and hopelessness.** *Journal of Clinical Sleep Medicine, 12*, 393-399. doi:10.5664/jcsm.5592 This study focused on the relationship between sleep disturbance and suicide risk, including a focus on identifying potential cognitive mediators. In a sample of 91 participants with trauma history and current PTSD symptoms, rates of suicidal behaviors were significantly higher than in those with nightmares (62% vs.20%). Beliefs about defeat, hopelessness and entrapment significantly mediated this relationship, suggested possible cognitive mechanisms by which disturbed sleep leads to suicidal behavior. The results of this study suggest that interventions to reduce suicidal behavior should target nightmares as well as these cognitive processes.

McLay, R. N., Klam, W. P., & Volkert, S. L. (2010). **Insomnia is the most commonly reported symptom and predicts other symptoms of post-traumatic stress disorder in U.S. service members returning from military deployments.** *Military Medicine, 175*, 759-762. doi:10.7205/MILMED-D-10-00193 McLay and colleagues conducted a search of electronic medical records data of military personnel who had received care at the Naval Medical Center San Diego and who had completed the PTSD Checklist (PCL) as part of routine screening. They found that, of all the PTSD symptoms assessed with the PCL, insomnia was the most frequently endorsed at 41% and also had the highest average severity rating. Those with insomnia also reported more severe PTSD symptoms overall.

Mysliwiec, V., Matsangas, P., Gill, J., Baxter, T., O'Reilly, B., Collen, J. F., & Roth, B. J. (2015). **A comparative analysis of sleep disordered breathing in active duty service members with and without combat-related posttraumatic stress disorder.** *Journal of Clinical Sleep Medicine, 11*, 1393-1401. doi:10.5664/jcsm.5272 In this study 109 military personnel who had returned from combat deployment were categorized into OSA and PTSD (*n*=24), OSA alone (*n*=68) or PTSD alone (*n*=17) using in-lab sleep studies. There was no difference in the severity of PTSD in those with and without comorbid OSA. Similarly, there was no difference in the severity of OSA in those with and without comorbid PTSD. These data, in contrast to prior studies, failed to find an increased rate of OSA in those with PTSD, nor was PTSD more severe in those with OSA.

Mysliwiec, V., O'Reilly, B., Polchinski, J., Kwon, H. P., Germain, A., & Roth, B. J. (2014). **Trauma associated sleep disorder: A proposed parasomnia encompassing disruptive nocturnal behaviors, nightmares, and REM without atonia in trauma survivors.** *Journal of Clinical Sleep Medicine, 10*, 1143-1148. doi:10.5664/jcsm.4120 Parasomnias are unusual behaviors during sleep and can include sleepwalking, sleep-related eating, and acting out of dream content during sleep. This was a case series of four male active duty military personnel who presented to the sleep clinic with nocturnal behaviors and nightmares. On overnight sleep study, all had elevated muscle tone during REM sleep, a classic feature of some REM-sleep parasomnias. Authors argue that this pattern represents a novel sleep disorder that they term Trauma Associated Sleep Disorder, rather than a comorbid parasomnia.

Petrakis, I. L., Desai, N., Gueorguieva, R., Arias, A., O'Brien, E., Jane, J. S., . . . Ralevski, E. (2016). **Prazosin for veterans with posttraumatic stress disorder and comorbid alcohol dependence: A clinical trial.** *Alcoholism: Clinical and Experimental Research, 40*, 178-186. doi:10.1111/acer.12926 There is evidence for noradrenergic dysregulation in alcohol dependence (AD), suggesting that prazosin may have efficacy in the treatment of PTSD comorbid with AD, a highly prevalent comorbidity with great clinical significance. In this RCT in Veterans with PTSD and comorbid AD, Petrakis et al. found that prazosin was not effective in reducing PTSD symptoms, improving sleep, or reducing alcohol consumption. The authors emphasized the importance of conducting RCTs in "real-world" patients with common comorbidities.

Raskind, M. A., Millard, S. P., Petrie, E. C., Peterson, K., Williams, T., Hoff, D. J., . . . Peskind, E. R. (2016). **Higher pretreatment blood pressure is associated with greater posttraumatic stress disorder symptom reduction in soldiers treated with prazosin.** *Biological Psychiatry, 80*, 736-742. doi:10.1016/j.biopsych.2016.03.2108 Investigating the effects of baseline standing systolic and other blood pressure parameters on PTSD outcome measures from a previously reported randomized placebo-controlled trial of prazosin, the authors found that, in prazosin, but not placebo, participants, higher baseline standing systolic and other blood pressure parameters were associated with greater reductions in PTSD symptoms at the end of treatment. These results are consistent with a role of alpha-1 adrenoceptor activation in the pathophysiology of PTSD and suggest that higher standing blood pressure is a biomarker for identifying Veterans with combat-related PTSD who are likely to benefit from prazosin.

Seda, G., Sanchez-Ortuno, M. M., Welsh, C. H., Halbower, A. C., & Edinger, J. D. (2015). **Comparative meta-analysis of prazosin and imagery rehearsal therapy for nightmare frequency, sleep quality, and posttraumatic stress.** *Journal of Clinical Sleep Medicine, 11*, 11-22. doi:10.5664/jcsm.4354 This meta-analysis compared the short term efficacy of prazosin and IR interventions alone or in combination. Fifteen RCTs were coded and analyzed, with 18 contrast groups reporting posttest effects from the treatment group compared to a control group for at least one of the three outcomes of interest: nightmare frequency, sleep quality, and PTSD symptoms. The results indicate that the interventions studied yield overall moderate effect sizes for nightmares, sleep quality and PTSD. The combination of IR with CBT-I performed significantly better at improving overall sleep quality than did prazosin, IR alone, and IR combined with other forms of psychological interventions.

Tamanna, S., Parker, J. D., Lyons, J., & Ullah, M. I. (2014). **The effect of continuous positive air pressure (CPAP) on nightmares in patients with posttraumatic stress disorder (PTSD) and obstructive sleep apnea (OSA).** *Journal of Clinical Sleep Medicine, 10*, 631-636. doi:10.5664/jcsm.3786 This study consisted of a retrospective review of medical records for 69 Veterans with a diagnosis of PTSD who were diagnosed and treated for OSA with CPAP. CPAP treatment led to a reduction in daytime sleepiness and, in terms of PTSD symptoms, a significant reduction in nightmares from 10.3 to 5.3 per week. The results of this study further support the need for routine screening and treatment of OSA in patients with PTSD.

VA Office of Research and Development. (2016). ***Cooperative Studies Program #563 - Prazosin and combat trauma PTSD (PACT)*** (Clinicaltrials.gov Identifier NCT00532493). Retrieved from https://clinicaltrials.gov/ct2/show/NCT00532493 This clinical trial

ADDITIONAL CITATIONS *continued*

was part of the VA Cooperative Studies Program and was designed to assess the efficacy of prazosin for treatment of nightmares and sleep disturbance in Veterans with PTSD. It was a 26-week randomized, double-blind placebo-controlled multisite study with 304 enrolled subjects. Surprisingly, there were no statistically significant treatment effects on the primary outcome measures. It is not clear why the results of this study were different from those of most prior studies but future exploration of the results may help to generate hypotheses.