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Sleep in Posttraumatic Stress Disorder

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Posttraumatic stress disorder (PTSD) is often associated with sleep disturbances. In this review, we focus on the published literature on subjective and objective findings of sleep in patients with PTSD. Insomnia and nightmares are most commonly reported subjective sleep disturbances. Polysomnographic investigations have frequently reported rapid eye movement (REM) sleep abnormalities in PTSD. However, studies have not been consistent about the type of REM sleep dysfunction in PTSD patients. Antidepressants such as nefazodone, trazodone, fluvoxamine, and imagery rehearsal therapy are found to be beneficial in the treatment of PTSD associated sleep disturbances as well as core symptoms of this anxiety disorder. We propose use of such modalities of treatment in PTSD patients with predominant sleep disturbances. Further studies are required to clarify polysomnographic sleep changes especially role of REM sleep dysregulation and treatment of sleep disturbances in PTSD.

KEY WORDS: PTSD; sleep; nightmares; REM sleep.

INTRODUCTION

Posttraumatic stress disorder (PTSD) is an anxiety disorder, which frequently becomes chronic, recurrent, or progressive. PTSD develops in individuals who experience a traumatic event capable of eliciting intense feelings of fear, helplessness, or horror (1). Epidemiological studies found a lifetime prevalence of PTSD from 7.8 to 9.2% in general population with rate in women two times higher than in men (2–5). This anxiety disorder is enormously costly to the patients, their families, health-care system, and society as a whole (6).

Patients with PTSD can present with constellation of symptoms such as intrusive recollection, avoidance of disturbing stimuli, and disturbance of attention and arousal. Sleep disturbances are part of diagnostic criteria for PTSD and are included in both the re-experiencing (Criterion B) and increased arousal (Criterion D) symptom cluster in the *DSM-IV-TR* (American Psychiatric Association 2000). According to *DSM-IV-TR* (7) patients with PTSD can have recurrent distressing dreams of the traumatic event or difficulty falling or staying asleep. In fact, some authors have labeled sleep disturbance as the hallmark of PTSD (8).

It is very common for patients with PTSD to complain of sleep disturbances. Patients with this anxiety disorder perceive their sleep quality as poor (9, 10) and frequently report difficulty falling asleep, increased awakenings while asleep, decreased sleep duration, and anxiety arousals or nightmares during sleep (11–14). However, the association of sleep disturbance with PTSD remains poorly understood. In this paper we review the current knowledge of sleep in PTSD.

INSOMNIA

Insomnia is a complaint of difficulty initiating or maintaining sleep or of nonrestorative sleep. Patients with PTSD report all types of insomnia (10, 11, 13). In response to sleep disorders questionnaire, 16 out of 18 Vietnam veterans with chronic PTSD reported insufficient sleep (2 of 10 controls), 13 had difficulty falling asleep (0 of 10 controls), and 16

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endorsed unrefreshing sleep (1 of 10 controls) (10). Similarly in a small sample of youth with *DSM-III-R* PTSD and conduct disorder 25–71% had trouble sleeping (15).

A sleep survey comparing sleep of combat veterans with versus without PTSD reported significantly fewer hours of sleep in combat veterans with PTSD (11). In this study, insomnia and nonrestorative sleep were endorsed as significant problem by 59 and 73% of the PTSD subjects, respectively. In contrast, among combat veterans without PTSD, 19% reported insomnia and 38% reported nonrestorative sleep. Among the insomnia patterns, middle insomnia (awakening in the middle of the night) was associated most specifically with PTSD. The survey relied on subjective and retrospective reporting, and factors affecting sleep (variable sleep/wake schedule, use of prescribed and nonprescribed medication to facilitate sleep) were not controlled.

Additionally, male war-theater veterans (who served in Vietnam and air, space, and water surrounding Vietnam) with current PTSD at the time when National Vietnam Veterans Readjustment Study was conducted reported difficulty initiating and staying asleep (13). Difficulties falling asleep occurred in 44% of combat veterans with PTSD, 5.5% of combat veterans without PTSD, 9.4% of era veterans (who served on active duty in the U.S. Armed Forces during the Vietnam era but not in the Vietnam theater), and 5 of civilian comparison subjects. Difficulty staying asleep occurred in 90.7% of combat veterans with PTSD, 62.5% of combat veterans without PTSD, 63.1% of era veterans, and 52.9% of civilian subjects. The study was limited due to retrospective measurement of combat exposure, and lack of standardized measure of sleep disturbance.

Patients with PTSD complain frequent awakenings and perceive their sleep as restless. In a study of 59 elderly war veterans, subjects with PTSD reported significantly more awakening and rated their sleep as more restless compared to that of veterans without PTSD (16). Among hurricane victims with psychiatric morbidity (most commonly PTSD, followed by depression) subjective quality of sleep was significantly more disturbed on Pittsburgh Sleep Quality Index (PSQI) measure. The PSQI is an instrument to assess sleep quality in past 1 month, with established reliability and validity (17). The group with psychiatric morbidity had significantly decreased sleep quality and increase in global severity, awakenings, and bad dreams compared to subjects without psychiatric morbidity (18). Insomnia and poor subjective sleep quality seems to be significantly higher in PTSD patients across most studies (Table 1).

Table 1. Sleep Disturbances in PTSD

Insomnia
Difficulty falling asleep
Sleep maintenance insomnia
Nonrestorative/unrefreshing sleep
Nightmares
Trauma-related nightmares
Nontrauma related nightmares
Other
Startle/fear awakenings (without dream)
Panic-like awakenings
Thrashing movements during sleep
Rapid eye movement (REM) sleep behavior disorder
Sleep disordered breathing

NIGHTMARES

Commonly reported parasomnia-like events by the patients with PTSD are nightmares of combat, noncombat nightmares, movements during sleep, and startle or panic-like awakenings (waking up suddenly with fear or startle without remembering a dream) (Table 1) (11). Among these, combat nightmares were most specifically associated with PTSD (11). Nightmares are defined as frightening dreams that arouses the sleeper from sleep. Behavioral activation (such as talking, screaming, thrashing about, or ambulating) rarely occurs, which helps to distinguish them from other types of parasomnias. On awakening individuals can usually describe the dream sequence and content in detail.

Among Vietnam combat veterans more than 60% had one or more nightmare per month (19, 20). However, it is not clear how many of them met *DSM-III-R* criteria for PTSD. Recurrent dreams of wartime or captivity events were reported by 80% of the wartime prisoners and the frequency of these dreams remained constant (39%), decreased (30%), or increased (17%) with aging (21). Fifty to Sixty-nine percent of these prisoners of war met *DSM-III-R* criteria for PTSD. The dream content of the nightmares in these prisoners of war was typically combat situations with pursuers closing in. Among Holocaust survivors, half of the sample met *DSM-III-R* criteria for PTSD and nightmares were found to be almost universal (22). In contrast, studies of healthy students suggest that 20–24% of normal young adult population have nightmares at a frequency of less than one per year (23, 24).

In an archival analysis of the National Vietnam Veterans Readjustment Study database, frequent nightmares appeared to be specific for PTSD. Nightmares occurred in 52.4% of combat veterans with PTSD, 4.8% of combat veterans without PTSD, 5.7% of era veterans, and 3.4% of civilian subjects (13). Combat exposure strongly correlated with frequency of nightmares. Alcohol abuse, chronic medical illness, panic disorder, major depression, and mania did not predict the frequency of nightmares after control for nonsleep PTSD symptoms. The study lacked standardized measure of sleep disturbance and relied on retrospective measurement of combat exposure.

The dream content of nightmare is not always related to traumatic event leading to PTSD (11, 25). However, trauma-related nightmares are significantly more common in patients with chronic, severe, combat-related PTSD (25). The trauma-related nightmare complaint is associated with increased awakenings during sleep, whereas nontrauma-related nightmare complaint is not. Nightmares are now considered to be the integral feature of this anxiety disorder (8, 26, 27) and have significant effect on well being while awake as well as social and occupational functioning (28).

OTHER SLEEP COMPLAINTS

Sleep complaints other than insomnia and nightmares have been reported by patients with PTSD (Table 1). Hospitalized veterans with PTSD reported startle or fear awakenings without dream-recall, panic-awakenings (with physiological symptoms), and thrashing movements in sleep diary recordings (11). This study was limited by lack of a comparison group, and the majority of these inpatients were on medication. Narcolepsy and sleep apnea are significantly increased in adults with childhood abuse or trauma compared to adults without childhood abuse or trauma (28). However, the prevalence of PTSD in these subjects was not known. Other documented sleep-related complaints in PTSD patients include REM sleep behavioral disorder (29) and sleep-disordered breathing (30).

Subjective assessment of sleep by PTSD patients does not correspond to the objective findings. They seem to overestimate their sleep difficulties (9). Subjects with sleep complaints consistently underestimate sleep duration and overestimate sleep latency (31–33). However, other studies in patients with PTSD have shown significant positive correlation between subjective and objective estimates of sleep duration and latency (34). Even though there was substantial absolute subjective judgement error, subjects with PTSD reporting longer time-in-bed tended to demonstrate more minutes asleep and minutes in bed in the lab, while those reporting longer sleep latencies generally demonstrated longer latencies. Polysomnographic (PSG) studies give more objective measures of sleep disturbances.

POLYSOMNOGRAPHIC RESEARCH

PTSD can occur following various traumatic events (e.g., sexual assault, burns, accident or injury, natural disasters), but most PSG research to date has been conducted in combat-related PTSD.

Many (but not all) PSG studies have reported rapid eye movement (REM) sleep abnormalities in patients with PTSD (Table 2) (10, 35). PTSD patients have been found to have increased REM density (36–38), decreased, normal, or increased REM latency, lower or higher percentage of REM sleep, increased REM activity, and increase in movement during REM sleep (16, 38–44). Although, the pattern of altered REM sleep parameters is not consistent across studies (14, 45), some type of REM-related abnormality is frequently found in patients with PTSD. Not surprisingly Ross *et al.* (8) implicated REM sleep dysregulation as a critical factor in the pathophysiology of PTSD.

Studies have also reported significant decrease (36, 37, 41, 48) as well as no difference in sleep efficiency (10, 38) among patients with PTSD compared to normal controls. Similarly, some investigators have shown a trend towards increased (18, 36) wake percentage (awakenings during sleep), whereas others did not find any increase (38) of wake percentage in the sleep of PTSD patients.

In a small sample of crime victims with PTSD, presenting to a nightmare and insomnia treatment program, 40 of 44 patients suffered from sleep-disordered breathing. Among these 22 patients had obstructive sleep apnea (OSA) and 18 patients satisfied upper airway resistance syndrome (UARS) criteria (30). The criteria for clinical diagnosis were based on the recent position paper of the American Academy of Sleep Medicine (49). This study suffered from a selection bias, lack of control subjects, and in addition, 73% of patients were using antidepressants, anxiolytic/sedatives, and/or pain medications singly or in combination.

Table 2. Case Controlled PSG Studies

PSG sleep variable	Increased*	Decreased*	No difference*
Sleep efficiency	None	P = 21, C = 8 (11); P = 20, C = 8 (36); P = 24, C = 9 (37); P = 7, C = 7 (46)	P = 18, C = 10 (10); P = 11, C = 8 (38); P = 12, C = 12 (47)
Entries to wake (no.)	P = 7, C = 7 (46)	None	P = 20, C = 8 (36); P = 24, C = 9 (37)
REM latency	P = 7, C = 7 (46)	None	P = 18, C = 10 (10); P = 21, C = 8 (11); P = 20, C = 8 (36); P = 24, C = 9 (37); P = 11, C = 8 (38); P = 12, C = 12 (47)
REM time	P = 11, C = 8 (38)	None	P=18, C = 10 (10); P = 12, C = 12 (47)
REM percentage	P = 30, C = 29 (16); P = 56, C = 14 (25); P = 11, C = 8 (38)	P = 7, C = 7 (46)	P = 18, C = 10 (10); P=20, C = 8 (36); P = 24, C = 9 (37); P = 12, C = 12 (47)
REM activity	P = 11, C = 8 (38)	None	P = 18, C = 10 (10)
REM density	P = 20, C = 8 (36); P = 24, C = 9 (37)	None	P = 18, C = 10 (10)
SWS time		P = 7, C = 7 (46)	P = 11, C = 8 (38)

Note. SWS = slow wave sleep; P = PTSD subjects; C = normal controls.
*$p < 0.05$.

In most of the sleep studies the subjects in the PTSD group had comorbid major depression and/or substance use disorders (36–38). However, when the subset of PTSD subjects who did not have current major depression was compared with the normal control group, REM sleep differences were still evident (38) but the possibility of depression contributing to REM sleep abnormalities cannot be excluded. Moreover, it is not clear whether comorbid substance use disorder has any effect on the sleep of patients with PTSD.

Lifetime prevalence of major depressive disorder (MDD) in patients with PTSD is around 60% (50, 51). Few researchers have attempted to understand the possible relevance of this comorbidity in terms of sleep findings. Patients with PTSD and MDD show weak trends of increase in REM density compared to PTSD without MDD group (35). Slow wave sleep (SWS) was significantly decreased in the PTSD with MDD group compared to PTSD without MDD group (35). However, there was no significant difference in REM latency in the PTSD with MDD group compared to PTSD without MDD group (35) as well as control group (45).

TREATMENT IMPLICATIONS

Sleep disturbances may exacerbate chronic PTSD. Considering that insomnia, nightmares, and REM sleep dysfunction are major sleep-related disturbances in PTSD, psychotropic medications and other modalities improving these sleep abnormalities might help PTSD patients (Table 3). Monoamine oxidase inhibitors (phenelzine) and tricyclic antidepressants (imipramine, amitriptyline) are more effective than placebo in treating patients with PTSD (52, 53). In spite of the fact that both monoamine oxidase inhibitors and tricyclic antidepressants are able to suppress REM sleep (54–56), only phenelzine has been shown to directly improve sleep-related symptoms of PTSD (57). In an open label study of 25 Israeli combat veterans with *DSM-III* PTSD, treatment with a median daily dose of 60 mg of phenelzine showed significant clinical improvement in sleep disturbance (57).

Selective serotonin reuptake inhibitors (SSRI) such as fluoxetine, paroxetine, and sertraline are effective in the treatment of PTSD (58–61). In fact this group of medications are considered to be the first line of agents for treatment of patients with PTSD (62). However, SSRIs are known to have arousing effects on sleep EEG such as increase in number of arousals, decrease in total sleep time, suppression of REM sleep, and increase in phasic REM sleep activity (63). Despite these adverse effects of SSRIs on sleep, fluvoxamine (64) and paroxetine (65) are found to improve sleep quality. Fluvoxamine significantly improved subjective quality of sleep in an open-label study of 21 Vietnam combat veterans with *DSM-IIIR/IV* PTSD (64). Another SSRI, paroxetine improved subjective sleep quality as measured by PSQI in an open, flexible dose trial of 14 patients with primary insomnia (65). Both these studies were limited by lack of a control group and small sample size.

Pharmacological agents acting at serotonin-2 (5HT2) receptors such as nefazodone, trazodone, and cyproheptadine are reported to improve sleep disturbances in PTSD patients (66–71). In an open-label clinical trial, nefazodone, a 5HT-2 receptor antagonist, is reported to be effective for treatment

Table 3. Possible Treatment Options for Sleep Disturbances in PTSD and Supporting Evidence

Pharmacological	Evidence
Nefazodone	Very few open-label, small sample studies
Trazodone	One open-label, small sample study; 1st line in expert consensus guidelines (62)
Fluvoxamine	One open-label study with small sample
Paroxetine	One open-label study (in primary insomnia)
Others	
Phenelzine	One open-label, small sample size
Zolpidem	Case series; Higher 2nd line in expert consensus guidelines (62)
Benadryl	Higher 2nd line in expert consensus guidelines (62)
Benzodiazepines	Higher 2nd line in patients without history of substance abuse; 3rd line in patients with history of substance abuse in expert consensus guidelines (62)
Behavioral	
Imagery rehearsal therapy	One randomized control trial and one open-label study
Anxiety management (using relaxation training, breathing retraining, positive thinking and self-talk, assertiveness training, and thought stopping)	Preferred psychotherapeutic technique recommended in expert consensus guidelines (62)
Sleep hygiene, stimulus control (eliminating learned sleep preventing associations), and sleep restriction (increasing sleep quality and efficiency by reducing time spent in bed) all together	Along with imagery rehearsal therapy in one open-label study

refractory PTSD patients with multiple comorbid Axis I psychiatric disorders (71). This study found significant decrease in number of awakenings and bad dreams and improvement in total sleep time, ability to fall sleep, and overall quality of sleep as measured by PSQI after treatment with nefazodone in comparison to baseline. Similarly, a recent open-label study of 12 chronic combat-related PTSD patients demonstrated improvement in subjective sleep quality and nightmares without significant changes in PSG sleep after 12-week treatment with nefazodone, in comparison to baseline (66). Another 5HT2 antagonist trazodone was found to be helpful by PTSD patients for treatment of insomnia and nightmares in survey using a questionnaire designed by the authors (70). More than 70% of the 60 PTSD patients who completed the study reported significant improvement in nightmares, sleep onset insomnia, and sleep maintenance. However, most of these patients were on other psychotropic agents (SSRIs, nefazodone, valproic acid, and benzodiazepines) and the questionnaire was not standardized.

Retrospective review of records and anecdotal reports have found cyproheptadine (antagonist at histamine 1 (H1) and 5HT2 receptor) as effective medications to reduce nightmares in patients with PTSD (67, 72, 73). In contrast, a double-blind, randomized, placebo-controlled study found cyproheptadine as ineffective for sleep problems or PTSD in males with combat-related PTSD (74). Instead this study suggests that cyproheptadine may exacerbate the sleep problems in such patient population. However, the study sample was small, which limits interpretation.

Other case reports have found improvement in nightmares in PTSD patients with guanfacine (α-adrenergic agonist) (75), prazosine ($\propto$-adrenergic antagonist) (76), zolpidem (non-benzodiazepine imidazopyridine) (77), and olanzapine (78). Even though, alprazolam, a benzodiazepine has been found to improve insomnia in PTSD patients (79), benzodiazepines (alprazolam, clonazepam) have not been found to be effective for core symptoms of PTSD (79, 80). Moreover, use of benzodiazepines increases the risk of dependence (81), and withdrawal symptoms are particularly severe after prolonged use (80, 82).

Among the psychotherapeutic modalities, imagery rehearsal therapy was initially found in anecdotal reports and case series (83–85) as beneficial for treatment of nightmares. Imagery rehearsal therapy is a form of cognitive behavioral therapy, which teaches patients to control nightmares and change them to any way wanted with imagery exercises and cognitive behavioral tools (86). Subsequently, an open-label study (87) of 62 crime victims with PTSD found significant improvement in nightmares, insomnia, and PTSD symptoms with imagery rehearsal therapy, sleep hygiene, stimulus control (eliminating learned sleep preventing associations) and sleep restriction (increasing sleep quality and efficiency by reducing time spent in bed). Additionally, a randomized controlled trial of female sexual assault survivors with PTSD by Krakow (86) and colleagues

demonstrated that imagery rehearsal therapy significantly improved disturbing nightmares, sleep quality (assessed by PSQI), and symptoms of PTSD. This study was limited by lack of a placebo control and large drop rates at follow up.

CONCLUSION

PTSD is often associated with frequent sleep complaints especially insomnia and nightmares (Table 1). Some investigators (13, 14) postulate that sleep onset insomnia in these patients is secondary to sleep phobia resulting from the experience of frequent frightening dreams (nightmares). Repetitive nightmares are seen in vast majority of patients with PTSD (8, 11, 13). Sleep studies have shown that nightmares or anxiety arousals occur during REM sleep (38) and nonrapid eye movement sleep (NREM) (27, 43). However, some investigators (8, 88) argue that nightmares of PTSD are of REM sleep related rather than NREM because of the content as well as ease of recall. This has lead researchers to hypothesize REM sleep dysregulation as a possible underlying mechanism in the pathogenesis of PTSD (8, 14, 38, 88).

Even though various REM sleep abnormalities (Table 2) have been identified (10, 16, 36–38) in patients with PTSD, type of REM sleep alterations reported across studies have been inconsistent. Moreover, high frequency of comorbid psychiatric disorders in patients with chronic PTSD makes it difficult to exclude an influence of other disorders on the polysomnographic findings. Additionally, it is not known whether PTSD subjects in earlier studies, especially studies reporting reduced REM sleep were receiving psychotropic medications with REM sleep suppressing properties such as monoamine oxidase inhibitors, tricyclic antidepressants, or benzodiazepines (54, 56).

Although, a causal role of sleep dysfunction in the pathophysiology of PTSD could not be established, it is clear that PTSD patients have frequent sleep complaints with disturbed sleep. This suggests the possibility that these sleep disturbances may aggravate or maintain other psychiatric symptoms of PTSD. Handful of uncontrolled studies have shown that there are pharmacological and behavioral modalities of treatment that are beneficial in independent amelioration of sleep disturbances in patients with PTSD. These include trazodone, nefazodone, fluvoxamine, and imagery rehearsal therapy (Table 3). Additionally they have been found to be effective in treatment of PTSD as a whole. Even though evidence is scarce, we suggest use of such modalities of treatment whenever sleep related symptoms are prominent.

To further strengthen the association between sleep and PTSD, sleep disturbances should be studied in PTSD patients controlling for other factors known to affect sleep (comorbid psychiatric disorders such as major depression and substance use disorders; pharmacological agents; caffeine intake). However, such an ideal study design may not be feasible or ethical. A recent prospective study of survivors of motor vehicle accident suggests the possibility of identifying patients who will develop PTSD based on sleep complaints as early as 1 month after trauma (89). This avenue needs to be explored. Randomized double-blind studies of pharmacological therapy for sleep disturbance in PTSD are needed. Future studies should focus on clarifying the PSG sleep changes and understanding the possible role of REM sleep disturbances in the biology PTSD.

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