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ORIGINAL ARTICLE

Sleep disorders in combat-related PTSD

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Abstract
Purpose We sought to assess the rate of sleep complaints and sleep disorders among active duty soldiers with deployment-related PTSD and to determine whether any clinical features differentiated those with sleep disorders.
Methods Retrospective review of consecutive soldiers diagnosed with PTSD. We recorded subjective measures of sleep and polysomnographic data. We compared clinical and demographic variables including psychoactive medication use, psychiatric comorbidity, and combat-related traumatic injury with the presence of sleep disorders.
Results One hundred thirty patients were included (91.5 % male, mean age of 35.1±10.6 years, mean body mass index (BMI) 28.9±4.4 Kg/m^2). About 88.5 % had comorbid depression, with the majority (96.2 %) taking psychoactive medications (mean 3.4±1.6 medications per patient). Over half of the cohort suffered combat-related traumatic physical injuries (54.6 %). The obstructive sleep apnea syndrome (OSAS) was diagnosed in 67.3 % (80 % of the cohort underwent polysomnography), with a mean apnea hypopnea index of 24.1±22.8 events/hour and a mean oxygen saturation nadir of 84.2±5.7 %. OSAS was significantly more common in the non-injured soldiers (72.9 vs. 38.0 %, $p<0.001$). In multivariate analysis, absence of physical injury showed a trend towards predicting OSAS.
Conclusions Sleep complaints are common among soldiers with PTSD. We observed significantly higher rates of OSAS among those without physical injuries, raising the possibility that underlying sleep-disordered breathing is a risk factor for the development of PTSD. This potential association requires further validation.

Keywords Combat related sleep disorder · Insomnia · Obstructive sleep apnea · Sleep-disordered breathing · Post-traumatic stress disorder

Abbreviations

AASM	American Academy of Sleep Medicine
DSM-IV-TR	Diagnostic and statistical manual of mental disorders, 4th ed, text revision
ESS	Epworth sleepiness scale
OEF	Operation enduring freedom
OIF	Operation Iraqi freedom
PCL-M	PTSD checklist-military version

Introduction

Sleep complaints are a hallmark of post-traumatic stress disorder (PTSD) and an evolving body of literature supports the

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view that sleep disorders may be implicated in the underlying pathophysiology of PTSD and not simply a consequence or manifestation of the disease [1–3]. Sleep disorders, to include sleep-disordered breathing, insomnia, nightmares, and parasomnias, are common in PTSD and correlate with worse outcomes [4, 3]. Adverse clinical outcomes including suicide are significant concerns for combat veterans, as well as civilians who have experienced traumatic events such as natural disaster, violent crime, sexual assault [5–10], and critical illness [11, 12].

The interrelationships between traumatic events, physical injury, and emotional dysregulation have been documented for decades. Freud and his contemporaries described accounts from WWI and WWII, analyzing the overlap of CNS damage and resultant neurotic sequelae [13, 14]. In recent years, a number of researchers have focused on the relationship between physical and psychological injuries and comorbid sleep complaints [15–17].

PTSD is associated with a variety of sleep disturbances. Sleep architecture itself may be disrupted, and abnormal rapid eye movement (REM) sleep is a central feature of PTSD [18]. Disruptions in non-REM (NREM) sleep may also exacerbate underlying psychopathology. A recent review has shown that fear response, memory processing, and mood disorders are all affected by the presence of insomnia and sleep-disordered breathing [19]. Data evaluating the prevalence of sleep disorders and medical conditions in recently deployed soldiers have shown a significant association between the likelihood of comorbid PTSD and insomnia [20]. This study and others have demonstrated that impaired sleep correlates with poorer outcomes in psychiatric disease [21, 22].

Just as PTSD can exacerbate sleep disorders, the converse is also true. Pre-deployment insufficient sleep and nightmares are risk factors for the development of PTSD and significantly worsened outcomes [23, 1]. A 2009 report of the average sleep duration in the USA reported that 41.8 % of military personnel obtained less than 5 h of sleep per night compared with 7.8 % in the general population. These data included soldiers who had not yet deployed [24]. Military-specific stressors including extended duty hours, frequent shift work, time zone changes, and deployment are all factors promoting insufficient sleep. Thus, behaviorally induced insufficient sleep syndrome may be superimposed on other sleep disorders, complicating evaluation and management [25]. It is conceivable that just as insufficient sleep may increase the risk of PTSD, preexisting sleep disorders may increase the possibility that a potentially emotionally traumatic event might lead to long-term psychological disturbances, perpetuating the cycle of disrupted sleep.

We sought to determine the rates of subjective sleep complaints and sleep disorders among active duty soldiers with PTSD, and to assess for clinical variables that differentiated those with and without sleep disorders.

Methods

Study design

We conducted a retrospective study of consecutive soldiers with PTSD receiving care at our facility between January 2008 and January 2010. All patients were 18 years of age or older and were diagnosed with PTSD following combat deployments to Iraq and/or Afghanistan. We excluded patients with preexisting OSAS prior to their PTSD diagnosis. Otherwise, no records were excluded from our review. This study was approved by our hospital's Institutional Review Board.

All soldiers received a diagnosis of PTSD following their combat tour. Diagnoses were based on a clinical encounter with a doctoral level behavioral health provider utilizing the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) criteria and a standardized military PTSD screening tool (the PTSD Checklist—Military Version, PCL-M Scoring Criteria) [26, 27]. The PTSD Checklist-Military Version is a subjective questionnaire that includes 17 questions (1–5 points each) addressing the DSM-IV criteria for PTSD. A cut-off score of 50 points was used to assess for the presence of PTSD (17–85 points possible) [26]. As part of the multidisciplinary care in the Warrior Transition Units in our military medical region, soldiers with a diagnosis of PTSD were referred for screening evaluations at the Sleep Disorders Center at our hospital during this time period.

Data were abstracted from a closed electronic medical record and included the initial sleep consultation, follow-up evaluations, and polysomnographic testing. Clinical variables included age, gender, BMI, and subjective assessments of sleep quality and daytime somnolence. Subjective assessments of excessive daytime somnolence (EDS) and daytime sequelae were assessed using the Epworth Sleepiness Scale (ESS) [28] and the Stanford Fatigue Visual Numeric Scale [29] (ranging from 0, "no fatigue" to 10, "severe fatigue"). Directed questioning during face-to-face clinical encounters with board-certified sleep medicine physicians was used to evaluate sleep quality and symptoms compatible with chronic insomnia (prolonged sleep latency (SL), sleep fragmentation (nocturnal awakenings and increased wake after sleep onset), non-restorative sleep, duration of symptoms for greater than 1 month, and daytime impairment).

A history of traumatic physical injury sustained during deployment was determined via review of the electronic medical record. Soldiers were included if they were greater than 3 months status post injury, thereby minimizing the confounding effect of the acute convalescent phase on the measured variables. Given the wide variety of injury type and severity inherent to combat related trauma, we used the term "injury" to dichotomize patients with versus without combat-related physical trauma.

Comorbid psychiatric diagnoses were reviewed. All psychoactive medications at the time of the initial sleep evaluation were recorded. Patients who underwent polysomnography were evaluated on their habitual medications.

Patients with a clinical suspicion for sleep-disordered breathing (habitual snoring, subjective sleep fragmentation, non-restorative sleep, witnessed apneas, or daytime somnolence not better explained by another process), underwent level I attended, nocturnal PSG. All polysomnograms were scored and interpreted by the study investigators in accordance with guidelines published by the American Academy of Sleep Medicine (AASM) [30]. No autoscoring techniques were utilized. Polysomnographic data used in this analysis included total sleep time, SL, sleep efficiency (SE), total arousal index (TAI), the apnea-hypopnea index (AHI), and oxygen saturation nadir by continuous pulse oximetry.

The presence of obstructive sleep apnea syndrome (OSAS) and insomnia was determined for each patient. The diagnosis of OSAS was based on an AHI≥5 events/hour plus clinical symptoms of sleep-disordered breathing in accordance with AASM criteria [31]. We defined insomnia as a subjective sleep latency ≥30 min, early morning awakenings, non-restorative sleep, and/or subjective sleep fragmentation (nocturnal awakenings), occurring over the majority of nights for greater than 1 month, associated with daytime impairment and not better explained by sleep disordered breathing, pain, or other identifiable factors [27].

Endpoints

Our primary endpoint was determining the rate of sleep disorders among soldiers with PTSD. Our secondary endpoint was to determine which clinical variables differentiated soldiers with and without sleep disorders.

Statistical analysis

Data are presented as the mean ± one standard deviation or median with interquartile ranges (IQR) as appropriate. Chi-square analysis and Fisher's exact tests were used to compare categorical variables. P values<0.05 were assumed to represent statistical significance. Continuous variables were assessed using the independent samples t test when normally distributed and the Mann–Whitney U test when non-normally distributed.

Variables were considered for inclusion in multivariate logistic regression analysis if they reached a p value≤0.20 on univariate analysis. Assessments for correlation were made using Pearson's correlation coefficient and Fisher's chi-square, and if a given variable showed a significant correlation with another it was excluded from the model. Data were analyzed using PASW 17 (SPSS Inc, Chicago, IL).

Results

Our cohort consisted of 130 consecutive adult patients with PTSD. The study population was predominantly male (91.5 %) with a mean age of 35.1±10.6 years and BMI of 28.1±4.3 Kg/m^2. Subjective sleep complaints were nearly universal (98.5 %), including poor sleep quality (86.9 %), excessive daytime sleepiness (87.7 %), and fragmented sleep (67.7 %). Most reported a history of comorbid depression (88.5 %) and 56.2 % met diagnostic criteria for insomnia. Approximately half of the cohort had a history of combat-related physical injury (54.6 %) (Table 1).

The majority of the cohort (80.0 %) underwent PSG to assess for clinically suspected sleep disordered breathing. Overall, sleep quality was poor among those undergoing PSG, with reduced sleep efficiency (84.5 %), increased total arousal index (19.7±13.5), increased NREM sleep, and decreased REM (13 %). OSAS was diagnosed in 67.3 % (53.8 % of the cohort overall). The mean AHI was 24.1±22.8 events/hour among those with OSAS (Table 2).

We compared clinical variables between injured and non-injured patients. The injured patients were younger (32.6±10.0 vs. 38.2±10.5, p=0.003) and had a lower BMIs (27.4±3.6 vs. 30.6±4.6, p<0.001) compared to those without injury. Rates of depression and use of psychoactive medications (including narcotic and non-narcotic analgesics) were also significantly greater among injured patients. PSGs were performed in a similar percentage of injured and non-injured patients (74.6 vs. 86.4 %, p=0.10). OSAS was significantly more common among non-injured patients (72.9 vs. 38.0 %, p<0.001). Rates of insomnia were not significantly different

Table 1 Demographic and clinical variables among 130 soldiers with PTSD

Variable	
Male gender (%)	91.5
Age (years)	35.1±10.6
BMI (Kg/m^2)	28.1±4.3
Neck circumference (inches)	16.4±1.4
Mallampati class (I–IV)	2.7±1.0
Epworth Sleepiness Scale (points, 1–24)	10.7±5.7
Stanford fatigue visual numeric scale (points, 0–10)	7.1±1.8
Traumatic injury during deployment (%)	54.6
Obstructive sleep apnea syndrome (OSAS), entire cohort (%)	53.8
Obstructive sleep apnea syndrome (OSAS), subjects with PSG (%)	67.3
Insomnia (%)	56.2
Depression (%)	88.5
Tobacco use (%)	41.5

Abbreviations: *BMI* body mass index, *OSAS* obstructive sleep apnea syndrome

Table 2 Polysomnographic (PSG) data (n=104; 80 % of cohort)

Variable	
Sleep efficiency (SE) (%)	84.5
Sleep latency (SL) (minutes)	30.3±33.3
Stage N1/N2 sleep (%)	63.9
Stage N3 sleep (%)	15.6
Stage REM sleep (%)	13.0
Total arousal index (TAI; events/hour)	19.7±13.5
Apnea-hypopnea index (AHI; events/hour)[a]	16.7±21.3
O_2 saturation (SpO_2) nadir[a] (%)	86.4
AHI; events/hour, among those with OSAS	24.1±22.8
SpO2 nadir, among those with OSAS (%)	84.2

[a] Data for all patients who underwent PSG in our cohort

Abbreviations: *SE* sleep efficiency (%), *SL* sleep latency (minutes), *REM* rapid eye movement sleep, *TAI* total arousal index (events/hour), *AHI* apnea hypopnea index (events/hour), *SpO2* pulse oximetry, *OSAS* obstructive sleep apnea syndrome

based on injury status (Table 3). We then compared patients with and without OSAS, and again found significantly higher rates of injury among those without OSAS. Rates of insomnia were nearly identical between those with and without OSAS (Table 4).

We performed a multivariate analysis to evaluate the predictors of OSAS in our population. While increased age was the only statistically significant predictor of OSAS, non-injured status showed a trend towards predicting OSAS (injury was associated with less OSAS). No other clinical variables were predictive of sleep apnea (Table 5).

The majority of patients (96.2 %) were receiving psychoactive medications. The mean number of psychoactive medication classes was 3.4±1.6 per patient. The rate of the overall polypharmacy (number of medications of any class) was also high, with 5.4±3.0 medications per patient. The most common medication classes included narcotics (36.9 %), serotonin reuptake inhibitors or serotonin and norepinephrine reuptake inhibitors (70.0 %), tricyclic antidepressants (22.3 %), atypical analgesics (gabapentin and pregabalin, 50.0 %), benzodiazepines (26.9 %), the alpha-receptor blocker prazosin (21.5 %), the atypical antipsychotic quetiapine (38.5 %), trazodone (26.2 %), and benzodiazepine receptor agonists (52.3 %) (Table 6). Comparing soldiers with and without traumatic injuries, the only significant differences in medication use was an increased number of psychoactive medications classes (3.7±1.6 vs. 3.0±1.5, p=0.01), narcotics (45.1 vs. 27.1 %, p=0.04), and atypical analgesics (63.4 vs. 33.9 %, p=0.001) among those who were injured (Table 3).

Table 3 Comparison of clinical variables between injured and non-injured soldiers with PTSD

Clinical variable	Injured (n=71)	Non-injured (n=59)	p value
Age	32.6±10.0	38.2±10.5	0.003
BMI	27.4±3.6	30.6±4.6	<0.001
PSG performed (%)	74.6	86.4	0.10
AHI (events/hour)	12.5±16.6	21.1±24.6	0.04
OSAS (%)	38.0	72.9	<0.001
Insomnia (%)	53.5	59.3	0.51
Depression (%)	94.4	81.4	0.02
On psychoactive medication (%)	97.2	94.9	0.51
# psychoactive medication classes	3.7±1.6	3.0±1.5	0.01
Antidepressant (%)	80.3	67.8	0.11
Narcotic analgesia (%)	45.1	27.1	0.04
Prazosin (%)	18.3	25.4	0.33
SSRI/SNRI (%)	74.6	64.4	0.21
TCA (%)	22.5	22.0	0.95
AED (%)	63.4	33.9	0.001
Trazodone (%)	23.9	28.8	0.53
NBRA (%)	52.1	52.5	0.96
Benzodiazepine (%)	26.8	27.1	0.96
Atypical antipsychotic (%)	42.3	33.9	1.00

Abbreviations: *BMI* body mass index, *OSAS* obstructive sleep apnea syndrome, *SSRI/SNRI* serotonin specific reuptake inhibitor/serotonin-norepinephrine reuptake inhibitor, *TCA* tricyclic antidepressant, *AED* anti-epileptic drug, *NBRA* non-benzodiazepine receptor agonist, *PSG* polysomnogram, *SL* sleep latency, *SE* sleep efficiency, *REM* rapid eye movement sleep, *TAI* total arousal index, *AHI* apnea hypopnea index, *SpO2* pulse oximetry

Table 4 Comparison of clinical variables between OSAS and non-OSAS patients

Clinical variable	OSAS (n=70)	Non-OSAS (n=60)	p value
Age (years)	39.3±10.4	30.4±8.7	<0.001
BMI (Kg/m^2)	30.1±4.4	27.4±3.9	0.001
Neck circumference (inches)	16.9±1.3	16.0±1.3	0.03
Mallampati class (I-IV)	2.9±1.0	2.5±0.9	0.03
Epworth sleepiness scale (ESS)	11.5±5.8	9.5±5.3	0.10
Stanford fatigue visual numeric scale	6.9±1.8	7.5±1.7	0.13
Insomnia (%)	54.3	58.3	0.65
Tobacco use (%)	34.3	50.0	0.07
Traumatic injury (%)	38.6	73.3	<0.001
Atypical antipsychotic medication (%)	31.4	46.7	0.076
Narcotic analgesia (%)	27.1	48.3	0.01
Anti-epileptic drugs (%)	44.3	56.7	0.16
Apnea hypopnea index (events/hour)	24.1±22.8	1.8±1.5	<0.001
SpO2 nadir (%)	84.2	90.8	<0.001

Abbreviations: *BMI* body mass index, *ESS* Epworth sleepiness scale, *SpO2* pulse oximetry

Table 5 Predictors of OSAS

Variable	*p* value	Odds ratio	95 % confidence interval	
			Lower	Upper
Absence of combat injury	0.09	2.39	0.87	6.56
Anti-psychotic medication	0.59	1.32	0.48	3.65
Age	0.001	1.10	1.04	1.16
ESS	0.09	1.08	0.99	1.18
BMI	0.50	1.04	0.92	1.18

Variable(s) entered on step 1: Absence of combat injury, anti-psychotic medication, Age, ESS, BMI

Discussion

Among recently deployed soldiers with PTSD, subjective sleep complaints were universal, and more than half were diagnosed with OSAS and insomnia. Our study suggests that patients with PTSD may have clinically significant differences based on the presence or absence of combat-related physical injury. When we compared injured to non-injured patients, the most significant difference was a higher rate of OSAS among non-injured patients. Additionally, when we compared those with and without OSAS, this finding was reinforced and maintained statistical significance. Because multiple confounders existed in our population (polypharmacy, psychoactive medication use, depression, insomnia, and poor quality sleep), we performed a multivariate analysis and non-injured status still showed a trend towards predicting OSAS.

Table 6 Psychotropic medication use among cohort

Variable	
Subjects on psychotropic medications (%)	96.2
# psychotropic medication classes	3.4±1.6
# medications (total)	5.4±3.0
Anti-depressant medications (%)	74.6
Narcotic analgesics (%)	36.9
Benzodiazepines[a] (%)	26.9
SSRI/SNRI (%)	70.0
Tricyclic antidepressants[b] (%)	22.3
Anti-epileptic drugs[c] (%)	50.0
Non-benzodiazepine receptor agonists[d] (%)	52.3
Atypical antipsychotics[e] (%)	38.5
Prazosin[f] (%)	21.5
Trazodone[g] (%)	26.2

[a] For anxiety disorders and sedative-hypnotic (clonazepam and diazepam)

[b] For atypical pain, narcotic sparing analgesia, headache, and sedative-hypnotic sleep aid (amitriptyline and nortriptyline)

[c] For neuropathic pain and/or sedative-hypnotic sleep aid (gabapentin, pregabalin)

[d] Sedative-hypnotic sleep aid (zolpidem, eszopiclone)

[e] Sedative-hypnotic sleep aid (quetiapine)

[f] Nightmares

[g] Sedative-hypnotic sleep aid

Our findings suggest the possibility of different phenotypes of combat-related PTSD with respect to injury and sleep-disordered breathing. Theoretically, non-injured PTSD patients may have been compromised by premorbid sleep-disordered breathing, rendering them less resilient for the challenges of deployment, and more prone to developing PTSD. Injured patients may have PTSD as a direct consequence of physical trauma.

Our findings reinforce those of recent studies demonstrating a high rate of insomnia and OSAS in combat veterans [32, 33]. Numerous studies have shown that rates of OSAS are increased among those with PTSD (40–91 %) [34–37, 7] compared to population norms [38]. In a study of Iraqi-Americans with PTSD who immigrated to America, there was a positive correlation between the presence of OSAS and psychosomatic disorders. The authors concluded that OSAS might have been partially responsible for PTSD-associated adverse health effects [39]. OSAS has also been shown to worsen cognitive functioning in veterans with PTSD [40], in addition to mental health outcomes. While the treatment of OSAS with CPAP has been shown to improve symptoms in PTSD [41, 42], efficacy is limited by lower CPAP adherence in this group [43, 44], potentially impacted by comorbid insomnia [33, 45].

Although preexisting OSAS has not been identified as a risk factor for the subsequent development of PTSD in clinical studies, subjective evidence of disrupted sleep prior to trauma has been shown predict an increase in post-traumatic psychiatric disorders, including PTSD [46]. In addition, increased OSAS severity has been linked to PTSD, and fragmented sleep (insomnia and nightmares) has been postulated to be a risk factor for PTSD [2, 1, 47].

The pathophysiology linking sleep-disordered breathing and PTSD is based on the premise that impaired sleep may limit one's ability to manage stress and to recover from traumatic events. There are several ways that poor quality sleep (insufficient or fragmented sleep) impacts PTSD. It may limit cognitive resources for managing stress, create a state of hyperarousal, confound environmental stressors (trauma), and hinder restorative sleep for recovery from traumatic events [46]. Sleep-disordered breathing has been theorized to be a risk factor for PTSD [48]. REM sleep is posited to consolidate emotional memory, which may be critical to recovery from traumatic events [49, 50]. Fragmented REM sleep, due to insomnia, nightmares, or sleep disordered breathing, can diminish this capacity. Sleep fragmentation in normal volunteers has been shown to cause upper airway instability, which may promote sleep-disordered breathing events [51].

Abnormalities in upper airway anatomy (narrowing) and function (instability) have been linked to functional somatic syndromes overall, anxiety, irritable bowel syndrome, fibromyalgia, poorer mental health, and symptoms among those with Gulf War Syndrome [52–58]. Alterations in the central nervous system (CNS) can increase noradrenergic tone and lead to deregulation of CNS negative feedback loops that dampen the stress response. The cycle is self-perpetuating, with fragmented sleep disrupting REM, impairing the role of sleep (Stage-REM in particular) in recovery from trauma, and increasing noradrenergic tone which may promote further sleep disruption, respiratory events, and nightmares [59, 60, 1, 2].

While the link between sleep-disordered breathing and PTSD has been delineated in the past, the majority of literature focuses on older veterans' populations. Our paper is the first to apply this to recent soldiers with combat-related PTSD.

Limitations

Our study's retrospective design may have created selection bias; however, we included all patients with PTSD that were available for screening, rather than PTSD patients referred specifically for sleep complaints. Polysomnograms were obtained only in those with a clinical concern for OSAS based on evaluation by a sleep medicine physician. However, this may have missed the diagnosis in some patients and altered the observed prevalence rates. Given that this was a retrospective study, we were unable to influence the practices of sleep providers. PSG analyses were conducted in patients taking their standard regimen of medications, which is reflective of their baseline condition, given the chronicity of their diagnoses. Universal polypharmacy with psychoactive medications precluded our ability to generate meaningful conclusions regarding the impact of particular medications on sleep disorders. In addition, it is notable that the non-injured patients with OSAS were older and had higher BMIs than the injured cohort, which may have confounded our results. Although there was a statistically significant difference in BMI between groups in univariate analysis, BMI was not a predictor of OSAS in multivariate analysis. A possible reason for this finding is that the BMI differences in our service members (between "overweight" and "obese") are not clinically significant. Comorbid insomnia has been shown to worsen the clinical and therapeutic outcomes in patients with OSAS, and is highly prevalent in recently evaluated veteran populations. Rates of insomnia did not differ significantly between the subgroups we evaluated, and the impact of insomnia in our population is unclear. Data regarding the number and type of deployments per service member were not available. This information could influence the likelihood of developing PTSD.

Conclusions

Sleep disorders are highly prevalent among patients with PTSD, with adverse implications on clinical outcomes. Our manuscript highlights a novel association between injury status and OSAS among our cohort of recently deployed combat veterans with PTSD. The underlying reasons why some patients subjected to traumatic events develop PTSD are complex and multifactorial. A potential explanation for our findings is that patients with PTSD differ based on the presence or absence of physical traumatic injury. Those with PTSD in the absence of injury may suffer from undiagnosed preexisting sleep disorders, such as OSAS, which fragment sleep and diminish resilience, thereby increasing the risk for subsequent worsened mental health outcomes. Future studies may further delineate whether distinct phenotypes of PTSD exist, with regards to injury status and sleep-disordered breathing. This could have significant implications on evaluation, management, and therapeutic expectations. Given the adverse implications of untreated sleep-disordered breathing, a formal sleep medicine evaluation and polysomnogram should be considered in all patients who are diagnosed with PTSD.

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Conflict of interest The authors have no conflicts of interest to disclose.

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