THEORETICAL REVIEW

Trauma associated sleep disorder: A parasomnia induced by trauma

Vincent Mysliwiec [a, *], Matthew S. Brock [a], Jennifer L. Creamer [b], Brian M. O'Reilly [b], Anne Germain [c, d], Bernard J. Roth [b]

[a] San Antonio Military Medical Center, Department of Sleep Medicine, 2200 Bergquist Drive, Suite 1, JBSA Lackland, TX 78236, USA
[b] Madigan Army Medical Center, Department of Pulmonary, Critical Care, and Sleep Medicine, Tacoma, WA, USA
[c] University of Pittsburgh School of Medicine, Department of Psychiatry, Pittsburgh, PA, USA
[d] University of Pittsburgh School of Medicine, Department of Psychology, Pittsburgh, PA, USA

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SUMMARY

Nightmares and disruptive nocturnal behaviors that develop after traumatic experiences have long been recognized as having different clinical characteristics that overlap with other established parasomnia diagnoses. The inciting experience is typically in the setting of extreme traumatic stress coupled with periods of sleep disruption and/or deprivation. The limited number of laboratory documented cases and symptomatic overlap with rapid eye movement sleep behavior disorder (RBD) and posttraumatic stress disorder (PTSD) have contributed to difficulties in identifying what is a unique parasomnia. Trauma associated sleep disorder (TSD) incorporates the inciting traumatic experience and clinical features of trauma related nightmares and disruptive nocturnal behaviors as a novel parasomnia. The aims of this theoretical review are to 1) summarize the known cases and clinical findings supporting TSD, 2) differentiate TSD from clinical disorders with which it has overlapping features, 3) propose criteria for the diagnosis of TSD, and 4) present a hypothetical neurobiological model for the pathophysiology of TSD. Hyperarousal, as opposed to neurodegenerative changes in RBD, is a component of TSD that likely contributes to overriding atonia during REM sleep and the comorbid diagnosis of insomnia. Lastly, a way forward to further establish TSD as an accepted sleep disorder is proposed.

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Introduction

Following traumatic experiences, sleep disturbances are frequently reported. The most common symptoms are insomnia and trauma related nightmares (TRN) [1]. The nightmares that trauma survivors develop are noted to be distinctly different than the nightmares which characterize idiopathic nightmare disorder [2,3]. Trauma related nightmares tend to be more severe and distressing to the individual, and in many (but not all) cases, associated with posttraumatic stress disorder (PTSD). Disruptive nocturnal behaviors (DNB) to include dream enactment behavior (DEB) and sympathetic activation are often reported in the context of TRN. Nocturnal movements with TRN can range from gross body movements to frank combative behaviors. These symptoms, which further distinguish TRN from idiopathic nightmares, have remained relatively poorly characterized. This is in part due to the frequent

association of TRN with PTSD as a variant of idiopathic nightmares, as well as the rare capture of nightmares and DNB in monitored settings [4].

Prior to the proposal of trauma associated sleep disorder (TSD) as a distinct parasomnia [5], these nocturnal phenomena was best described by Raskind: "The physiology of PTSD trauma nightmares differs from that of 'normal' dreams. Trauma nightmares are largely expressed during light sleep and disrupted rapid eye movement (REM) sleep, and often are accompanied by motor activity. Normal dreams, whether pleasant or unpleasant, most often arise from REM sleep that is characterized by a relative paralysis of large muscle movement" [6]. This description highlights the characteristics which distinguish TSD from nightmare disorder, most notably the presence of motor activity, but also that the nightmares potentially emanate from both non-rapid eye movement (NREM) and REM sleep. Additionally, this constellation of findings occurs exclusively while asleep, thus differentiating TSD from the diagnosis of PTSD.

In this article, we report on the historical findings consistent with TSD and develop the clinical and potential neurobiological

* Corresponding author. Wilford Hall Ambulatory Surgical Center, Sleep Disorders Center, 2200 Bergquist Drive, Suite 1, JBSA-Lackland, TX 78236, USA. Fax: +1 210 292 4325.
E-mail address: vincent.mysliwiec.mil@mail.mil (V. Mysliwiec).

Abbreviations

ACC	anterior cingulate cortex	NREM	non-rapid eye movement
CPAP	continuous positive airway pressure	OIF/OEF	Operation Iraqi Freedom/Operation Enduring Freedom
CNS	central nervous system	OSA	obstructive sleep apnea
DNB	disruptive nocturnal behaviors	PLM	periodic limb movements of sleep
DEB	dream enactment behaviors	PSQI-A	Pittsburgh sleep quality index-addendum
EEG	electroencephalographic	PSG	polysomnography
EMG	electromyogram	PTSD	posttraumatic stress disorder
GABA	gamma-aminobutyric acid	REM	rapid eye movement
HPA	hypothalamic-pituitary-adrenal	RBD	REM sleep behavior disorder
IRBD	idiopathic REM sleep behavior disorder	RPLA	REM sleep phasic leg activity
LC	locus coeruleus	RWA	REM sleep without atonia
mPFC	medial pre-frontal cortex	SLD	sublaterodorsal nucleus
NE	norepinephrine	SSRI	selective serotonin reuptake inhibitors
		TRN	trauma-related nightmares
		TSD	trauma associated sleep disorder

mechanisms of TSD. As there is a paucity of articles on nightmares and DNB emanating solely from traumatic experiences in the absence of PTSD, we review the scientific literature which has evaluated patients with PTSD and in some cases, REM sleep behavior disorder (RBD). In a portion of the literature evaluated, the patient's symptoms and overall clinical picture is, in our opinion, more consistent with the proposed criteria for TSD.

Initial reports of complex sleep disturbances after traumatic experiences

The effects of combat related trauma on sleep have long been recognized. Descriptions of complex behaviors associated with nightmares were reported during the Civil War. Wallace Woodford, a Union soldier who survived the Confederate prison in Andersonville, where many soldiers died from disease and starvation, "flailed in his sleep, dreaming that he was still searching for food" [7]. Marked sleep disturbances were reported in association with combat exhaustion that Bartemeier et al. described in World War II veterans [8]. While insomnia was the primary sleep component of combat exhaustion, "difficulties were experienced also in staying asleep because of sudden involuntary starting or leaping up, or because of terror dreams, battle dreams and nightmares of other kinds" [8]. In these historical reports, the observances of abnormal behaviors and movements in sleep in association with TRN were described relatively shortly after the inciting trauma. The concept that these sleep disturbances were only nightmares remained until Ross et al. reviewed the literature assessing sleep disturbances in PTSD [9]. One question they asked was if the dreams associated with PTSD were true nightmares or another sleep disorder. They compared and contrasted PTSD nightmares to night terrors and the newly proposed REM parasomnia, RBD. Two primary reasons supported PTSD dreams as night terrors (a NREM parasomnia): PTSD dreams tended to occur early in the sleep period and could have associated gross body movements. However, as most dreams occur during REM sleep and Schenk et al. [94] reported REM sleep without atonia in RBD patients, PTSD dreams may be a REM-related phenomenon.

Inciting factors for TSD

Combat exposure is the most frequently reported cause of TRN [10—12], although TRN are reported after maritime disasters [13], sexual trauma [14], burns [15], and other traumatic experiences [16]. The severity of the traumatic exposure is generally associated with nightmare intensity with increasing trauma severity typically associated with more intense nightmares [16,17]. Less severe

trauma can incite nightmares, but has not been reported to result in the other clinical manifestations of TSD. A cohort of college students who survived an earthquake experienced more nightmares than a control group [18]. However, nightmare severity was not more intense than controls and DNB were not reported. The context and setting in which the trauma occurs also appears to play a role in the development of TSD. Whereas military personnel in combat and sailors are typically exposed to extremely stressful situations and prolonged work periods with both acute and chronic sleep deprivation, other trauma survivors often lack such austere living situations. Sleep deprivation coupled with fragmented sleep have long been recognized as contributing factors to the sleep disturbances ensuing after combat [8,19]. These additional stressors likely contribute to the development of TSD as opposed to only TRN. A proposed model for the development of TSD is presented in Fig. 1.

Previous reports consistent with TSD

There are only a few studies [5,10,19—22] that have assessed trauma survivors and documented the occurrence of findings consistent with TSD. The first study performed polysomnography (PSG) in three men (ages 25, 29, and 35 y) with combat fatigue who were 2—4 wk removed from their combat experiences and medication-free at the time of their evaluation [19]. They were all classified as having substantial sleep deprivation prior to their evacuation from combat with the resultant symptoms of "severe insomnia, and recurrent nightmares with vocalization and much body movements." On their PSGs there were many body movements and bursts of tachycardia. Traumatic nightmares were reported in stage two sleep and one patient had a violent awakening with vocalizations. "Our case 1 awoke particularly violently, jumping out of bed screaming and hallucinating." The other notable finding was generalized elevated electromyogram (EMG) tone throughout the PSG, to include during REM sleep.

The second study to report patients with TSD-like findings evaluated 15 Vietnam veterans with PTSD [21]. Participants underwent a semi-structured psychiatric interview and five nights in a sleep lab. Nightmares were reported by 13 of 15 patients, with a typical onset between 01:00 and 03:00 h. The nightmares consisted of replays of prior combat experiences with body movements and reports of attacks by the patients on their bed partners. The in-lab PSG documented two patients with DNB. During REM sleep one patient removed the electrodes and walked around the room, stating he was in an ambush. Another patient had non-descript body movements in N2 associated with a dream of a gunfight. On the subsequent night, this patient awakened from REM sleep, thrashing about after a nightmare of mutilated bodies.
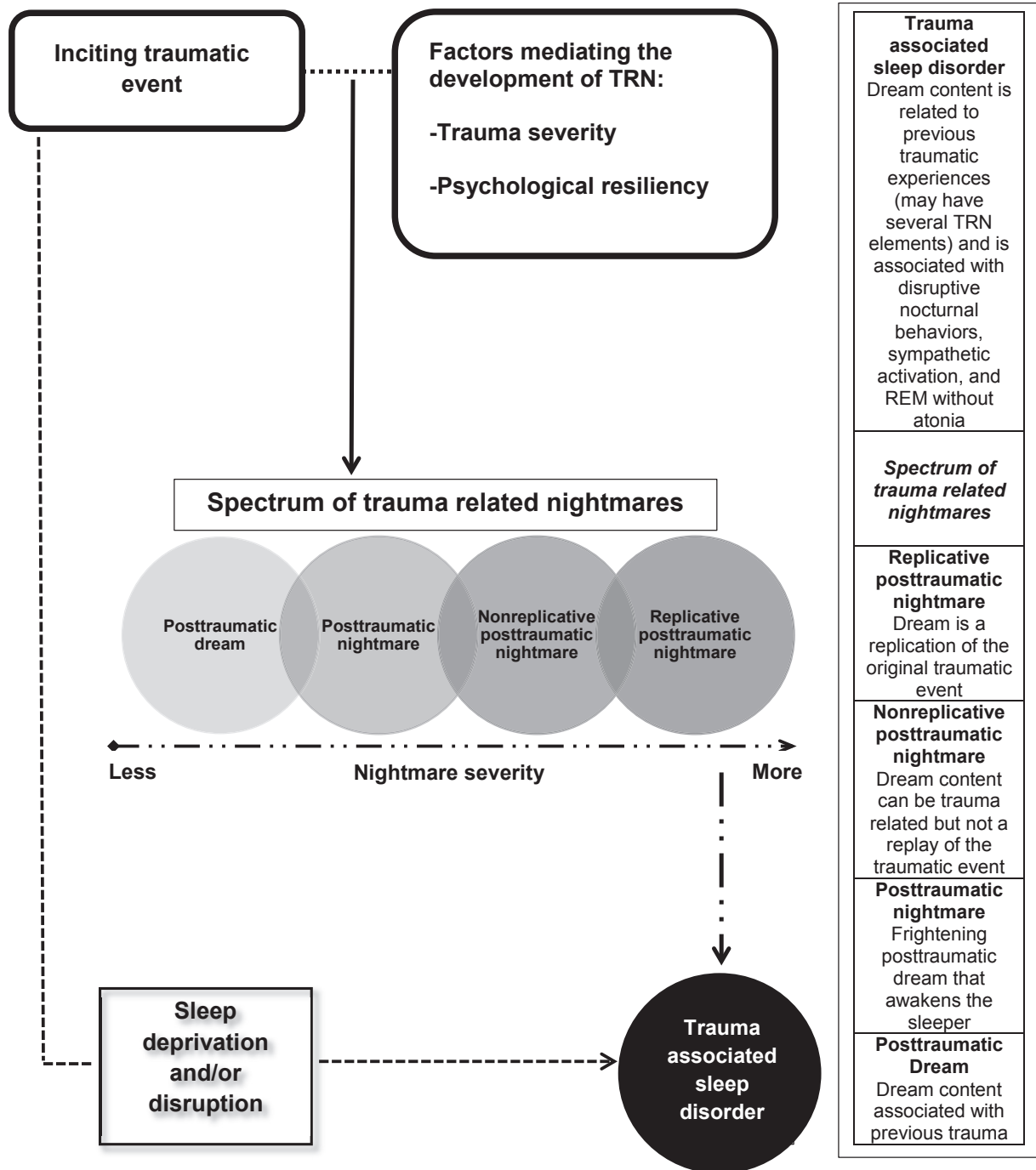
Fig. 1. Proposed model for the development of trauma associated sleep disorder (TSD). Trauma related nightmares (TRN) develop following a traumatic event and advance along a spectrum based on the severity and duration of the trauma exposure, the individual's psychological resiliency, and if sleep deprivation and/or disruption were present in the peri-traumatic period. Increasing trauma severity is typically associated with more intense and disruptive nightmares. TSD represents the extreme end of this spectrum, whereby the individual not only has TRN but develops disruptive nocturnal behaviors and rapid eye movement (REM) without atonia. Definitions for TSD and spectrum of TRN are included.

Hefez et al. reported two patients who appeared to have TSD [10]. In their study, 11 patients with posttraumatic sleep disturbances were evaluated with PSG for two to five nights and were awakened 10–15 min after every REM period. Two patients, ages 20 (taking chlorpromazine, an antipsychotic medication) and 25 y old (taking chlordiazepoxide, a benzodiazepine), survived separate maritime disasters, and were evaluated 6 and 12 mo after their trauma exposure, respectively. "One of the maritime survivors showed complex motor activity during REM, which at one time resulted in actual escape from the bedroom." His nightmares consisted of reliving the maritime disaster. The other patient had similar nightmare content but did not have DNB, although REM-related motor activity was noted for this patient as well. An additional two patients, one a 45-year-old Holocaust survivor and a 33-year-old combat veteran, who were further removed from their traumatic experiences, had nightmares documented after awakenings from N2 and REM. Notably, the combat veteran had explosive motor activity when he was awakened from sleep during a subsequent hospitalization. While the combat veteran had

characteristic symptoms of TSD, there was not enough detail in the report to render this diagnosis.

In our initial case series, we described four male soldiers, ages 22–39, who each had a traumatic experience with the subsequent development of nightmares, DNB, and insomnia [5]. Their clinical characteristics were notable for two patients taking selective serotonin reuptake inhibitors (SSRI) and one patient having PTSD. All four men had a PSG performed relatively soon after their respective traumatic experience. One patient had a documented nightmare with DNB in an early onset REM period. During the nightmare the patient had vocalizations, REM sleep without atonia (RWA) with observed defensive limb movements, and associated tachycardia and tachypnea. After his PSG he reported a nightmare consistent with his usual combat related nightmares. We reported the additional findings of variable RWA ranging from 13.7 to 37.6% (using the "any" mentalis EMG criteria) and the presence of mild obstructive sleep apnea (OSA) in three of the soldiers. In our study, all of the patients were treated with prazosin and had decreased nightmares and DNB. Additionally, the patients with OSA were treated with continuous positive airway pressure (CPAP), which may have contributed to their overall improvement.

In evaluating these studies, there are a number of similarities in the patients and their PSG findings. The patients were relatively young men who worked in stressful occupations such as military service or the maritime industry that likely predisposed them to sleep deprivation and/or disruption [19]. In the cases that nightmares and DNB were documented, each patient underwent PSG evaluation in temporal proximity to his traumatic event. This aspect of temporal proximity was first noted by Hefez, with the maritime disaster patient who was 6 mo removed from his trauma having the most profound movements in REM [10]. Additionally, many of the patients spent multiple nights in the sleep lab, allowing them to acclimate to this new sleeping environment. The nightmares were nearly always replays of the patient's prior traumatic event and the DNB occurred during REM sleep with profound body movements and an absence of the normal atonia of REM. However, there is a report that DNB can occur in NREM sleep. Lipper et al. proposed a theory that sleep disturbances developing after trauma potentially have inappropriate transitions, whereby REM and NREM phenomena may occur [23]. Thus, while in our initial report we focused on nightmares and DNB associated with REM, it is also likely that nightmares and DNB occur in NREM sleep. As dreams in NREM sleep are not as vivid as those in REM, this may help explain to a degree the lack of dream recall reported in patients with TSD.

Studies reporting features of TSD

Trauma related nightmares

There are a number of studies which used variable methods to describe clinical and polysomnographic findings of TSD. Nightmares are one of the most frequent sleep disturbances following trauma and were assessed following either induced or spontaneous awakenings in two studies. In a study assessing sleep and dreams in nine male combat veterans with war neuroses (defined as persistent, repetitive war nightmares, startle reactions, marked irritability or difficulty in controlling anger, and severe feelings of hopelessness and helplessness), three nights of sleep were evaluated [24]. During the study, patients either slept without awakenings or had induced awakenings after each REM period. Nightmares only occurred in two patients during the study and were associated with REM sleep. This was in marked contrast to each patient's report of frequent nightmares at home. Kramer et al. evaluated nightmares in four veterans with a remote history (>10 y ago) of military service with three nights in a sleep laboratory [25]. After spontaneous periods of

wakefulness lasting at least 60 s, participants were questioned about their dreams. A nightmare in this study was defined as a dream with associated anxiety or fright. A total of four nightmares were associated with REM sleep and 21 with NREM in this study.

Nocturnal movements in sleep after traumatic experiences

Eleven veterans (ages 24–33) with psychiatric and sleep disturbances including nightmares, who were 2–2.5 y removed from their combat experiences, were compared to controls in a sleep lab [26]. While the data from this study are limited as it focused on nocturnal movements and respiration, it suggested that patients with combat-related sleep disturbances had increased movements and respiratory rates consistent with increased autonomic activity. Ross et al. assessed the sleep of 12 veterans with chronic PTSD and compared them to a control group of 10 veterans [22]. The participants underwent three nights of PSG with the first night in the lab as an adaptation night. The veterans with PTSD had increased REM sleep and more notably, an increase in phasic activity in REM. During this study, which included 32 nights of recorded sleep, one patient had a nightmare resulting in awakening from REM sleep. This nightmare occurred in the first REM period, with an associated high REM density and high REM sleep phasic leg activity (RPLA) index. The findings reported in this study are suggestive of RWA. In a subsequent report, these authors assessed RPLA in this same cohort [27]. Phasic leg movements were defined as activity in either leg EMG that was ≥ 1.5 s in duration and $\geq \frac{1}{2}$ the amplitude of the biocalibration ankle flexion response. The veterans with PTSD had a significant increase in RPLA index compared to controls (4.6/h vs 1.3/h); the patients with PTSD also had increased periodic limb movements of sleep (PLM). Increased nocturnal movements have also been reported in children that suffered abuse. In a study of 19 pre-pubertal children with a history of abuse, actigraphic assessment documented increased nocturnal movements as compared to controls and children with depression [28]. One study reported elevated PLM indices during REM and NREM sleep in both posttraumatic and idiopathic nightmare sufferers compared to controls [29]. The authors suggested that PLM potentially correlated with the intense negative dream content. Thus, there appears to be different nocturnal movements in TSD, one which is non-specific and consistent with PLM, and the other which is related to nightmares, manifested as more purposeful DEB.

Multiple sleep disturbances following combat related trauma

Sleep disturbances in Vietnam veterans were characterized utilizing questionnaires and PSG by Mellman et al. [30]. The veterans, who were far removed from their combat experiences, had chronic symptoms and were between 39 and 48 y old. Veterans with PTSD reported the following symptoms: disturbing combat-related dreams (65%), thrashing and violent movements (59%), startle-panic awakenings (51%), and screaming or shaking while sleeping (38%). Each of these symptoms was reported more frequently in veterans with PTSD. During the PSGs, 18 symptomatic awakenings were documented. Threatening dream content was associated with three awakenings and 15 were associated with symptoms of startle or fear, but no dream recall. There were increased body movements in the PTSD patients but purposeful movements were not reported. Physiologic arousal, characterized by tachycardia and tachypnea, were noted after REM sleep. Notably, 47.6% of the patients with PTSD had OSA; it is unknown how sleep disordered breathing contributed to their overall symptomatology. In an observational study of 30 young Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) veterans with a mean age of 31, all of whom had insomnia and returned from combat within 35 mo, Wallace et al. performed actigraphy, sleep diaries, and a PSG

to evaluate their sleep disorders [31]. Nightmares were diagnosed in 89% of patients with PTSD and 80% of those with PTSD/traumatic brain injury. Their nightmare content included reenacting combat experiences. Additionally, four patients had RWA, DNB, and sleep related injuries. These patients, all of whom were taking SSRI, were diagnosed with RBD.

Chronic PSG findings following trauma

In a study evaluating the sleep of 63 medication-free veterans with chronic PSTD, Woodward et al. reported that veterans with nightmares had increased wakefulness after sleep onset [32]. There was no difference in REM latency or duration in those with nightmares vs those without. A second study by this same group studied 88 male combat veterans with chronic PTSD (20 y after combat), noting they had decreased movement time on an attended in-lab PSG compared to controls [33]. Movement time was scored when more than one-half of an epoch had dense, large-amplitude findings in the electroencephalographic (EEG) and EMG channels. Additionally, nightmares were strongly associated with decreased movement. Similar findings were reported by Lavie et al. whereby patients with chronic PTSD had elevated arousal and awakening thresholds [34]. They proposed that acutely following trauma exposure, nightmares and night terrors develop, resulting in awakenings from NREM and REM. Over time there is active blocking that develops through modification of awakening thresholds and sleep architecture, decreasing awakenings from nightmares. These studies suggest that TSD evolves over years, and there is potentially less DNB over time.

Assessment of nightmares and DNB with the Pittsburgh sleep quality index-addendum

Non-PSG methods have also been developed to assess nightmares and DNB after trauma. Germain et al. developed a clinical instrument, the Pittsburgh sleep quality index-addendum (PSQI-A), to assess the DNB that occur in trauma survivors, both with and without a diagnosis of PTSD [4]. The PSQI-A assesses nightmares related and not related to trauma and addresses DNB with the following questions: "Had episodes of terror or screaming during sleep without fully awakening; Had episodes of 'acting out' your dreams, such as kicking, punching, running or screaming; Feeling hot flashes." In a study of 375 recent OIF/OEF veterans using the PSQI-A, 59.1% had a total score of >4, which is consistent with PTSD [35]. The specific components of "acting out your dreams" or "episodes of terror or screaming" in sleep were not reported. However, nightmares were one of the most frequent symptoms and participants reported excessive body movements during sleep.

Clinical characteristics of TSD

Here we develop the overall clinical picture of TSD. We relate these characteristics to the aforementioned cases and clinical descriptions. See Table 1 for the proposed diagnostic criteria for TSD and Fig. 2 for a characteristic epoch of sleep in a patient with this disorder.

1) **Inciting traumatic experience**. All of the cases we assessed as TSD developed after trauma [21,30,36], which was the inciting event for the onset of DNB and nightmares. The majority of cases were provoked by combat [5,19,21]; however, two other cases occurred shortly after a maritime disaster [10]. These experiences were extremely stressful and more than likely long in duration, i.e., lasting many hours to days.

Table 1
Proposed diagnostic criteria for trauma associated sleep disorder.

1. Onset after combat or other extreme traumatic experience
2. A history of altered dream mentation that is related to prior traumatic experience
3. Self or witnessed reports of disruptive nocturnal behaviors (DNB) to include at least one of the following:
   a. Abnormal vocalizations
      i. Screaming or yelling
   b. Abnormal motor behaviors in sleep
      i. Tossing, turning, or thrashing
      ii. Combative behaviors such as striking bed partner
4. Symptoms of autonomic hyperarousal or polysomnogram (PSG) monitoring demonstrates one of the following:
   a. Tachycardia
   b. Tachypnea
   c. Diaphoresis
   d. If documented on PSG, these findings occur in association with rapid eye movement (REM) sleep without atonia or DNB, and are not due to sleep disordered breathing
5. PSG may demonstrate:
   a. REM sleep without atonia; "any" EMG activity index is variable
   b. Dream enactment behavior in REM sleep
6. Absence of electroencephalographic (EEG) epileptiform activity on PSG

(Adapted from) Ref. [5] with permission.

2) **Sleep deprivation and disruption around the time of trauma**. Sleep deprivation and disruption as contributing factors to the onset of TSD was first appreciated by Schlosberg when he evaluated soldiers with combat fatigue [19]. Military personnel in combat environments and shortly upon returning home are known to have disrupted, insufficient sleep and at times, total sleep deprivation [37]. Similar sleep disturbances also likely occurred in the maritime disaster patients.

3) **Temporal proximity to the traumatic event**. Nightmares and DNB are reported to occur within weeks to months after the inciting trauma [5,10,19]. In some cases, there appears to be an initial prodrome of nightmares after the initial traumatic experience with subsequent onset of DNB following repeated combat exposures as we have previously reported [5].

4) **Nightmares**. The nightmares that patients with TSD experience are related to their traumatic experience. Specifically, the nightmare content varies depending on the inciting trauma, similar to TRN [38]. Nightmares may include prior combat experiences, elements of death, dying, or threats to the patient's safety with associated symptoms of fear, anxiety, or emotional content that occurred at the time of the trauma. Yet, some patients lack specific dream recall [24,39,40], which is also reported in patients with PTSD. In these cases, the bed partner typically reports the occurrence of nightmares in which the patient grunts, yells out orders, or screams. As previously discussed, nightmares are reported to occur in both NREM [19,25] and REM sleep [9,10,21].

5) **Disruptive nocturnal behaviors**.
   a) Gross body movements described as thrashing and tossing about are frequently described [21,30]. In our initial case series, we described self-reported symptoms of frankly combative behaviors such as striking at or choking of the bed partner [5] which are more purposeful and consistent with DEB. The occurrence of nightmares and DNB in a monitored setting is rare and reported to take place only in close temporal proximity to the trauma. A potential reason for a lack of nightmares and DEB in the laboratory environment was first suggested by Fisher et al. who postulated that another person, in the vicinity
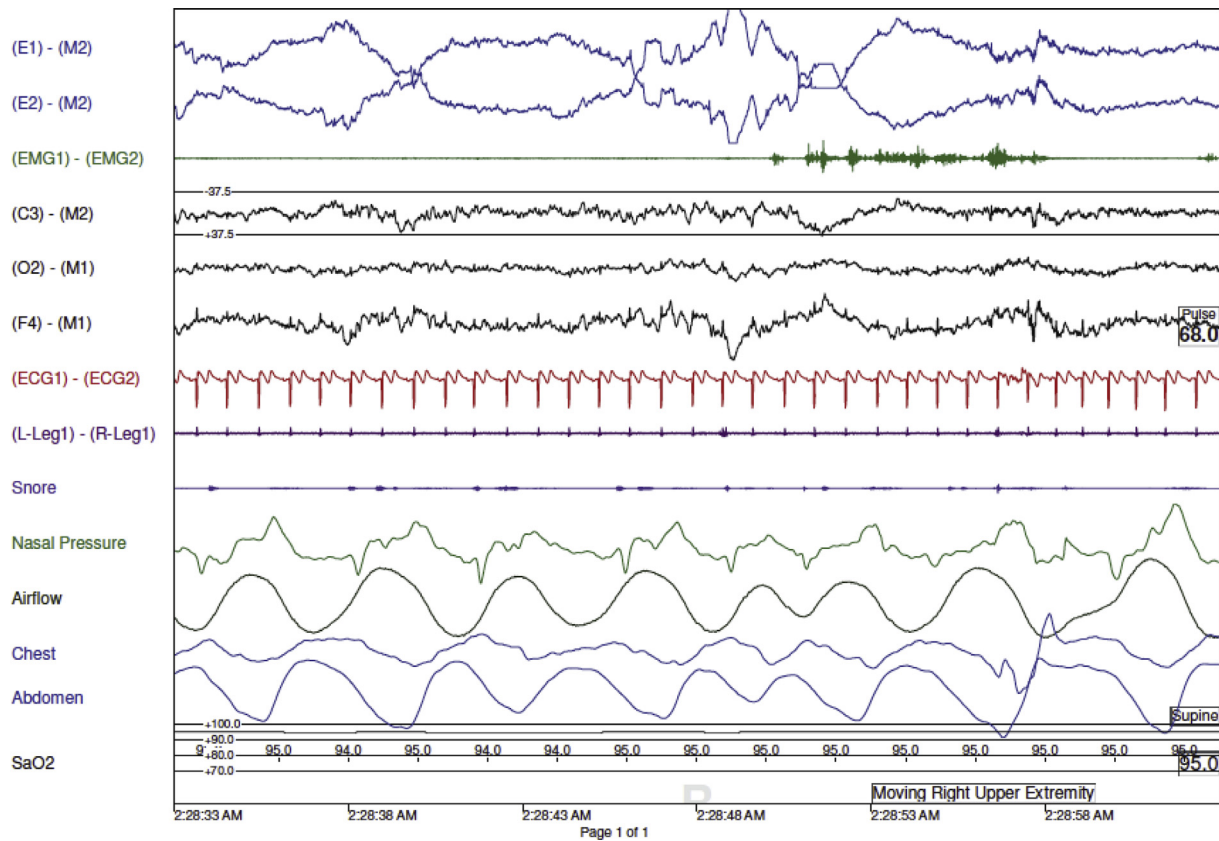
Fig. 2. A 30-s epoch of rapid eye movement (REM) sleep in a 37-year-old male with posttraumatic stress disorder and chronic insomnia who presented with frequent combat-related nightmares and disruptive nocturnal behaviors. He reported symptoms of tachycardia, tachypnea, and night sweats as well as awakening from his nightmares with purposeful movements. His symptoms dated to 2006 after returning from a combat deployment to Iraq with a recrudescence in the two preceding years due to increased stress. The epoch is unambiguous REM with rapid eye movements and initially, atonia in the chin electromyogram (EMG) leads. There is increased EMG tone during the latter half of the epoch corresponding with semi-purposeful right upper extremity movements. His polysomnogram (PSG) was otherwise essentially normal except for decreased N3. At the time of the study, he was not taking any antidepressant medications. Based on the patient's symptoms and PSG findings he was diagnosed with TSD.

of the patient, might reduce the probability of a nightmare [41]. In the cases documented in sleep labs, the DEB was purposeful and has ranged from defensive posturing to escape from the sleep lab [5,10].

b) Vocalizations ranging from grunting and groaning to yelling out and frank screaming are reported [5,19,21]. The vocalizations are usually related to nightmare content and may at times be repetitive with little night-to-night variability.

6) **Sympathetic activation**. Tachycardia, tachypnea [30], and night sweats are symptoms frequently reported in patients with TSD. Induced arousals during NREM sleep in veterans with disturbed dreaming have been reported to result in excessive physiologic activation. In our index case who had DNB associated with a nightmare, there was marked tachycardia and tachypnea [5]. Similar findings were reported by Schlosberg and Mellman [19,30]. However, sympathetic activation is relatively non-specific and can be found with other disorders to include OSA, which is frequently comorbid with TSD [5] and PTSD [42].

7) **REM sleep without atonia**. During PSG, there appears to be increased phasic EMG abnormalities during REM. Yet, based on the available literature, this appears variable and potentially focused during periods when nightmares are occurring (Fig. 1). During the initial case we reported with DNB in REM, the patient had profound RWA, but otherwise did not have an abnormal amount of RWA using the Sleep Innsbruck Barcelona criteria for the "any" mentalis EMG activity. This

contrasts with two of the other patients we reported who had a higher percentage of RWA, but no DNB on PSG. It is currently unknown if patients with TSD have a pathologic increase in RWA or primarily focal periods of RWA associated with nightmares or DNB.

8) **Comorbid sleep disorders**. Insomnia and OSA appear to occur frequently with TSD. As reported by Schlosberg and Benjamin [19], the sleep of soldiers was severely disrupted, consistent with insomnia. Similar findings have been reported by multiple authors, noting that insomnia is reported in up to 74% of combat veterans with PTSD symptoms and nightmares [43]. Similarly, there appears to be an association with OSA, noting that in patients with PTSD, 50—60% assessed for sleep disordered breathing will meet criteria for this disorder [42].

9) **Comorbid PTSD**. PTSD appears to frequently co-occur with TSD. However, in our initial report of TSD, only one of the four patients was diagnosed with this disorder.

10) **Efficacy of prazosin**. Prazosin, an alpha-1-adrenergic receptor antagonist which is active in the brain, has demonstrated efficacy in reducing nightmares in veterans with PTSD [6]. In subsequent studies by Raskind et al. prazosin decreased the frequency and intensity of nightmares, and improved PTSD symptoms and overall sleep quality [44,45]. However, the majority of patients continued to experience substantial residual PTSD symptoms. Conversely, in a study of veterans with PTSD and comorbid alcohol dependence, prazosin did not demonstrate any improvement in either PTSD or sleep

symptoms compared to placebo [46]. There was a significant effect, whereby both PTSD and sleep symptoms improved over time independent of prazosin treatment. While limited, it has been our clinical experience that prazosin is efficacious in ameliorating the symptoms of TSD.

11) **Clinical course**. In TSD, the clinical severity appears to be most intense early in the disorder with nightmares and DNB occurring frequently (i.e., 5–7 nights per week and sometimes more than once nightly). While nightmares and DNB persist, their frequency and severity tends to diminish over time. Specifically, the frequency of nocturnal symptoms appears to decrease 2–3 y into the course of the illness, with less frequent nightmares and DNB. Engdahl et al. evaluated 59 elderly males with and without PTSD who were in combat 28–50 y prior to their evaluation [47]. Those with PTSD had a significant increase in REM sleep and decreased arousals from NREM sleep; otherwise the sleep was similar between the groups. The authors concluded that the initial sleep disturbances experienced by the combat survivors diminished over time. It is likely that TSD follows a similar course.

Differentiating TSD from other sleep disorders

TSD fulfills the essential criteria of a parasomnia as defined in the International classification of sleep disorders 3rd edition as it encompasses abnormal dreams, sleep-related movements, behaviors, and autonomic nervous system activity that are not better explained by another clinical disorder [2]. The clinical features of TSD overlap to some degree with the current parasomnias of RBD and nightmares. However, TSD has unique features which distinguish it from these parasomnias. The relatively acute onset of DNB and nightmares in close temporal proximity to trauma is not consistent with the usual presentation of RBD [19]. While stressful situations (robbery, fraud, cancer diagnosis, surgical procedure) have been associated with the onset of idiopathic RBD (IRBD), these patients did not have clinical features that otherwise differed from the rest of the IRBD cohort (based on personal communication with the author) [48]. Additionally, the sympathetic overdrive that is observed during REM sleep in TSD appears to be relatively specific to this disorder. The most notable distinction between patients with nightmare disorder and TSD is the occurrence of excessive movements and at times, complex motor behaviors [2]. Additionally, nightmares in TSD appear to occur in both NREM [25] and REM sleep [24] and in some cases of TSD, patients do not recall their nightmares. The nightmares of TSD are TRN, which can vary in their dream content and can be classified as replicative/replay, non-replicative/symbolic, or mixed [49]. Combat survivors are likely to report replicative nightmares that consist of fairly accurate portrayals of prior traumatic events [21,49] which is characteristic of the nightmares reported in patients with TSD.

Differentiation of TSD from PTSD

The diagnostic criteria for PTSD include two specific sleep symptoms: repetitive and distressing dreams in which the content relates to the traumatic event(s), and insomnia [3]. While nightmares and insomnia are the most prevalent sleep disturbances reported by trauma-exposed adults with PTSD, other DNB are also commonly found when sleep habits and patterns are more thoroughly assessed. For instance, DNB, such as nocturnal panic attacks, night sweats, simple and complex vocalizations, and DEB that may or may not resemble actual events are far more frequent in trauma-exposed civilians and military samples than in the general population [4]. There are a number of reasons why TSD should be

recognized as a distinct parasomnia and not merely a severe variant of PTSD nightmares. Dream enactment behavior, which more than likely involves overriding the atonia of REM sleep, does not occur with nightmares, severe or otherwise. Whereas nightmares in PTSD have previously been ascribed different clinical characteristics to include injury to bed partners and movements, it is our contention that this would then constitute a separate sleep disorder, TSD. The other major reason is that patients with TSD do not necessarily have PTSD. TSD may indeed be comorbid with PTSD, but the prevalence of the co-occurrence of these two disorders is unknown. Failure to recognize that trauma can incite a singularly nocturnal disorder, with profound clinical symptoms, can result in continued speculation. Do trauma survivors truly have the nocturnal symptoms they report? Providers may mistakenly believe these are transient symptoms or a *forme fruste* of PTSD and thus not address what is a significant sleep disorder. Since an in-depth clinical sleep-focused interview and in-lab sleep evaluation are not regularly included in the evaluation of trauma patients (and conversely, trauma evaluation in sleep patients), assessment and treatment planning can be suboptimal for individuals who present with symptoms of TSD. For instance, prazosin or imagery rehearsal therapy can be effective for PTSD-related nightmares, but their efficacy for TSD is unknown. While there is little information regarding the benefits or risks of first-line PTSD psychological or pharmacological treatments on TSD, there are other treatment aspects of TSD which should be addressed. Specifically, patients with DNB and DEB, which potentially pose a hazard to themselves or their bed partner, should have instructions on safe sleeping practices which are not part of the usual treatment regimen of PTSD.

Clinical conclusion

There are multiple sleep disorders which develop after traumatic experiences; TSD is the extreme nocturnal manifestation of traumatic experiences, encompassing nightmares, DNB, and comorbid insomnia. While TSD is relatively recently proposed, the unique presentation of this parasomnia has long been described. Clinical recognition of this sleep disorder is essential so that affected patients can seek diagnosis, treatment, and counseling. The requirement for counseling regarding a safe sleeping environment is critical for the patient and their bed partner. In order to better characterize TSD, and posttraumatic sleep disorders, there is a dire need for a systematic approach. The emerging study of RWA with microepochs and automated scoring is required to establish if atonia is substantially altered throughout REM sleep or only during nightmares. Chronological evaluations will prove essential to determine if the symptoms of TSD are worse in temporal proximity to the traumatic experience or are persistent. Treatment regimens for TSD will prove challenging and require a multidisciplinary approach, as patients frequently have comorbid OSA and PTSD.

Developing a neurobiological hypothesis of TSD

The neurobiological correlates of TSD remain largely unexplored [50]. However, the growing body of pre-clinical and clinical research on trauma and PTSD provides insight into how traumatic experiences and disrupted sleep may trigger TSD. Ross and colleagues originally described sleep disturbances, with an emphasis on REM sleep disturbances and nightmares, as the hallmark of PTSD [9]. There is now substantial evidence that both REM and NREM sleep are dysregulated following trauma (see review by Germain et al.) [51]. Despite occurring in NREM sleep [30], nightmares are conceptualized as exclusively REM phenomena [2]. Based on clinical findings, the characteristic features of TSD, including RWA, appear to occur primarily during REM [5].

Neurobiological correlates of dreaming and nightmares

Despite the distressing content of nightmares, autonomic activation, as measured by heart rate and respiratory rate, is low or absent during a nightmare [52]. Based on the less than expected sympathetic activity during nightmares, Fisher and colleagues postulated REM dreaming possessed a mechanism for modulating anxiety and "desomatizing the physiologic response to it" in order to help master traumatic experiences [41]. Along these lines, a recent neurocognitive model for nightmares proposed by Nielsen et al. suggests the purpose of dreaming is to facilitate fear memory extinction. During normal dreaming there are four regions of the brain [amygdala, medial pre-frontal cortex (mPFC), hippocampus complex, and anterior cingulate cortex (ACC)] that operate in a coordinated manner to control emotional processes [17]. With increasing levels of stress there is dysfunction in this interactive network and a spectrum of dream related disturbances can ensue.

Neurobiological substrates of TSD

The psychological stress of trauma leads to metabolic and structural changes in the brain [53]. Recent research utilizing functional neuroimaging has explored volumetric changes and cerebral blood flow patterns during wake and sleep in response to traumatic experiences [50,51,54]. Many of the changes occur in structures responsible for REM sleep, dreaming, and nightmares with potential implications for the clinical manifestations of TSD.

Amygdala

The amygdala is critical in dreaming and nightmare models [50,51,54], with increased activity during REM sleep [55,56]. In response to fear and anxiety, amygdalar projections cause physiologic changes to include sympathetic nervous system activation and modulation of heart rate, blood pressure, and respiratory rate [57–59].

Fear results in norepinephrine (NE) and serotonin release on motor neurons via amygdala activation of the locus coeruleus (LC) and pontine raphe nuclei respectively, enhancing motor activity which may contribute to RWA in TSD. Additionally, the amygdala has projections to the nucleus reticularis pontis caudalis involved in the fear startle reflex, and trigeminal and facial motor nuclei that may facilitate reflexive blinking, jaw movements, and facial expressions of fear. Based on animal studies, stimulation of the amygdala results in locomotor activity [60]; whereas, amygdala outputs to the striatum may mediate escape behavior [61] and projections to the central gray facilitate freezing and vocalizations in conditioned fear [58,62]. These findings provide a basis for the amygdala in generating DNB and vocalizations in patients with TSD. Functional neuroimaging in PTSD patients and controls with trauma related sleep disturbances demonstrates increased amygdalar activity and decreased volume [54]. Thus trauma exposure, even in the absence of PTSD, appears to cause amygdalar hyperactivity, which is likely critical in the neurobiology of TSD.

Other central nervous system structures

Hyperadrenergic function of the LC and peri-locus coeruleus characterizes PTSD and contributes to its pathology [30,63,64]. In patients with PTSD, central nervous system (CNS) alpha-1 adrenoreceptors may be hypersensitive to NE; stimulation of the adrenoreceptors fragments REM sleep and facilitates release of corticotropin-releasing hormone, promoting "fight or flight" processes [45,65]. The excessive adrenergic activity leads to hyperarousal and direct stimulation of motor neurons [66,67], creating a sleep state that is rich for the DNB, RWA, and sympathetic output characteristic of TSD.

Compared to wakefulness, the frontal lobes are relatively deactivated during REM and especially NREM sleep [50,55,68]. Therefore, sleep is inherently more susceptible to unopposed limbic system activity [55,68]. After sleep deprivation, the frontal lobes may be so deactivated that they are unable to inhibit the limbic system during sleep [69]. This may trigger violent or aggressive impulses [70] that manifest as the DNB component of TSD. The dorsal mPFC modulates activity in the subcortical limbic regions (i.e., the amygdala) during REM sleep and is critical for fear extinction [57,71]. Impairment or hypoactivity of the dorsal mPFC following trauma has been linked to the facilitation of nightmares and sleep disturbances [50,51].

There are several other CNS structures which are likely integral to the development of TSD. The hippocampus consolidates traumatic memories, the ACC modulates the amygdala and is involved in emotional reactivity to pain [17,72], and the insular cortex processes emotions and is involved in autonomic control [73]. Sleep disturbances and trauma result in volume loss in all of these structures [74–76] which can result in fear, REM sleep disruption, and TRN [68]. Increased activity of the precuneus is reported in PTSD patients; this can contribute to TSD symptoms by fostering re-experiencing of trauma during sleep as well as disrupting REM sleep [54,68]. The exact interplay of these and other CNS structures that contribute to the development of TSD requires further research.

Physiologic hyperarousal following trauma contributes to TSD

Stress and sleep disruption following trauma are closely associated with central and peripheral physiologic hyperarousal in humans [77,78]. Sinha expands upon this concept in his recent review of trauma-induced insomnia, noting "hyperarousal is not a unitary construct and may encompass symptoms with different underlying mechanisms" [79]. The hyperarousal model of insomnia is based on activation of central arousal centers with increased sympathetic activity through activation of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in physiologic arousal and sleep disruption. Hyperarousal following trauma likely differs and is exaggerated from the central hyperarousal encountered in insomnia, although there is overlap [71,79]. It appears that hyperarousal in TSD is likely a reflection of increased autonomic and limbic activity with dysfunctional processing of memories and emotions similar to PTSD [80], though occurring exclusively during sleep. Mellman et al. reported that in the acute posttraumatic period patients with and without PTSD had increased heart rate variability in REM sleep [81]. This suggests trauma exposure alone can cause peripheral sympathetic activation in REM (i.e., symptoms of tachycardia reported in TSD patients) [79,81]. Furthermore, hyperarousal is frequently episodic [33] and central hyperarousal in PTSD can actually be uncoupled from physiological activation. Specifically, despite generalized hyperarousal, PTSD patients do not necessarily manifest tachycardia in their sleep [82]. These findings offer one possible explanation why manifestations of hyperarousal are typically not observed in trauma victims undergoing polysomnography.

Sleep deprivation and disruption: priming factors for the development of TSD

Sleep deprivation or sleep disruption, especially when combined, are substrates for the development of TSD. Fear extinction is inhibited by sleep deprivation [83] and sleep disturbances play a key role in PTSD symptom development by disrupting sleep-

dependent affective and memory processing [71,84—86]. Sleep deprivation enhances neural response to negative stimuli by potentiating amygdala activation and decreasing activation of the mPFC. The mPFC regulates output from the amygdala in an inhibitory, top-down fashion which is critical for fear extinction and contextually appropriate emotional responses [51,87]. Further, sleep deprivation reduces the connectivity between the amygdala and the mPFC as well as the ACC, another key structure in the neurocognitive model for nightmares [87,88]. Conversely, sleep and primarily REM sleep, is associated with increased emotional memory consolidation, reduced anger and fear, and increased reactivity to positive stimuli. Central adrenergic activity is suppressed during REM and amygdala-hippocampal networks process and depotentiate prior experiences to reduce their emotional intensity [89,90]. Van der Helm and colleagues demonstrated "REM sleep physiology is associated with an overnight dissipation of amygdala activity in response to previous emotional experiences, altering functional-connectivity and reducing subsequent next-day subjective emotionality" [89]. The authors predict similar sleep-dependent downstream adaptive reductions in reactivity in the peripheral nervous system. These results offer insight into disorders in which amplified emotional reactivity and sleep disruption are comorbid, including TSD.

Disturbances in REM sleep are predicted to amplify emotional reactivity and compromise resilience [51]. In survivors of life-threatening experiences, those with sleep disturbances in REM were at higher risk for developing PTSD [91]. Individual variability in REM propensity and childhood exposure to stressors or trauma may impact REM physiology [51]. Insana et al. showed that REM sleep fragmentation in combat veterans was associated with adverse childhood experiences in addition to DNB as an adult [92]. Trauma, particularly at a young age, may disrupt REM sleep and subsequently potentiate fear and the risk of developing TSD. Though REM appears to mediate many of the effects of stress and trauma, animal and human studies support that the effects may not be limited to REM alone. Sleep, in general, appears to be directly involved in emotional and memory processes related to trauma and stressors [51]. This is consistent with observations that TSD symptoms are reported to occur in both REM and NREM sleep and with the hypothesis that REM and NREM mechanisms underlie the production of TRN [9,50,64,93].

Neurobiological hypothesis of TSD

We propose the interplay of extreme trauma and concurrent sleep deprivation or disturbance can incite measurable changes in the volume, activity, and function of CNS structures that are integral to dream processing and REM sleep, manifesting in the symptomatology of TSD. REM sleep, normally protective for depotentiating traumatic experiences, is disrupted in TSD patients. Multiple factors contribute to the alterations in REM including sleep deprivation and hyperarousal from trauma; these factors lead to hyperactivity of the amygdala during REM. Frontal lobe activity, already reduced in REM, is further impaired in TSD by sleep deprivation and comorbid insomnia, increasing the potential for violent or aggressive behavior. In particular, there is a blunted increase in the activity of the mPFC, which regulates the amygdala. The combination of these changes results in fear and many accompanying downstream effects including increased neuroendocrine activity (via direct stimulation of the HPA axis by the amygdala) that perpetuates hyperarousal in sleep as well as physical expressions of fear (DNB, vocalizations, facial expressions of fear, startle reflex, etc.). The state of hyperarousal present in TSD is further compounded by direct amygdalar stimulation of brainstem REM-off nuclei including the LC, resulting in increased adrenergic activity and the "fight or flight" sympathetic response which has been observed in TSD patients. Additionally, excessive NE release by the LC inhibits REM-on nuclei such as the laterodorsal tegmental and pedunculopontine tegmental nuclei, which may cause RWA and further fragmentation of REM sleep. Trauma also results in dysfunction of other CNS structures including the precuneus and limbic structures such as the hippocampus, ACC, and insula, further contributing to REM sleep disruption and nightmare generation. The clinical manifestations of TSD likely result from the combination of these neurobiological changes, along with others that are not yet discovered or fully elucidated.

Practice points

1) Trauma associated sleep disorder is a unique parasomnia incited by extreme trauma and sleep deprivation or disturbance that negatively impacts the sleep quality of the patient and bed partner.
2) While disruptive nocturnal behaviors are frequently reported in patients with trauma associated sleep disorder, they are rarely captured during polysomnography.
3) Hyperarousal during sleep underlies the clinical manifestations of trauma associated sleep disorder.

Research agenda

1) Standardized sleep assessments including both validated instruments and sleep studies are essential to characterize and better differentiate the sleep disorders (insomnia, nightmares, and trauma associated sleep disorder) that develop in trauma survivors.
2) Randomized controlled studies to determine the optimal pharmacologic management of the nightmares and disruptive nocturnal behaviors of trauma associated sleep disorder are required.
3) Investigations into the early recognition and treatment of sleep disturbances and nightmares that develop in temporal proximity to trauma as a novel approach to potentially prevent the development of trauma associated sleep disorder.

Conflict of interest

The authors do not have any conflicts of interest to report.

Disclosure statement

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