

The Effect of Continuous Positive Air Pressure (CPAP) on Nightmares in Patients with Posttraumatic Stress Disorder (PTSD) and Obstructive Sleep Apnea (OSA)

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SCIENTIFIC INVESTIGATIONS

Objectives: Post-Traumatic Stress Disorder (PTSD) is increasingly prevalent among Veterans characterized by recurrent nightmare and disrupted sleep. Veterans with PTSD also have a high prevalence of obstructive sleep apnea (OSA) and untreated OSA worsens the sleep-related symptoms of PTSD. In our study, we hypothesized that among PTSD-afflicted Veterans with OSA, CPAP therapy may reduce the frequency of nightmares and a better CPAP compliance may be associated with increased symptom improvement.

Methods: We retrospectively reviewed medical records to identify OSA patients treated in a VA medical center who also carried a diagnosis of PTSD (n = 69). Data about patient characteristics and polysomnographic findings were extracted. Repeated-measures t-tests were performed, comparing mean nightmare frequency and Epworth sleepiness score (ESS) before and after CPAP treatment. Multiple linear regressions were done to identify factors predicting CPAP compliance. A logistic regression analysis was also done to estimate the odds of subjective improvement in PTSD symptoms with CPAP.

Results: CPAP therapy reduced the mean ESS from 14.62 to 8.52 (p < 0.001) and the mean number of nightmares per week from 10.32 to 5.26 (p < 0.01). Reduced nightmare frequency after CPAP treatment was best predicted by CPAP compliance (p < 0.001). Every 10% increase in CPAP compliance almost doubled the odds of benefitting by CPAP (odds ratio = 1.92, 95% CI = 1.47-2.5)

Conclusions: In Veterans with PTSD and OSA, CPAP therapy reduces PTSD-associated nightmares and improves overall PTSD symptoms. We recommend that all PTSD patients should be screened clinically for symptoms of OSA and receive CPAP treatment whenever possible to improve PTSD symptoms.

Keywords: sleep apnea, PTSD, CPAP

Citation: Tamanna S, Parker JD, Lyons J, Ullah MI. The effect of continuous positive air pressure (CPAP) on nightmares in patients with posttraumatic stress disorder (PTSD) and obstructive sleep apnea (OSA). *J Clin Sleep Med* 2014;10(6):631-636.

About 26% to 31% of veterans in the US are estimated to be affected by posttraumatic stress disorder (PTSD) in their lifetime.¹ Individuals with PTSD often report sleep disturbances including trouble in falling and maintaining sleep, recurrent nightmares about trauma, and other disruptive nocturnal behaviors such as anxiety and night terrors during sleep.²⁻⁶ The need for an inventory assessing the quality of sleep in the posttraumatic stress disorder (PTSD) The re-experiencing of the traumatic event in the form of repetitive nightmares and dysfunctional REM sleep mechanism may be involved in the pathogenesis of PTSD related sleep disturbance.⁷ Most of these nightmares are vivid and can be recalled by the patients when they wake up and this usually happens in the early morning when the REM sleep occurs for longer periods and with increased REM density. Previous studies indicated that persons with PTSD tend to have more stage 1 sleep and less slow wave sleep, shorter total sleep time, and more REM sleep than those without PTSD.^{8,9}

Veterans with PTSD have higher prevalence of obstructive sleep apnea (OSA) than the general population.¹⁰ Untreated OSA accentuates the sleep-related symptoms of PTSD, especially the number and intensity of nightmares, repeated awakenings, difficulty falling back to sleep, and increase in daytime

BRIEF SUMMARY

Current Knowledge/Study Rationale: Post-Traumatic Stress Disorder (PTSD) is increasingly prevalent among Veterans characterized by recurrent nightmares. Veterans with PTSD also have a high prevalence of obstructive sleep apnea (OSA) and untreated OSA worsens the sleep-related symptoms of PTSD.

Study Impact: Our study shows that the Veterans with concurrent PTSD and OSA, CPAP therapy reduces PTSD-associated nightmares and improves overall PTSD symptoms. Screening of all PTSD afflicted Veterans for OSA symptoms and treating them with CPAP as appropriate will improve the overall quality of life of these patients.

sleepiness and tiredness.¹¹⁻¹⁴ A growing body of evidence suggests that disturbed sleep is more likely to be a core feature of PTSD rather than just a secondary symptom.^{5,15} Hypoxia, sympathetic discharge from respiratory disturbances, dysfunctional REM sleep, and abnormal REM mechanism have been areas of interest in finding a connection between sleep apnea and PTSD symptoms.^{16,17}

Chronic sleep disruption associated with nightmares decreases the efficacy of first-line PTSD treatment; therefore, targeted sleep treatments have been recommended to accelerate

recovery from PTSD.¹⁸ A few studies in the past have reported some improvement in sleep quality, nightmares and overall PTSD symptoms with continuous positive airway pressure (CPAP) use,^{15,19-21} but adherence to CPAP has been reported to be low among veterans with PTSD.²² In our study, we hypothesized that among PTSD-afflicted veterans with OSA, CPAP therapy may reduce the frequency of nightmares, and better CPAP compliance would be associated with increased symptom improvement. Since dysfunctional REM sleep has been suggested to be one of the core features of PTSD, we also sought to determine if the effectiveness of CPAP on nightmares differed among patients whose sleep disordered breathing is more prominent in REM sleep.

METHODS

Patient Selection

The study was approved by the institutional review board of the Veterans Affairs (VA) Medical Center at which the data were collected. We retrospectively reviewed medical records to identify patients treated in a major VA Medical Center sleep clinic between May 2011 and May 2013 who had been previously diagnosed with both PTSD and OSA. The inclusion criteria for patients in our study were as follows: (1) must carry both the diagnoses of OSA (diagnosed by a polysomnography) and PTSD (diagnosed by a board certified psychiatrist ≥ 1 year prior to the sleep clinic visit); (2) CPAP had been prescribed; (3) had a follow-up visit in the sleep clinic ≥ 6 months after the initiation of CPAP treatment; (4) CPAP adherence data (percentage of nights with > 4 h CPAP use) were downloaded from the CPAP machine and documented in the chart; (5) mean number of nightmares per week reported by the patient were documented in the chart by the sleep physician both before and after CPAP use; and (6) the polysomnography report was available for review. Nightmare was defined as repeated nighttime awakenings accompanied by detailed recollections of frightening dreams.²³ A total of 69 patients were identified who met all of the above criteria.

Data Extraction

The computerized medical records from the VA sleep clinic visits were reviewed to identify the veterans who had PTSD and OSA and qualified for our study with above inclusion criteria. No medical records from the mental health clinic visits were reviewed. We extracted demographic data on age, gender, race, body mass index (BMI), and the combat era during which each veteran served. Polysomnographic (PSG) data including total apnea hypopnea index (AHI), REM AHI, REM sleep percentage, lowest oxygen saturation (nadir) on diagnostic polysomnography, and CPAP pressure prescribed were obtained from the sleep study report. Epworth Sleepiness Scale (ESS) scores and the mean number of nightmares per week (pretreatment and up to 6 months after CPAP prescription) were extracted from the sleep clinic progress notes. During each visit to the sleep clinic, a questionnaire was routinely administered to assess the sleep quality and factors affecting their sleep at night. One of the questions asked was “Do you wake up at night due to nightmares? If yes, then how many of such episodes happened in

the last one week?” This response was used to document the frequency of pre and post CPAP treatment nightmares in the chart.

A large number of patients with PTSD are referred to our VA sleep clinic due to their concomitant OSA and other sleep related issues. We have found that many of these patients sometimes had difficulty in initiating or maintaining sleep with the CPAP mask on; some reported that the CPAP mask sometimes reminded them of the gas masks used during the war. This sometimes brings back the traumatic memory back and makes the CPAP use difficult for these patients. In order to identify and troubleshoot these difficulties, all of our patients with PTSD on CPAP are routinely asked several questions in their sleep clinic follow-up visits to explore the factors affecting their CPAP usage and PTSD symptoms. One of these questions asked is, “do you feel your symptoms of PTSD have improved after you have started CPAP treatment?” The responses are documented in the chart as “yes” or “no” answers. We have used these responses in our study to determine if they felt benefitted or not in terms of PTSD symptom improvement with CPAP therapy.

Diagnosis of OSA

OSA was diagnosed with overnight polysomnography using American Academy of Sleep Medicine standard criteria of AHI ≥ 15 events/h or AHI ≥ 5 /h in patients who reported any of the following: fatigue, excessive daytime sleepiness, unrefreshing sleep, insomnia, waking up breath-holding, gasping or choking, or the bed partner describing snoring or breath interruption during sleep.²⁴ All sleep studies were interpreted by a physician board certified in sleep medicine. Baseline PSG was examined to identify REM-related OSA. REM OSA was defined when the REM sleep AHI was twice or more than the NREM sleep AHI in the diagnostic part of the study. A CPAP machine with optimal pressure was given from the VA sleep clinic with instructions for use. Compliance data were downloaded from the CPAP machine when the patients came back for follow-up visits 6 months after initiation of CPAP therapy.

Diagnosis of PTSD

The diagnoses of PTSD were made by a psychiatrist at least 1 year prior to the sleep clinic visit following DSM IV criteria, and patients were being followed by the mental health provider in the VA medical system. Psychotropic or antidepressant medications were prescribed by the mental health provider who followed the patient. Medication adjustments were independent of the sleep lab visits. All patients with PTSD and OSA were asked to report a mean number of nightmares per week before and after CPAP use.

Statistical Analysis

Baseline polysomnograms determined patients' assignment to REM or NREM-related OSA cohorts. The characteristics of different groups of patients were compared using χ^2 tests. Repeated-measures *t*-tests were performed, comparing mean nightmare frequency (per week) and degree of daytime sleepiness (using ESS) before and after treatment. Instead of assessing CPAP adherence by counting cumulative “hours per night” or “number of nights per week,” we have used the “percentage of nights the patient has used the CPAP treatment for a minimum

of 4 hours for the previous 6 months.” For example, a CPAP compliance of 80% or 0.8 means that the patient has used the CPAP machine in 80% of nights for ≥ 4 h for the last 6 months. Even though there is a linear relationship of number of hours of CPAP use with its beneficial effect,²⁵⁻²⁷ using the “percentage of nights with CPAP usage for > 4 h” may be a more robust way of assessing compliance.²⁸

Multiple linear regression analyses were conducted to identify factors predicting 2 separate outcome variables: *CPAP compliance* and mean *number of nightmares (per week)*. All independent variables were tested in the initial regression models (age, gender, BMI, total AHI, REM AHI, ratio of REM/NREM AHI, REM sleep percentage, CPAP pressure, nadir oxygen saturation), and stepwise regressions were used to eliminate variables that were statistically insignificant (p value > 0.05). A logistic regression analysis (using the dichotomous outcome variable “patient reported PTSD symptom improvement after CPAP therapy = yes/no”) was also performed to estimate the odds of subjective improvement in PTSD symptoms with CPAP therapy, adjusting for potential confounders including age, BMI, total and REM AHI, pre-treatment ESS, and mean number of nightmares per week (using similar stepwise regressions). Model fit was determined by the Hosmer-Lemeshow goodness-of-fit test. The statistical analyses were performed using STATA software, version 12.1 (StataCorp, College Station, TX).

RESULTS

Sixty-nine ($n = 69$) patients had complete data; 43% were Caucasian, and 97% were male; 69% served in Vietnam, 19% in Gulf war, and 12% in other wars (**Table 1**). Thirty-four patients had REM-related OSA, and 35 patients had NREM related OSA (**Table 2**). CPAP therapy significantly reduced daytime sleepiness and nightmare frequency in all patients. The mean (\pm standard deviation) ESS decreased from 14.62 (± 3.21) to 8.52 (± 2.14) ($p < 0.001$), and the mean number of nightmares per week decreased from 10.32 (± 3.41) to 5.26 (± 1.25) ($p < 0.01$) with CPAP. There were no differences in mean age, BMI, or severity of OSA between African American and Caucasian participants, but the CPAP compliance ($p = 0.04$) and

nadir oxygen saturation during diagnostic polysomnography ($p = 0.03$) were lower in African American patients (**Table 3**).

When REM and NREM related OSA cohorts were compared, REM percentage ($p = 0.001$) and REM AHI ($p = 0.007$)

Table 1—Baseline characteristics of veterans with OSA and PTSD.

	Total (n = 69)	REM OSA (n = 34)	NREM OSA (n = 35)
Race	n (%)	n (%)	n (%)
African American	39 (57)	19 (56)	20 (57)
Caucasian	30 (43)	15 (44)	15 (43)
Female	2 (3)	1 (3)	1 (3)
Male	67 (97)	34 (97)	33 (97)
Combat era			
Vietnam	47 (68)	20 (59)	27 (77)
Gulf	13 (19)	9 (26)	4 (11.5)
Other	9 (13)	5 (15)	4 (11.5)

Table 2—Characteristics of patients by presence or absence of REM related OSA.

Variables	REM OSA (n = 34)	NREM OSA (n = 35)	p value
	Mean (SD)	Mean (SD)	
Age, years	56 (1.98)	60 (2.08)	0.154
BMI, kg/m ²	32.76 (0.88)	33.28 (0.85)	0.643
Total AHI, /h	13 (2.61)	28 (3.77)	0.002
REM AHI, /h	43 (9.05)	16.69 (3.23)	0.007
Compliance, %	52 (6.53)	64 (6.62)	0.21
ESS before CPAP	14 (0.91)	15 (0.78)	0.494
ESS after CPAP	9 (0.83)	8 (0.66)	0.615
Nightmare/week before CPAP	10.6 (1.11)	9.9 (1.21)	0.678
Nightmare/week after CPAP	5.4 (0.94)	5.1 (0.99)	0.772
Nadir O ₂ saturation, %	81 (1.5)	80 (1.91)	0.673
REM percentage	14 (1.12)	6.86 (1.46)	0.001
CPAP pressure, cm H ₂ O	11 (0.66)	11 (0.56)	0.467

AHI, apnea hypopnea index; ESS, Epworth Sleepiness Scale; O₂, oxygen.

Table 3—Characteristics of patients by race.

Variables	Total (n = 69)	African American (n = 39)	Caucasian (n = 30)	p value
	Mean (SD)	Mean (SD)	Mean (SD)	
Compliance (%)	58.82 (4.67)	51 (6.27)	69 (6.65)	0.041
Age (years)	58 (12.05)	57 (11)	58 (12)	0.653
BMI (kg/m ²)	33 (5)	33 (5.06)	32.5 (5.11)	0.451
Total AHI (/h)	21 (2.46)	24 (3.78)	16.85 (2.76)	0.184
REM AHI (/h)	30 (4.98)	30 (4.72)	30 (9.80)	0.972
REM percentage	10.32 (1.01)	10.4 (1.28)	10 (1.65)	0.941
CPAP pressure (cm H ₂ O)	11 (3.59)	11 (3.84)	10.83 (3.3)	0.695
ESS before CPAP	15 (4)	15 (4.85)	14.6 (5.14)	0.972
ESS after CPAP	9 (4.3)	9 (4.5)	8 (4.26)	0.488
Nightmare/week before CPAP	10 (6.8)	11 (7.62)	9.43 (5.55)	0.342
Nightmare/week after CPAP	5.3 (0.68)	6.23 (0.9)	4 (1.02)	0.101
Nadir O ₂ saturation (%)	80.7 (10.09)	78.48 (12)	83.6 (4.7)	0.032

Figure 1—Percentage of REM sleep and number of nightmares per week before CPAP therapy.

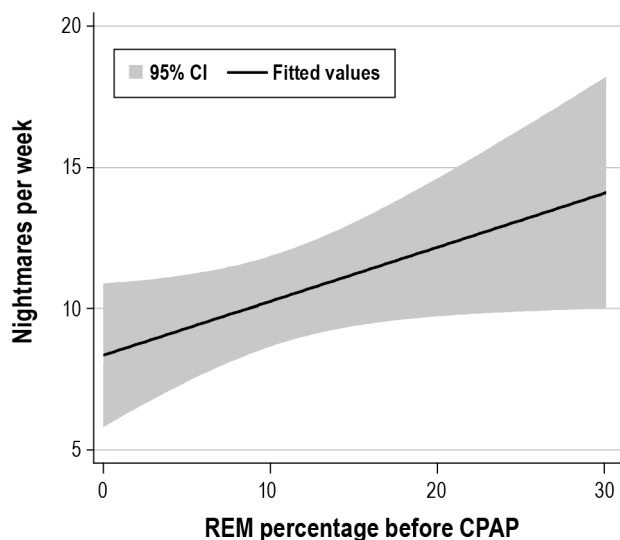
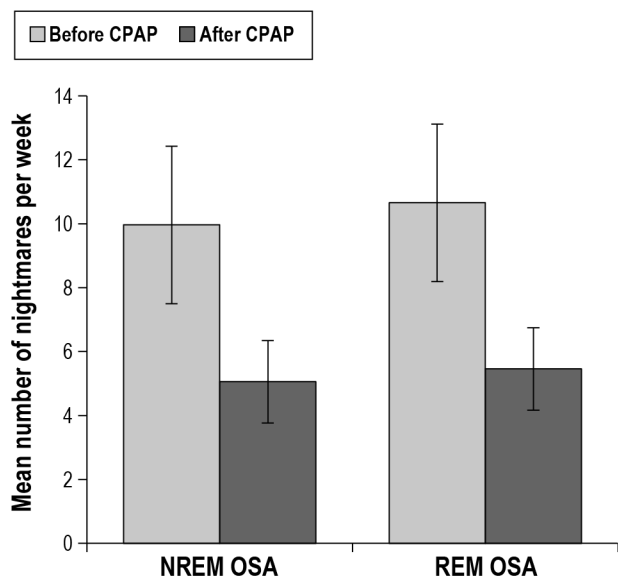


Figure 3—Mean frequency of nightmares before and after CPAP by REM/NREM OSA (with 95% CI).



were significantly higher among patients with REM-related OSA, but the total AHI ($p = 0.002$) was higher in NREM OSA (**Table 2**). REM sleep percentage was positively correlated with the number of nightmares before CPAP ($r = 0.24$, **Figure 1**) whereas REM AHI was negatively correlated with CPAP compliance ($r = -0.32$, **Figure 2**). CPAP compliance did not differ between these 2 groups. The mean number of pre-treatment nightmares per week was similar in both groups (10.6 [± 1.11] in REM OSA, 9.9 [± 1.21] in NREM OSA), and decreased significantly in both groups (5.4 [± 0.94] in REM OSA, 5.1 [± 0.99] in NREM OSA, $p < 0.001$) after 6 months of CPAP treatment (**Figure 3**).

Figure 2—REM AHI and percentage of CPAP compliance.

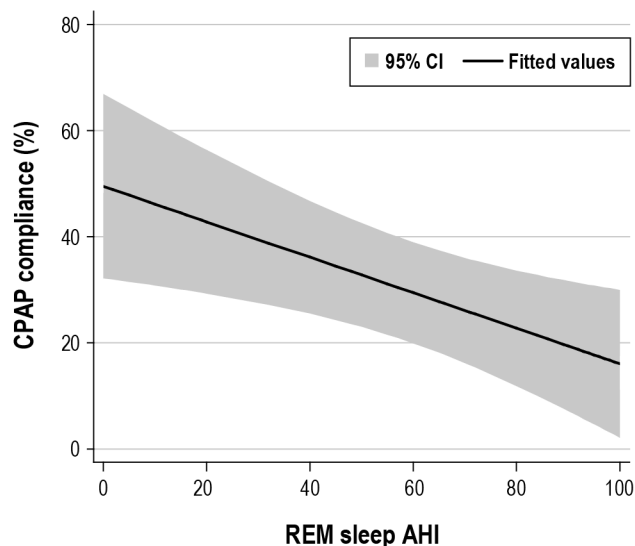
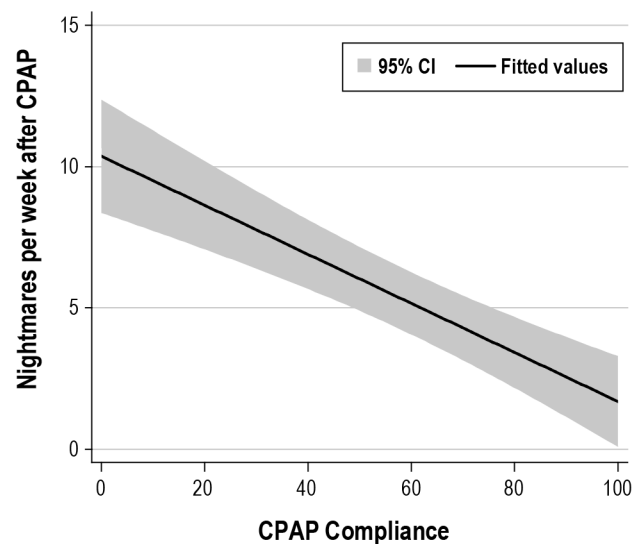


Figure 4—CPAP compliance and number of nightmares per week after CPAP therapy.



Reduced nightmare frequency after CPAP treatment was best predicted by CPAP compliance ($p < 0.001$; **Figure 4**) and percentage of REM sleep ($p = 0.04$). Every 10% improvement in CPAP compliance decreased the mean number of nightmares by 1 per week (β coefficient = -0.08931 , 95% CI = -0.117 to -0.062). CPAP compliance was also the only significant predictor of overall subjective improvement in PTSD symptoms since beginning CPAP therapy. Every 10% increase in CPAP compliance almost doubled the odds of benefitting by CPAP (odds ratio = 1.92, 95% CI = 1.47-2.5)

DISCUSSION

Our study showed that treatment of OSA with CPAP is associated with decrease in the number of nightmares and daytime

sleepiness in PTSD patients. CPAP compliance was found to be the single most important predictor of these benefits. REM-related sleep apnea did not show any significant relationship with frequency of nightmares, but increasing REM percentage was related to increase in nightmares before CPAP use. Krakow et al. (N = 14) previously reported improved nightmares with CPAP treatment,¹⁹ but their study relied on self-reported CPAP compliance, which often yields an overestimate of compliance.²⁹ Our findings confirm the effectiveness of CPAP in reducing nightmares in a larger sample using compliance data downloaded from the CPAP machine.

The mean CPAP compliance was 58% in our study, which is similar to other studies. Overall CPAP compliance was reported to be poor (41% vs. 70% in PTSD and control group) among PTSD veterans in a recent study.²² Collen et al. also found lower CPAP adherence among PTSD sufferers compared to control (61% vs. 76.8%, $p = 0.001$) group.¹⁰ We did not find any difference in compliance between REM and NREM OSA groups.

African Americans were less compliant than Caucasians in CPAP use (51% [± 6.27] vs. 69% [± 6.65], $p < 0.05$), and their mean nadir oxygen saturation was lower (78% [± 12] vs. 84% [± 4.7], $p = 0.03$) during the sleep study (**Table 3**). This is consistent with the finding of a recent study of 191 subjects where CPAP adherence was significantly lower among African Americans than Caucasians (47% vs. 65%, $p < 0.01$).³⁰ There was no racial difference in severity of sleep apnea in our study even though other studies have found higher mean AHI among black patients.³¹ Vietnam veterans comprised the highest percentage (69%) of our treatment-seeking PTSD/sleep apnea veteran population, which is supportive of previous literature.³² A recent study has suggested that there may be a gender difference in susceptibility to development of PTSD symptoms, with greater frequency of nightmares and disruptive nocturnal behaviors in female after exposure to a traumatic event.² We had only two females in our study; therefore it was not possible to appreciate any difference in treatment response to CPAP by gender.

This study also showed positive correlation of REM sleep percentage with the number of nightmares. This supports the hypothesis that a dysfunctional REM sleep mechanism may be involved in the pathogenesis of PTSD. Many previous studies have tried to explore this link with conflicting results.³³⁻³⁵ A recent study reported that REM AHI and interrupted sleep at night were independent predictors of nightmares in OSA patients, and CPAP therapy results in significant improvement in nightmare occurrence.²⁰ Apparently, when a patient spends more time in REM, likelihood of having nightmares becomes higher.³⁶ REM suppression with prazosin, an α -1 inhibitor, showed improvement in combat-related PTSD nightmares and sleep quality in active-duty soldiers in a recent trial.³⁷ This may indicate that suppressing the “dysfunctional REM” in PTSD patients may have helped reduce symptoms. We did not have follow-up polysomnography after 6 months to see if there was a difference in REM sleep percentage after CPAP therapy. If the REM sleep percentage remains the same or actually increases after CPAP therapy but a decrease in nightmare occurrence continues, this may suggest that treatment of obstructive sleep apnea addresses nightmares by reducing this “dysfunctional REM” in PTSD patients.

We did not find any significant correlation between REM AHI and number of nightmares, suggesting that obstructive events during REM sleep may not be the only triggering factor for nightmares. There was no significant difference in CPAP compliance between REM and NREM OSA groups, which is consistent with a recent finding by Conwell et al.³⁸ That study reported a prevalence of REM related OSA of 13.5% to 36.7%, whereas we found a higher prevalence (49%) among veterans with PTSD. Increased REM-related respiratory disturbance may lead to higher REM dysfunction with worsening PTSD symptoms. Future clinical studies looking at changes in REM sleep mechanism after exposure to psychological trauma may help explain its underlying mechanism.

We had several limitations in our study. Since it was a retrospective study and the data were extracted from the existing chart, the results may have been subjected to several biases. The self-reported mean weekly frequency of nightmare before and after the CPAP left the possibility of errors for quantification of nightmares, as there may be week-to-week variability in occurrence of nightmare. We did not take into account any change in the medication regimen during the study period which may have had some effects on change in PTSD symptoms. The reported improvement in nightmare frequency by the patients during their follow-up visit might have been subject to recall bias. This can be overcome by designing a prospective study where the patients are asked to keep a diary of their nightmares before and after CPAP treatment. Due to the retrospective nature of the study, there was no quantitative assessment of the severity of PTSD symptoms before or after the CPAP therapy by a mental health provider available. The overall subjective improvement in PTSD symptoms may be better assessed by using the standard PTSD check list (PCL), which has been validated in many previous studies.³⁹⁻⁴³ An unbiased pre- and post-CPAP evaluation by administering the full PCL questionnaire by a mental health professional would be much more accurate and valid, which can be only done in a prospectively designed study. The small sample size is another limitation of the study which limited the power to assess the large number of covariates in the regression models.

In summary, CPAP therapy is associated with decrease in frequency of PTSD-associated nightmares in veterans with either REM- or NREM-related OSA, and compliance predicts the magnitude of treatment benefit. We recommend that all PTSD patients should be screened clinically for symptoms of obstructive sleep apnea and that those who screen positive then undergo polysomnography to establish the diagnosis. If diagnosed with OSA, treatment with CPAP should be recommended and every effort should be made to improve the CPAP compliance to maximize the benefit in reducing the PTSD-related nightmares.

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SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication September, 2013

Submitted in final revised form December, 2013

Accepted for publication January, 2014

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DISCLOSURE STATEMENT

This was not an industry supported study. The study was performed at G.V. (Sonny) Montgomery VA Medical Center, Jackson, MS. The authors have indicated no financial conflicts of interest.