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Recent Advancements in Treating Sleep Disorders in Co-Occurring PTSD

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Abstract

Purpose of Review—Comorbidity of posttraumatic stress disorder (PTSD) and insomnia, nightmares, and obstructive sleep apnea (OSA) is high. We review recent research on psychotherapeutic and pharmacological interventions for sleep disorders in PTSD.

Recent Findings—PTSD treatments decrease PTSD severity and nightmare frequency, but do not resolve OSA or insomnia. Research on whether insomnia hinders PTSD treatment shows mixed results; untreated OSA does interfere with PTSD treatment. Cognitive behavioral therapy for insomnia is the recommended treatment for insomnia; however, optimal ordering with PTSD treatment is unclear. PTSD treatment may be most useful for PTSD-related nightmares. CPAP therapy is recommended for OSA but adherence can be low.

Summary—Targeted treatment of sleep disorders in the context of PTSD offers a unique and underutilized opportunity to advance clinical care and research. Research is needed to create screening protocols, determine optimal order of treatment, and elucidate mechanisms between sleep and PTSD treatments.

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Compliance with Ethical Standards

Conflict of Interest P.J.C., L.D.S., C.S., L.A.G., and S.B.N. each declare no potential conflicts of interest.

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Keywords

PTSD; Sleep disorders; Insomnia; Obstructive sleep apnea; Treatment

Introduction

Comorbidity of posttraumatic stress disorder (PTSD) and sleep disorders is staggeringly high, with 70–91% of individuals with PTSD reporting sleep disturbances [1–3]. The most common sleep disturbances include insomnia [1, 4], obstructive sleep apnea (OSA) [5, 6••], and nightmares [4], with prevalence rates in PTSD that are considerably higher than in unaffected individuals. Furthermore, sleep disorders, even when controlling for PTSD symptoms, contribute to major depression, substance abuse, impaired daytime functioning [7], negative long-term health consequences [8], and suicide risk [7]. Treatments for sleep disorders, in the context of co-occurring PTSD, offer opportunity to advance client-centered clinical care and research.

We review recent research on pharmacological and psychotherapeutic interventions for the most common sleep disturbances in PTSD: insomnia, nightmares, and OSA. First, we review sleep disorder prevalence and assessment in patients with PTSD and the relationships between sleep disorders and PTSD severity. Second, we review sleep disorder treatments in patients with PTSD. Finally, we make suggestions for screening (see Fig. 1) and research to advance sleep treatments with co-occurring PTSD.

Prevalence of Sleep Disorder with PTSD

Prevalence of Insomnia in PTSD

“Difficulty sleeping” was reported by up to 90% of individuals with PTSD [9] whereas application of DSM-5 criteria for insomnia suggest a range of 35–61% [1–3, 5]. Interestingly, civilian and military samples with PTSD showed similar rates of insomnia [1, 2]. However, the rates of insomnia depend on a range of factors that include definition of insomnia (“trouble sleeping,” DSM-5 criteria), sample characteristics (treatment seeking, community), trauma type (sexual assault, combat, natural disaster), objective/ subjective measurement (self-report questionnaire, actigraphy), instrument (sleep items from PCL, validated sleep questionnaire), time from incident trauma (childhood, adult), co-occurring disorders (depression/OSA/TBI), and age [1, 2, 4, 5, 9–14].

Prevalence of Nightmares in PTSD

Recurrent nightmares are one of two sleep items in the PTSD diagnosis and are highly prevalent in PTSD. Prevalence estimates range from 50 to 96% [4, 15]. Nightmare frequency was estimated at more than five per week in a sample of sexual assault survivors with PTSD [5], while increased combat exposure in Vietnam veterans was related to increased nightmare frequency [4]. Rates of nightmares seems to depend upon criteria, assessment, and methodology [16]. In a retrospective review of 500 active military personnel, Creamer et al. [17•] found 31.2% had nightmares weekly, but only 3.9% reported nightmares as a reason for seeking treatment.

Prevalence of OSA in PTSD

Sleep-disordered breathing (SDB) is a spectrum [18] ranging from mild upper airway resistance (e.g., snoring) to severe OSA. OSA is defined by repeated episodes of apneas (pauses in breathing) and hypopneas (shallow breathing) with decreases in blood oxygenation during sleep. The apnea–hypopnea index (AHI) per hour is the most commonly used metric of OSA severity. Research suggests that individuals with PTSD have higher rates of OSA than the general population; estimates range from 13.5 to 83% [19, 20]. However, not all studies found a higher prevalence of OSA in PTSD [21]. Rates of OSA seem to depend on objective/subjective measurement, diagnostic criteria (SDB, OSA), AHI thresholds, sample characteristics (military, civilian), age, body mass index (BMI), and sex (see Gupta et al. [22•] and Zhang et al. for reviews [23••]). In a meta-analysis on CPAP [23••], pooled variance % of OSA was reported in 10 studies on individuals with PTSD (mean age 42.4 years). OSA prevalence was 75.7% when using criteria of AHI > 5 and 43.6% when using AHI > 10; rates are significantly higher in individuals with PTSD than without. Of note, a majority of their studies ($N=9$) used veteran samples, limiting generalizability to civilian samples. Their analyses showed no difference in rates of OSA by U.S. compared to non-U.S. or mixed samples (60.4 vs. 42.4%). They did, however, find differences based on veterans and non-veterans (62.5 vs. 7.0%), but the civilian numbers may be skewed. While the pooled variance is similar to findings in studies not included in the review, increasing confidence in the findings [24], Zhang et al. noted that they could not control for psychotropic medications that may affect OSA prevalence (e.g., benzodiazepines, opioids). Gupta et al. noted that no conclusion could be drawn about the role of medications on OSA prevalence due to the wide range of medications and quality of the studies but suggests that medications that lead to weight gain (e.g., antipsychotics) or affecting upper airway and breathing (e.g., benzodiazepines) may be risk factors for OSA.

There is increasing evidence that the classic predictors of OSA, such as BMI and age, may not apply to younger veterans with PTSD. Two recent studies found 67.3–69.2% were at high risk of OSA in younger veterans (mean age = 33.40–35.1 years) with lower BMI (BMI = 19.08–28.9) [6, 25]. Similarly, in a recent PSG study comparing Iranian veterans with and without PTSD, AHI was higher and BMI lower in the PTSD group compared to the non-PTSD group, and that AHI was unrelated to BMI [26•].

Relationship Between Sleep Disorders and PTSD

Relationship Between Insomnia and PTSD

Although sleep disturbances are symptoms of PTSD, insomnia may be best considered a co-occurring and independent disorder [27•, 28]. For instance, insomnia may precede the trauma and predict the development of PTSD [29–33]. This is especially true in military populations where short sleep duration and irregular sleep patterns are common [9, 34]. Second, when insomnia initially occurs as a symptom of PTSD, it can become an independent disorder when the behavioral and cognitive responses to acute insomnia lead to perpetuating factors (e.g., napping, sleeping pills) and conditioned arousal [35]. Additionally, nightmares and hyperarousal symptoms may lead to the pairing of the bed with wakefulness (i.e., conditioned arousal). Thus, perpetuating factors and conditioned arousal

are often responsible for the maintenance of insomnia even in the absence of PTSD [36]. This suggests that insomnia may need to be assessed and treated separately from, or in conjunction with, PTSD.

Relationship Between Nightmares and PTSD

Nightmares in PTSD are associated with increased anxiety, depression, and suicide [37, 38]. Similar to both insomnia and OSA, the temporal relationship between nightmares and PTSD is unknown; however, there is evidence that nightmares may precede PTSD [4, 39, 40]. Nightmares may also influence insomnia through conditioned arousal (e.g., chronic nightmares pair the bed with arousal) and OSA (e.g., nighttime fragmentation leading to increased AHI).

Relationship Between PTSD and OSA

Both PTSD and OSA are associated with common medical comorbidities including heart attacks, hypertension, stroke [41–43], pain [43], and diabetes [41, 43]. However, there is a dearth of research examining both OSA and PTSD together on health outcomes. In a study of 187 sexual assault victims with PTSD, patients with both PTSD and SDB had worse physical functioning, bodily pain, less energy, and worse social/emotional/mental health functioning than patients with PTSD alone [5]. One study found that while PTSD was not associated with a higher prevalence of OSA, AHI predicted PTSD severity [21].

While no definitive conclusions can be drawn about the temporal relationship between OSA and PTSD, there may be a bidirectional relationship through which PTSD/chronic arousal affects OSA onset and severity, and a pathway through which OSA negatively affects PTSD and chronic arousal [44]. Jaoude et al. [45••] suggests several possible shared pathways between OSA and PTSD including HPA axis dysfunction [46, 47] and reduced fear extinction [48]. Additionally, there is evidence that SDB or nighttime fragmentation, when paired with trauma, may decrease processing, resiliency, and coping capacity and lead to higher likelihood of stress symptoms [25, 49].

Relationships among PTSD, OSA, and Insomnia

Despite high co-occurrence among PTSD, OSA, and insomnia [14, 26•, 50, 51], clear diagnosis of each disorder is often underreported due to symptom overlap [45••] and absence of differential diagnostic criteria [52•]. One study compared PSG patterns of OSA in veterans and found that those with PTSD were more likely to also have insomnia compared to those without PTSD [26]. Further, recent studies suggest that having PTSD, OSA, and insomnia all together shows a more severe clinical profile than PTSD/OSA or PTSD/insomnia combinations. A nationally representative sample found individuals with OSA and insomnia had worse hypertension and cerebrovascular disease than those with OSA alone [53]. In a sample with PTSD, it was found that veterans with PTSD, insomnia, and OSA had worse quality of life, sleep, and depression than veterans with just PTSD/OSA [54•].

Assessment of Sleep Disorders

Due to the high overlap of symptoms between sleep disorders and PTSD, accurate assessment of sleep disturbance is necessary prior to treatment.

Assessment of Insomnia

One option is to extract existing sleep items from measures of PTSD, such as the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) interview [55] or PTSD Checklist for DSM-5 (PCL-5) self-report questionnaire [56]. While this approach may reduce patient burden, it provides only very basic information about sleep and is inadequate for research or treatment planning. Several validated subjective measures are available to assess the severity, duration, and nature of disruptions to sleep more thoroughly. The Pittsburgh Sleep Quality Index (PSQI) [57] is an 18-item self-report questionnaire which measures global sleep quality over the past month. The Insomnia Severity Index (ISI) [58] is a seven-item measure, evaluating perceived severity of sleep difficulties with sleep satisfaction, daily functioning, and impairment. Prospective sleep diaries allow for measurement of an individual's sleep over several days, including bed times, wake times, sleep latency, wake after sleep onset, total sleep time, and sleep efficiency.

Validated actigraphy offer a convenient option for objective, prospective measurement of sleep. Actigraphy involves wearing an activity monitor, typically similar to a wristwatch, that generates estimates of sleep and wake based on movement. Though collecting several days of sleep data is always ideal, it is particularly important in the case of PTSD, as sleep has been shown to be more variable than in primary insomnia patients without PTSD [59]. Note that actigraphy is not considered a valid methodology for the measurement of sleep stages or arousals from sleep. In contrast to medical-grade actigraphs, consumer-grade activity watches have not been validated in individuals with PTSD and cannot be recommended. Furthermore, proprietary and changing algorithms in many popular, non-clinical devices create difficulties conducting research or measuring clinical change.

Assessment of Nightmares

Similar to insomnia, researchers often extract the nightmare item from the CAPS-5 interview or PCL-5. Less utilized is the Disturbing Dream and Nightmare Severity Index, which assesses the frequency, intensity, and severity of nightmares [60]. Often sleep diaries include the number of nightmares and distress from night-mares. This is important to track in PTSD as there have been significant associations between number of daily stressors and sleep latency, number of nightmares, and distress from night-mares [61].

Assessment of OSA

Common screening measures such as the STOP-BANG [62] and Berlin [63] have not been validated against polysomnography (PSG) in PTSD populations. PSG is the gold standard method for the evaluation of sleep apnea and sleep architecture (e.g., stages of sleep, sleep spindles). PSG has traditionally been conducted in the hospital setting, but this might not be advantageous when assessing patients with PTSD where environmental factors may alter symptom severity [64]. Ambulatory PSG may offer a better option for those with PTSD to

reflect their sleep in their home environment. There is increasing use of validated portable devices for the detection of sleep apnea that are increasingly affordable and easy to use. While these devices cannot report stages of sleep or sleep architecture, they accurately track apneas/ hypopneas. Jaoude [45••] suggests that overestimation of AHI may be encountered when interpreting PSG in patients with PTSD due to PTSD specific arousals and awakenings.

Pharmacological Treatments of Sleep Disorders

Selective serotonin reuptake inhibitors (SSRI) and serotonin– norepinephrine reuptake inhibitors (SNRIs) are recommended as first-line treatments for PTSD [65]. However, the effects of SSRI/SNRI on sleep are typically modest or even adverse. Accordingly, adjunctive medication is commonly indicated for the treatment of insomnia.

GABA Receptor Agonists

Benzodiazepines are commonly used, but controversial in the treatment of insomnia. A recent meta-analysis revealed that short-acting benzodiazepines have modest, beneficial effects on sleep in PTSD; their use is not recommended due to the emergence of tolerance, and their association with depression, aggression, and worse psychotherapy outcomes [66••]. In a review of benzodiazepines and OSA, results suggest that benzodiazepine use was associated with reduced upper airway muscle tone, decreased ventilatory response to hypoxia, increased AHI and oxygen desaturations, and prolonged apneas [67]. It is suggested that benzodiazepines should be avoided in patients with OSA [68].

The non-benzodiazepine hypnotics carry fewer risks, but need further evaluation with PTSD patients. In a meta-analysis in non-PTSD samples, non-benzodiazepine hypnotics were found to have only slight improvements in sleep over placebo [69]. In 24 subjects with PTSD, eszopiclone was shown to have greater beneficial effects than placebo on sleep quality, duration and latency, while reducing waking and improving daytime function [70]. In a meta-analysis, non-benzodiazepine hypnotics in patients with OSA were shown to improve objective sleep quality without worsening AHI [71]; however, this has not been examined in a PTSD sample.

Trazodone and Nefazodone

Two 5HT_{2A} antagonists, nefazodone and trazodone, cause sedation and promote sleep. In small unblinded studies, trazodone has been shown to promote sleep and reduce nightmares in PTSD and depressed patients [72, 73]. Trazodone may be particularly helpful for patients with alcohol use disorders [74] and OSA [75], where GABA receptor agonists are contraindicated. However, the use of trazodone is limited by common side effects including cognitive and motor impairment [76], and tolerance [73].

Antipsychotics Drugs

Many atypical antipsychotic drugs are sedating and show evidence of efficacy in PTSD related insomnia and nightmares. In a placebo-controlled trial, adjunctive olanzapine was reported to have beneficial effects on sleep over 12 weeks in subjects who had failed to

respond fully to SSRI [77]. Similar effects were shown for risperidone. In a large, 24-week study of 267 veterans, risperidone significantly improved scores on the PSQI and reduced nightmares [78]. In a 12-week, placebo-controlled study of quetiapine monotherapy, there were only modest and transient effects on insomnia, even as there was an overall improvement in PTSD symptoms [79]. Antipsychotic drugs are commonly associated with high rates of adverse events [80]. Antipsychotic are associated with weight gain that may also increase risk of OSA [22]. Therefore, patient selection may be especially important with antipsychotics to identify those with favorable clinical profiles.

Adrenergic Drugs

Prazosin is an alpha1 receptor antagonist and is the best-supported drug treatment for insomnia in PTSD. Including case series, more than 10 trials have reported favorable effects of prazosin in PTSD on sleep, improving insomnia, and reducing nightmares across a range of civilian, military, and veteran groups [81, 82]. In a meta-analysis of six randomized trials encompassing 240 subjects, prazosin had significant effects on promoting sleep quality and reducing nightmares [83]. However, a recent multi-center study of prazosin in veterans found no effects on sleep or any other PTSD symptom cluster [84]. This large, well-powered study found relatively strong placebo effects that could have limited the ability to detect prazosin effects. Moreover, as prazosin was already commonly used in veterans with PTSD during the study, treatment-naïve patients may have been difficult to recruit, perhaps leading to selection bias. However, the work indicates that additional studies are needed to identify the circumstances and patients under which prazosin treatment should be selected.

For OSA, there are currently no studies examining the effects of prazosin for decreasing AHI. However, it is possible that prazosin, as a REM suppressor, may decrease nighttime arousals, and thus AHI [85].

Others

Diphenhydramine, gabapentin, hydroxyzine, and tiagabine are commonly used in the general insomnia population but are not well supported by evidence [86]. For example, the only study examining hydroxyzine in a PTSD sample found that hydroxyzine decreased nightmares and improved sleep better than placebo, and prazosin outperformed both [87]. These agents have not yet been systematically evaluated in PTSD. Melatonin agonists (e.g., ramelteon), orexin antagonists (e.g., suvorexant), and low-dose doxepin are approved treatments for insomnia in the general population but have not yet been systematically evaluated in PTSD.

Non-Pharmacological Treatment of Sleep Disorders

Effect of PTSD Treatment on Sleep Disorders

While insomnia tends to improve over the course of PTSD treatment, it often remains disturbed post-treatment. For example, two studies comparing prolonged exposure therapy (PE) and cognitive processing therapy (CPT) [88, 89] and one study examining cognitive-behavioral therapy (CBT) for PTSD [90] found that while sleep improved over the course of treatment, sleep disturbance remained above the clinical cut-off. Further, some of the sleep

improvements deteriorated by the 6-month post-treatment assessment [90]. More recently, in a study of active-duty military personnel randomized to group CPT or group present-centered therapy (PCT) [91••], sleep disturbance was the most frequently reported symptom of PTSD both before and after treatment. Of 108 participants, 92% reported sleep disturbance pre-treatment and 74–80% (CPT and PCT, respectively) reported sleep disturbances post-treatment. Among participants who no longer met criteria for PTSD post-treatment, 57% still reported sleep disturbances.

Nightmares were more responsive to PTSD treatment than insomnia. In one study, 69% reported nightmares pre-treatment and 49–55% at follow-up. However, among participants who no longer met criteria for PTSD, only 13% continued to report nightmares. This is consistent with previous findings showing nightmares decreasing following PTSD treatment [92, 93•]. Finally, a study of PE compared to client-centered treatment found that both insomnia and night-mares decreased, but that while only 20% of participants endorsed nightmares, 55.1% still reported residual insomnia following treatment [94••].

Studies examining whether baseline insomnia affected change in PTSD symptoms over the course of psychotherapy have shown mixed results. Individuals with residual sleep problems following PE were predictive of smaller treatment gains [95•]. In a study of 246 patients who received CT-PTSD, poorer self-reported sleep together with greater depression symptoms were associated with worse PTSD treatment out-comes [96••]. Finally, a study of CBT for PTSD found that individuals with residual sleep difficulties following treatment experienced worse residual PTSD [90]. Beyond PTSD symptoms, one study examining PE to client-centered therapy found that baseline insomnia and nightmares predicted worse quality of life up to 6 months following treatment [94••]. On the other hand, initial sleep duration was not associated with treatment outcomes in a sample of 121 individuals who received CT-PTSD, supportive therapy, or were waitlisted [97••]. Similarly, one study ($N=21$) found that while higher PSQI scores were related to higher baseline PCL scores, PSQI scores were not associated with reduced effectiveness of PE treatment or slope of PTSD symptom changes [98••].

Studies that examined whether baseline OSA affected change in PTSD symptoms over the course of psychotherapy were more consistent. A retrospective study of Veterans who had completed CPT at a VA found that those with OSA ($n=69$) showed less symptom improvement than those without OSA ($n=276$) [99••]. However, those with OSA who were being treated with CPAP showed more improvement than those who were not engaging in OSA treatment. Reist et al. [100••] found similar finding in a smaller sample ($N=18$) undergoing PE, where PCL scores reduced by 28.25 points in those without SDB and only 7.17 points in the SDB group. Reist et al. suggest that OSA and insomnia may have differential impacts on PTSD treatment effectiveness and should both be assessed for treatment planning.

Treatment of Insomnia in PTSD

Non-pharmacological treatments may be more effective to treat insomnia in individuals with PTSD than pharmacological treatments. Cognitive-behavioral therapy for insomnia (CBT-I) is considered to be the front-line treatment for insomnia by the American College of

Physicians [101] and shows promise in PTSD patients. CBT-I is a protocol typically involving (1) sleep restriction, or limiting patients' time in bed to more closely correspond to total sleep time; (2) stimulus control, or instructing patients to use bed for sleep only in order to strengthen the association between bed and sleep; (3) sleep hygiene, or providing additional suggestions for behavioral modifications to improve sleep; and (4) modification of dysfunctional thoughts about sleep. CBT-I can be delivered individually or in group format over 4 to 8 weeks [102].

Efficacy of CBT-I has been established in patients with primary insomnia [103] and has been shown to outperform sleep medication in studies conducted in primary insomnia patients [104, 105]. Several studies have also shown that CBT-I improves insomnia symptoms in PTSD patients; recent meta-analyses show large effect sizes for CBT-I in reducing insomnia symptoms in PTSD [106••] and medium effect sizes for reducing PTSD symptoms [107••]. For example, in an RCT involving mostly civilian PTSD patients, eight-session individual CBT-I improved subjective insomnia and increased objective total sleep time in comparison to waitlist control [108]. However, both groups showed decreases in PTSD, limiting the conclusions on the effects of CBT-I on PTSD symptoms. Other studies support the use of CBT-I in veterans with PTSD as a part of routine clinical care [61]. Taken together, these studies support the use of CBT-I in patients with PTSD.

Several studies in veterans with PTSD used CBT-I and Imagery Rehearsal Therapy (IRT, described below) together, which improved insomnia and PTSD symptoms as compared to treatment as usual [109]. An RCT conducted in veterans with PTSD used combined CBT-I and IRT and showed improvements in insomnia, PTSD, and depressive symptoms compared to the waitlist [110]. It is unclear if combined treatment is more effective than either treatment alone.

As supplemental treatments to trauma-focused or pharmacotherapy interventions, several other behavioral interventions for insomnia have been studied in PTSD, including physical exercise [111], mind-body bridging [112], acupuncture [113], and hypnotherapy [114•, 115], with improvements across a variety of insomnia measures. Additionally, due to the overlap of insomnia and OSA, there is some suggestion that treating both together can improve insomnia symptoms better than either insomnia or OSA treatment alone [67]. The research on these interventions is preliminary and improvements are modest. If supported by larger and more rigorous trials, these interventions have the potential to provide additional options for treating insomnia in PTSD.

Taken together, research suggests CBT-I is the best-supported intervention for treating insomnia in PTSD patients.

Treatment of Nightmares in PTSD

Several non-pharmacological interventions show promise for treating nightmares related to PTSD. Imagery rehearsal therapy (IRT) has been the most researched. IRT involves (1) psychoeducation about sleep and nightmares; (2) relaxation training, (3) rescripting selected nightmares, i.e., writing out the nightmare and changing the storyline, ending or any part of the dream to be more positive; and (4) rehearsing these scripts during the day. Several

studies have suggested IRT improves subjective sleep quality and reduces nightmares in PTSD patients, with large effects in several studies (see Casement and Swanson [116] and Hansen et al. [117] for meta-analyses). Notably, most studies included in these meta-analyses lacked controls, not all were conducted in PTSD samples, and several versions of IRT were used. Some research suggests that IRT may be more beneficial for patients with a primary nightmare disorder than for patients with PTSD and nightmares [118]. One of the few studies with an active control condition only showed small effects of IRT and no differences between groups on nightmare frequency [119]. An RCT comparing IRT to prazosin suggested that both treatments outperformed placebo in reducing insomnia and PTSD symptoms, but did not find differences between the two active treatments [120]. Findings from a recent meta-analysis suggest combining IRT with CBT-I may enhance treatment outcomes in comparison to IRT alone [121••], though it is unclear whether combined treatment outperforms CBT-I alone [122]. Finally, in 108 veterans randomized to CBT-I or IR + CBT-I, no differences were found between the groups in frequency or distress of nightmares [123••]. They conclude that IR may not be a necessary additive to CBT-I.

Another non-pharmacological treatment for nightmares is exposure, relaxation, and rescripting therapy (ERRT). Similar to IRT, this therapy involves rescripting selected nightmares during the day. ERRT involves an exposure therapy component that includes (1) psychoeducation regarding trauma; (2) discussion of the trauma; and (3) identifying trauma-related themes evidenced in the nightmare; thus, ERRT combines elements of trauma-focused psychotherapy with elements from nightmare-specific treatment [124]. Two RCTs have shown ERRT to be more effective than waitlist control in improving nightmares and reducing PTSD symptoms [125, 126]. Recently, a small pilot study showed ERRT may be efficacious in veterans with PTSD [127]. Interestingly, ERRT was less effective in those with suspected OSA as compared to the non-apnea group [128•]. As with IRT, future research in studies with larger study samples and active control conditions would provide additional evidence of ERRT's efficacy as a non-pharmacological treatment for nightmares in PTSD.

Treatment of OSA in PTSD

Continuous Positive Airway Pressure Therapy (CPAP)

Nasal continuous positive airway pressure (CPAP) is the gold-standard treatment for OSA, with meta-analytic reports showing improvement in daytime sleepiness and health-related quality of life [129]. The standard prescription is to use CPAP whenever asleep, including during daytime naps. However, despite CPAP being the most *efficacious* treatment available to OSA patients, adherence is substandard (3 to 5 h per night), thereby significantly limiting its *effectiveness* [130].

Early studies of CPAP in patients diagnosed with OSA and PTSD were primarily concerned with investigating adherence. A recent meta-analysis found that CPAP adherence was lower in patients with both OSA and PTSD than OSA alone [23]. One study found that less use of CPAP was associated with greater baseline nightmare severity and greater daytime sleepiness [131]. Other studies found that greater use of CPAP was associated with a lower nightmare frequency [132, 133, 134••]. Additionally, one study found that CPAP use

decreased nightmare frequency (from 10.32 nightmares per week to 5.26 with CPAP) and was predicted by CPAP adherence [85].

More recent studies directly examined the effect of CPAP therapy on PTSD symptom reduction. Three studies of CPAP therapy found small but consistent decreases in PTSD severity at 12 weeks [135•] and 6 months [136•, 137•]. Due to the dose response with outcomes, increasing adherence with desensitization requires further review [138]. While treating OSA only moderately affects PTSD severity, it may be considered a barrier to successful PTSD treatment and requiring intervention prior to initiating treatment.

Mandibular Repositioning Devices (MRDs)

AASM Clinical Guidelines for the treatment of snoring and OSA with oral appliances state that they are indicated for the treatment of mild to moderate OSA in patients (1) who prefer oral appliances to CPAP, (2) who do not respond to CPAP, (3) who are not suitable for treatment with CPAP, or (4) for whom treatment attempts with CPAP are unsuccessful [139]. There are two main classes of oral appliances: (1) mandibular repositioning devices (MRDs) and (2) tongue-retaining devices. Most research has been performed on MRDs. MRDs work through protruding the mandible to increase the anteroposterior dimensions of the oropharynx and the patency of the upper airway. A review of the literature suggests that 65% of patients experience a 50% reduction in AHI and that 35–40% of patients experience a normalization of the AHI (i.e., AHI \leq 5) [140]. When compared directly to PAP in cross-over trials, PAP consistently shows greater improvements in AHI [141, 142]. Only one study examined MRDs in individuals with PTSD. One study compared CPAP to MRDs and found that while CPAP was more efficacious in reducing AHI, both treatments had mild reductions in PTSD severity [135•]. Importantly, the reported adherence to MRDs was significantly higher than CPAP with 58% preferring MAD to CPAP. MRDs may offer a viable alternative for veterans with OSA and PTSD who are non-adherent to CPAP.

Weight Loss/Exercise

Weight gain is a risk factor for OSA, with one study showing a dose–response relationship between weight gain and OSA such that a 10% weight gain is associated with a sixfold increase in the odds of moderate to severe OSA and a 32% increase in the AHI [143]. A meta-analysis found that while CPAP was the most efficacious in decreasing AHI, exercise training and dietary weight loss also were associated with decreases in AHI [144••]. While this was not examined in a co-occurring PTSD sample, it may be reasonable to assume these findings could carry over especially as PTSD is associated weight gain and low CPAP adherence [133].

Combined Sleep and PTSD Treatments

There are a limited number of studies examining combined treatment for sleep and PTSD. There is a case study that used CBT-I prior to trauma-specific exposure therapy which suggests that CBT-I helped transition the patient into the trauma therapy [145]. An RCT compared hypnosis prior to CPT to symptom monitoring prior to CPT found that both conditions showed improvement in sleep and PTSD, but the hypnosis condition showed significantly greater improvement than the control condition in sleep and depression, but not

PTSD [114•]. Finally, a recent pilot study examined CBT-I prior to PE in veterans and found large effects for decreases in insomnia and PTSD symptoms and increases in quality of life [146••].

Summary and Future Directions

Advancement of evidence-based treatment of sleep disorders in the context of co-occurring PTSD offers a unique and underutilized opportunity to improve clinical care and research. While PTSD treatments are effective for PTSD symptom reduction, insomnia and OSA seem to require direct intervention. Our review suggests that PTSD treatments decrease PTSD severity and nightmare frequency, but do not fully resolve insomnia. There are no studies examining change in AHI over the course of PTSD treatment, but it is unlikely that PTSD treatment would affect OSA. While there are mixed findings as to whether insomnia affects PTSD treatment outcomes, untreated OSA seems to interfere with PTSD treatment.

There are currently no clinical guidelines for screening for sleep disorders in PTSD. We suggest a sleep and PTSD treatment decision tree (see Fig. 1). Clinically, we recommend a comprehensive sleep assessment to include OSA and insomnia screening, with treatment planning to match. Unfortunately, OSA is rarely screened due to the overlap with PTSD and insomnia symptoms. Due to the detrimental effect of OSA on PTSD treatments and health outcomes, we strongly recommend screening and treating OSA, even in lighter, younger individuals with PTSD prior to the start of PTSD treatment. We also recommend using independent measures for insomnia, such as the ISI or PSQI.

For sleep-specific interventions, CPAP therapy is recommended for OSA; however, there is lower CPAP adherence in PTSD samples. Given the importance of CPAP adherence to health and symptom outcomes, other treatment modalities and/or combination therapies may be warranted, such as CPAP desensitization, mandibular devices, exercise, or weight loss. For insomnia, CBT-I is the recommended treatment. While optimal sequencing with PTSD treatment is unclear, there is preliminary evidence that treating sleep prior to PTSD has benefits to sleep, PTSD, and quality-of-life outcomes. Nightmares significantly decrease with PTSD treatment and CBT-I, but nightmare-specific treatments are also effective and may be most beneficial for patients with primary nightmare disorder.

For pharmacological interventions for addressing sleep disturbances, we recommend following the 2017 VA/DOD guidelines [65], which are evidence-based and mimic the findings from our review. Specifically, there is a strong recommendation against the use of benzodiazepines for PTSD or insomnia due to a myriad of negative side effects. However, non-benzodiazepine hypnotics carry fewer risks, do not seem to increase risk of OSA, and increase sleep duration/quality, but need further evaluation with PTSD patients. While there are mixed reviews of prazosin, there is substantial evidence that it decreases nightmares, increases sleep quality, and may decrease nighttime arousals. However, future research is needed to identify the circumstances under which prazosin treatment should be selected and its effect on OSA. Antipsychotics are not recommended for routine use due to limited evidence supporting their efficacy and high propensity for adverse side effects. Finally, there are a host of commonly prescribed drugs (e.g., trazodone, hydroxyzine) that have

insufficient evidence for recommendation for or against that require future research. Taken together, behavioral treatments, such as CBT-I for insomnia or CPAP for OSA, should be the first-line interventions for sleep disturbances in PTSD.

Future research is needed to examine the sequencing/combination of PTSD and sleep treatments and to elucidate the mechanisms between sleep and PTSD treatments outcomes (e.g., memory, concentration, extinction/safety learning). Moderating factors to consider in research for co-occurring PTSD and sleep disorders will be demographics (gender, age, ethnicity/race), type of trauma exposure (interpersonal, combat), medications, and sample (military, civilian). While future research is unlikely to identify a unique set of PTSD-specific sleep difficulties, examining sleep disorders offers potential to increase client-centered care and advance efficacy of current treatments.

There is limited research examining the role of treating sleep in individuals with PTSD and other co-occurring disorders. Anxiety, depression, chronic pain, traumatic brain injury, and substance use show the highest prevalence with PTSD [147], and each negatively affects sleep. Similar to previous findings where insomnia did not resolve following PTSD treatment, there is evidence that insomnia does not resolve when PTSD and the co-occurring disorder are adequately addressed [148]. This suggests that sleep disturbances may need direct intervention even when PTSD and the co-occurring disorder are treated.

Offering sleep treatment to individuals with PTSD is patient-focused and prudent. First, it addresses a common and impairing co-occurring disorder. Treating sleep in those with PTSD may translate to higher patient satisfaction and better quality-of-life outcomes. Second, offering sleep treatments may be a “stepping stone” before starting PTSD treatment. Third, addressing sleep problems first may impact the mechanisms involved with trauma-focused treatment. Better sleep may influence fear learning/recall, decrease emotional reactivity, increasing emotional coping and emotional processing, and increase cognitive abilities/concentration necessary for successful trauma-focused therapy. Together, increasing focus on sleep treatment among those with PTSD offers a logical, innovative, and empirically informed method for expanding patient care, augmenting existing treatments, and optimizing global outcomes.

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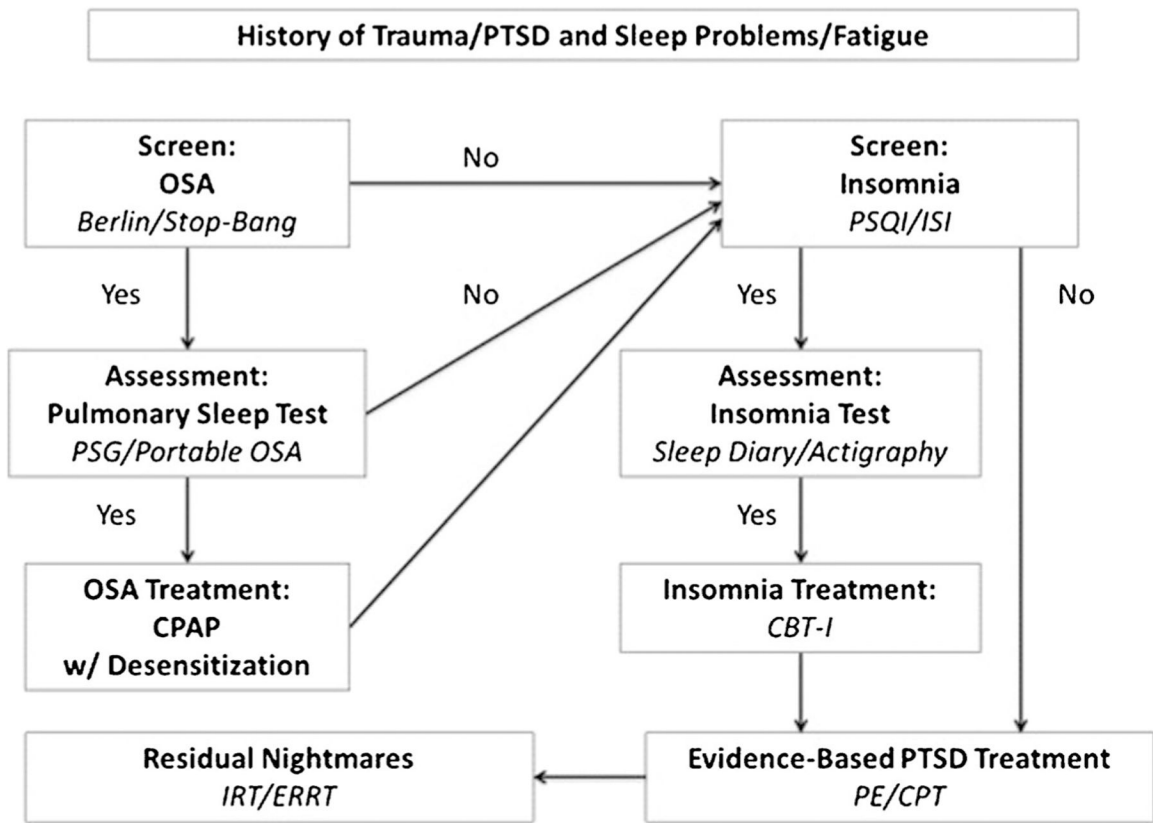


Fig. 1. Flow chart for assessment and treatment of sleep disorders in PTSD