The Extreme Nocturnal Manifestation of Trauma: Trauma Associated Sleep Disorder

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Illustrative Case of TSD

A 31-year-old active duty soldier presented with a 10-year history of restless sleep and disturbing nightmares occurring three to four times per week. He reluctantly discussed the content of his nightmares which involved experiences from his first deployment to Iraq. During his deployment, he had multiple prolonged missions without sleep. His combat-related nightmares primarily related to his duties as a medic when he encountered mutilated bodies and ensured enemy combatants were killed. Other nightmares involved life-threatening situations he experienced; however, in his nightmare he would not survive. The patient's wife reported he frequently acted out his dreams with violent punching, slapping, rolling, and kicking that have injured her on multiple occasions. During some of his nightmares, he vocalized with sounds ranging from crying out to panicked or angry speech related to his combat experiences. His past medical history was notable for PTSD that is treated with bupropion, and he suffers from daytime symptoms including flashbacks and visual hallucinations of enemy snipers or roadside bombs. Diagnostic polysomnography revealed a reduced sleep efficiency (77%), increased arousal index (25/h), and REM without atonia associated with thrashing body movements and increases in heart rate. He was diagnosed with trauma associated sleep disorder (TSD). Treatment with 10 mg of nightly prazosin and imagery rehearsal therapy decreased nightmare frequency (less than once per week) without changing nightmare severity. His disruptive nocturnal behaviors persisted.

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Introduction

Sleep disturbances are frequent following a traumatic experience [1, 2]. Ross and colleagues originally described sleep disturbances, with an emphasis on REM sleep disturbances and nightmares, as the hallmark of posttraumatic stress disorder (PTSD) [3]. There is now substantial evidence that both REM and NREM sleep are dysregulated following trauma [4]. Additionally, a variety of sleep disturbances arise in trauma survivors with and without PTSD including insomnia, trauma-related nightmares (TRN), autonomic hyperarousal, and disruptive nocturnal behaviors (DNB) consisting of dream enactment, vocalizations, and complex motor behaviors [3, 5–10]. Many of these disturbances, such as TRN or trauma-induced insomnia, do not conform to currently accepted sleep disorders; however, they are sometimes recognized as distinct nosological entities with novel neurobiological models [5]. More often, patients who present with the symptoms of posttraumatic nightmares and DNB are considered to have symptoms of PTSD or variants of existing sleep disorders such as nightmare disorder or REM sleep behavior disorder (RBD) [11, 12]. For these reasons, and because TRN and DNB are rarely captured during polysomnography, these posttraumatic sleep disturbances remain relatively poorly characterized [6].

Trauma associated sleep disorder (TSD) is a proposed parasomnia that encompasses the TRN, sympathetic activation, and DNB occurring during sleep in patients following trauma [13]. Though TSD may be associated with PTSD in some (but not all cases), its symptomatology is confined to sleep. Clinical features of TSD differentiate it from other sleep disorders, including established parasomnias. This chapter will discuss the clinical characteristics of TSD and distinguish it as a unique sleep disorder. Historical findings consistent with TSD and potential neurobiological

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mechanisms of TSD will also be described. Recognition of TSD as a unique parasomnia that develops after trauma is critical to furthering our understanding of this disorder and developing effective therapies.

The onset of profound sleep disturbances after trauma has long been recognized. In their historical account of psychotraumatology, Crocq and Crocq [14] detail multiple distinct accounts of TRN and DNB. They noted the following in Lucretius' poem, De Rerum Natura, which was written in 50 BC (Book IV, translation William Ellery Leonard):

"Again, the minds of mortals …
Often in sleep will do and dare the same
In manner like. Kings take the towns by storm,
Succumb to capture, battle on the field,
Raise a wild cry as if their throats were cut
Even then and there. And many wrestle on
And groan with pains, and fill all regions round
With mighty cries and wild, as if then gnawed
By fangs of panther or of lion fierce.
Many amid their slumbers talk about Their mighty enterprises…
Many meet death; many, as if headlong
From lofty mountains tumbling down to earth
With all their frame, are frenzied in their fright;
And after sleep, as if still mad in mind,
They scarce come to…

This historical account details many of the characteristic features of TSD to include TRN, vocalizations, dream enactment behavior, and frequent lack of dream recall. Similar symptoms have long been reported and continue to be reported by trauma survivors and their bed partners; however, as noted such profound clinical manifestations are only rarely documented during PSG. Based on the existing literature, there are 11 cases to date that have PSG-documented abnormalities consistent with TSD (see Table 18.1). The reasons for this lack of documentation

Table 18.1 Previous cases of polysomnographic documentation of patients with findings consistent with TSD

Article	Patients consistent with TSD	Demographic	PSG findings	Self-reported DNB	Nightmare content
Mysliwiec et al. [13]	4 ($N = 4$)	Male soldiers (ages 22–34)	Patient 1: defensive limb movements and repeated vocalizations, "oh f***, leave me alone!" Sleep stage: REM All patients: RWA, phasic bursts	Patient 1: screaming and combative movements Patient 2: thrashing movements; episode of choking wife Patient 3: somnambulism, combative movements Patient 4: "screaming, crying, throwing pillows, and cursing" and witnessed punching/kicking wall with vocalization of "I am going to kill you"	Patient 1: assailants pursued and threatened him Patient 2: combat-related experiences Patient 3: flashbacks to combat environment Patient 4: related to personal relationship
Hefez [10]	2 ($N = 11$)	Male maritime disaster survivors (ages 20 and 25)	Patient 1: violent body movement and vocalizations; 2 reports of falling out of bed Sleep stage: REM Patient 2: REM-related motor activity and vocalizations Sleep stage: REM	None reported	Patient 1: reliving sea disaster Patient 2: nightmares related to disaster
Schlosberg and Benjamin [19]	3 ($N = 3$)	Male soldiers (ages 25–35)	Patient 1: "awoke particularly violently, jumping out of bed screaming and hallucinating" Sleep stage: N2 All patients: numerous body movements with RWA	None reported	All patients reported recurrent nightmares; descriptions not provided
Van der Kolk et al. [8]	2 ($N = 15$)	Male Vietnam veterans (ages not reported)	Patient 1: removed electrodes and walked around the room; later reporting thinking he was in an ambush Sleep stage: REM Patient 2: body movements and thrashing Sleep stage: REM	Reported body movements accompanying nightmares with occasional physical attacks on bed partners	Patient 1: thought he was in an ambush Patient 2: memory of being in gunfight; coming upon mutilated bodies

Abbreviations: *DNB* disruptive nocturnal behaviors, *PSG* polysomnogram, *RWA* REM without atonia, *TSD* trauma associated sleep disorder

remain speculative, with some suggesting that being watched/monitored while sleeping decreases nocturnal hyperarousal, which is likely part of the pathophysiologic mechanism for TSD.

Besides the patient's symptomatology and PSG, there is a clinical instrument which evaluates posttraumatic sleep disturbances. The Pittsburgh Sleep Quality Index Addendum (PSQI-A) assesses the DNB that occur in trauma survivors with and without PTSD [6]. This instrument was initially developed to evaluate DNB in patients with PTSD but is now recognized as a better measure of trauma-related sleep disturbances as opposed to PTSD [15]. One study assessed 375 combat veterans using the PSQI-A and reported 59.1% had a score of >4, consistent with PTSD [16]. Nightmares were one of the most frequent symptoms, and participants reported abnormal movements during sleep, potentially suggestive of TSD. More recently, Thordardottir et al. evaluated the sleep of avalanche survivors 16 years after the inciting trauma using the PSQI-A [2]. They reported that compared to matched controls, survivors who were children at the time of the trauma had increased DNB, whereas adult survivors had TRN. Based on the previous cases consistent with TSD, the reports using the PSQI-A, and our clinical experience, the following features of TSD are outlined below.

Clinical Features of TSD

There are distinct clinical characteristics that define TSD and differentiate it from existing sleep disorders. See Table 18.2 for the proposed diagnostic criteria for TSD:

Table 18.2 Proposed diagnostic criteria for TSD

1. Onset after combat or other traumatic experiences (often in the setting of sleep deprivation/disruption)
2. A history of altered dream mentation that is related to prior traumatic experience
3. Self- or witnessed reports of disruptive nocturnal behaviors 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 PSG monitoring demonstrates one of the following:
(a) Tachycardia
(b) Tachypnea
(c) Diaphoresis
(d) If documented on PSG, these findings are not due to sleep-disordered breathing
5. PSG may demonstrate:
(a) REM sleep without atonia (variable amounts of RWA)
(b) Dream enactment behavior in REM sleep
6. Absence of EEG epileptiform activity on PSG

Adapted from Mysliwiec et al. [13]; with permission

1. *Onset/precipitating factors*: Every previously described case that is consistent with TSD developed following a traumatic experience [8, 17, 18]. In most cases, combat was the inciting event [8, 13, 19], though maritime disasters have also been described [10] and exposure to natural disasters [2] or other traumatic experiences are a potential trigger. These experiences typically occurred under extreme duress and more than likely lasted for a prolonged period of time, suggesting that the traumatic experience must be extremely stressful to induce TSD. Sleep deprivation or disruption also appears to contribute to the onset of TSD [19]. Military personnel serving in combat are exposed to disrupted, insufficient sleep or total sleep deprivation [20], and sailors likely experience similar conditions. Notably, sleep after trauma exposure appears to decrease the intensity and frequency of traumatic memories [21]. After the inciting trauma, symptoms including nightmares and DNB typically develop relatively acutely, within weeks to months [10, 13, 19]. In some cases, nightmares of the traumatic experience may precede DNB, or repeated exposure to trauma is required to unmask DNB [13].
2. *Patient demographics*: In the majority of cases consistent with TSD, patients were young adult males [8, 10, 13, 17, 19]. This is likely due to increased combat exposure in males and under-recognition of TSD. To date, we have diagnosed TSD in two females, both of whom had substantial combat exposure. In the study by Thordardottir et al. [2], children ages 2–12 who had trauma exposure during their developmental years had more severe nocturnal symptoms (i.e., DNB) than adults. This finding suggests that the development of TSD in the pediatric population may not necessarily require concomitant sleep disturbance as this cohort likely had normal sleep prior to their traumatic exposure. Though further research is required, it is conceivable that TSD could develop at any age in individuals with trauma exposure and concurrent sleep disruption.
3. *Nightmares*: Patients with TSD suffer from nightmares that are related to their traumatic experience. Nightmare content varies depending on the nature of the trauma [22], but may include elements of death or dying, combat, and imminent threat to the patient's safety. Associated symptoms of anxiety, fear, or emotions felt at the time of the trauma may accompany the nightmare. Nightmares in TSD appear to occur primarily in REM sleep [3, 8, 10], but nightmares in NREM sleep [19, 23] have also been reported. The occurrence of nightmares in NREM sleep may account for the fact that some patients lack specific dream recall [24–26]. In those cases, the patient may vocalize or act out the dream, as reported by the bed partner, which results in the patient seeking clinical care.

4. *Disruptive nocturnal behaviors*: Perhaps the most distinctive characteristic of TSD is the DNB that can accompany TRN. These symptoms, often reported by the bed partner, range from gross body movements to vocalizations. Some patients have limb movements or thrash and toss about [8, 17], whereas others report more purposeful movements consistent with dream enactment behavior (DEB) including combative behaviors such as striking or choking a bed partner [13]. A smaller number of patients experience vocalizations ranging from grunts and groans to yelling out expletives and frank screaming [8, 13, 19]. In documented cases, vocalizations are often related to the content of the nightmare and may occur repeatedly. Unfortunately, the patient's nightmares and DNB that are reported to frequently occur in the habitual sleeping environment are difficult to characterize due to rare capture on PSG. One potential explanation for this phenomenon is that the monitored environment and presence of another person in the vicinity of the patient afford a feeling of safety which may reduce the probability of having a nightmare [27]. In the few cases that have documented DNB in the sleep lab, movements were typically purposeful and ranged from defensive posturing to escaping from the room [8, 10, 13, 19].
5. *Autonomic hyperarousal*: Symptoms consistent with sympathetic nervous system activation including tachycardia, tachypnea, and night sweats are common in patients with TSD. Similar findings have been reported acutely and chronically in combat veterans with and without PTSD [17, 19]. Stress and sleep disruption are closely associated with physiologic hyperarousal in humans [28]. The hyperarousal physiology likely results from specific trauma exposure, such as that experienced during combat [29]. In TSD, the hyperarousal is likely a reflection of increased autonomic and limbic activity with dysfunctional processing of memories and emotions similar to PTSD [30], though occurring exclusively during sleep. Relative tachycardia during REM sleep, which is associated with phasic RWA, is the most common finding of autonomic hyperactivity on PSG.
6. *REM sleep without atonia*: Patients with TSD have increased phasic EMG activity during REM sleep on PSG. Using the Sleep Innsbruck Barcelona criteria for "any" mentalis EMG activity [31], the amount of RWA may vary. It is suspected that the RWA coincides with the occurrence of nightmares with or without associated DNB. For this reason, the RWA may appear intermittently in REM with phasic bursts, and the overall "any" EMG activity may not be pathologically increased [13]. Figure 18.1 demonstrates a characteristic finding of RWA and DNB in a previously unreported patient with TSD.
7. *Associated illnesses and comorbid sleep disorders*: Posttraumatic stress disorder appears to frequently co-occur with TSD. Though trauma incites both disorders, they are distinct and can be mutually exclusive; only one of four patients with TSD had PTSD in our initial report [13]. Sleep disorders, including insomnia and obstructive sleep apnea (OSA), are also commonly comorbid with TSD. Multiple authors have reported insomnia in up to 74% of combat veterans with nightmares and symptoms of PTSD [19, 32]. Additionally, approximately half of patients with TSD have OSA, with the majority having mild sleep-disordered breathing. A similar association of OSA with PTSD has been posited, noting that in a review of sleep studies in PTSD patients, over half met clinical criteria for sleep-disordered breathing [33].
8. *Therapy*: Potential therapies for TSD should target the core symptoms of the parasomnia. Enhanced sympathetic activity may be counteracted using prazosin, an alpha-1 adrenergic receptor antagonist that is active in the central nervous system (CNS). This medication has been effective in reducing nightmares in veterans with PTSD [34] and the nightmares and DNB of patients suffering from TSD [13]. Imagery rehearsal therapy may also have a therapeutic role in TSD given its efficacy in treating nightmares [35], but this remains to be determined. Clonazepam, a medication effective in controlling movements in RBD [18, 36], does not appear to be effective in counteracting the DNB of TRN in combat veterans [37]. Counseling regarding a safe sleep environment is essential for both the patient and his/her bed partner. Further research is required to determine additional treatment options, but a multidisciplinary approach including pharmacotherapy and behavioral therapy will likely be required to address the spectrum of TSD symptomatology.
9. *Clinical course*: The nightmares and DNB of TSD appear to be most severe early in the disease course. In close proximity to the trauma (i.e., weeks to months), symptoms may occur nightly and sometimes more than once per night [13]. While nightmares and DNB persist over time, their frequency and severity tends to diminish. In a study of 59 elderly men with and without PTSD who had combat experiences 28–50 years prior to their evaluation, sleep was similar between the groups with the exception of increased REM sleep and decreased arousals in those with PTSD [38]. Notably, recrudescence of nightmare symptomatology can result from increased stress [39]. The clinical course of TSD likely follows a similar pattern, though longitudinal studies are required to determine the chronic nature of this disease.

Differentiating TSD from Established Parasomnias and Other Sleep Disorders

TSD has characteristics that overlap with other sleep disorders including the established REM parasomnias, RBD, and nightmare disorder. However, TSD has features that distinguish it from these diagnoses, and TSD fulfills the necessary

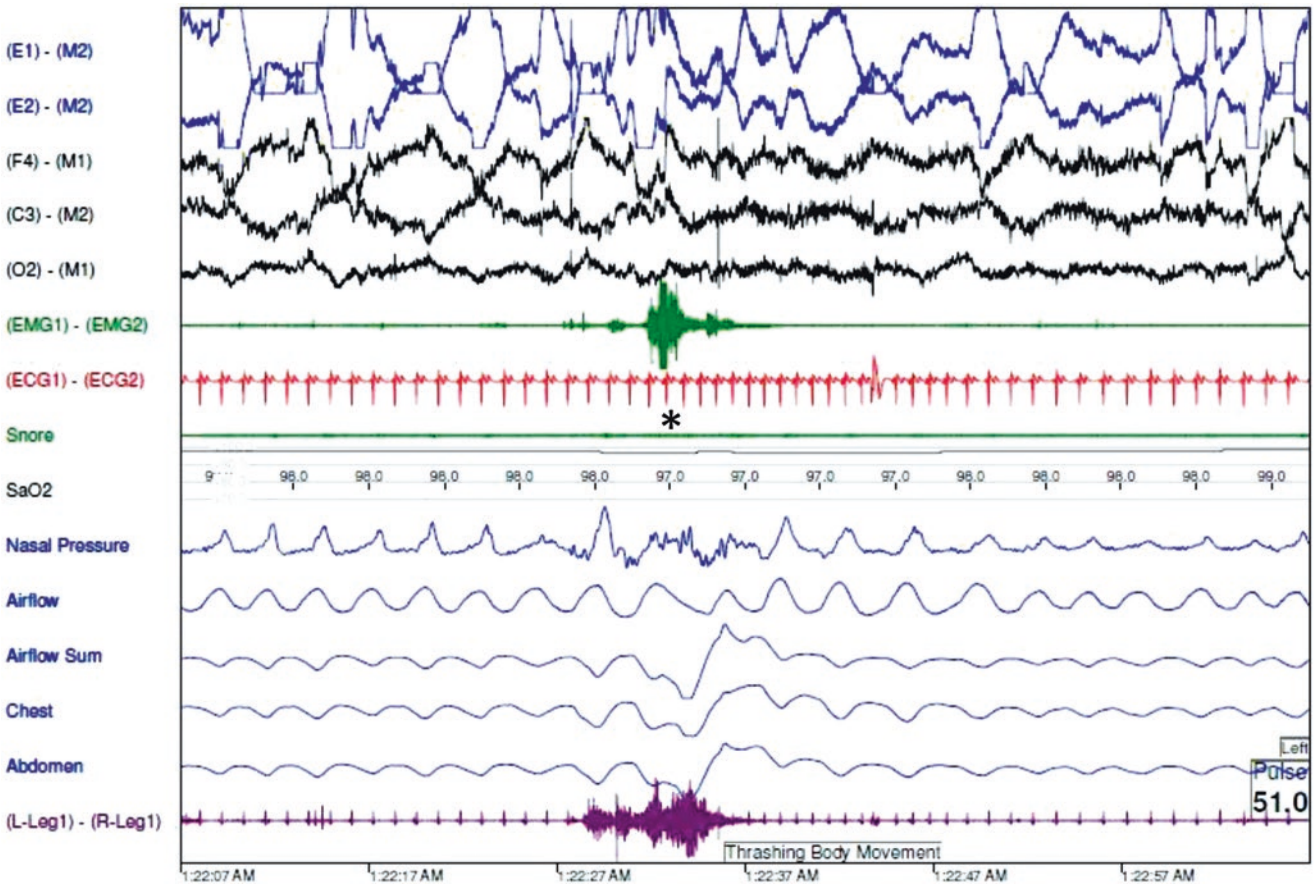

Fig. 18.1 Epoch of REM sleep depicting characteristic findings of TSD. A 60-s epoch of REM sleep in a 31-year-old male with posttraumatic stress disorder who presented with nightmares and disruptive nocturnal behaviors. These symptoms developed after deployment to Iraq. His nightmares occurred >3 times per week and entailed reenactments of combat. The nightmares were accompanied with thrashing and falling out of bed. His episodes of thrashing included slapping, kicking, and rolling into his spouse. The epoch demonstrates REM without atonia (*RWA*) with increased electromyogram (*EMG*) tone in the submental and left lower extremity corresponding with a thrashing body movement. A 15-beat increase in heart rate was associated with this event (onset at *). His PSG was otherwise normal except for multiple similar occurrences of RWA

criteria of a parasomnia with abnormal dreams, sleep-related movements and behaviors, and autonomic nervous system activity that are not better explained by another disorder [12]. Comparing and contrasting TSD with RBD and nightmare disorder bolsters its recognition as a distinct parasomnia (see Table 18.3).

REM Sleep Behavior Disorder

Vivid dreams with DNB, nightmares, and DEB that may be injurious are the presenting symptoms for RBD, and similar symptoms are present in patients with TSD [18, 36]. However, the relatively acute onset of DNB and nightmares in close temporal proximity to trauma is not consistent with the presentation of RBD [19]. There are reports of stressful situations such as being the victim of robbery or fraud, receiving a cancer diagnosis, or having a surgical procedure, which have been associated with the onset of idiopathic RBD (IRBD). Yet, these patients had clinical features which were otherwise consistent with IRBD [40]. RBD is associated with α-synucleinopathies, whereas TSD appears to have an association with PTSD [13, 41, 42]. Clinically, despite the report of frequent DNB by patients with TSD, it is rarely captured on PSG [6, 24, 43]. In contrast, DEB is frequently documented in RBD with two studies reporting a single PSG with video monitoring confirms the diagnosis of RBD in >80% of patients [40, 44]. Another distinguishing characteristic of TSD is the increased sympathetic output reported, most notably tachycardia [13, 19]. Conversely, even with vigorous DNB, there is a relative absence of autonomic activity in patients with RBD [36, 45]. In RBD, sleep quality is usually undisturbed, with 70% of patients reporting good sleep quality [40]. Disturbed sleep is present in all patients with TSD, with most patients meeting diagnostic criteria for insomnia. Regarding treatment, clonazepam, the drug of

Table 18.3 Characteristics of TSD compared to other parasomnias

Characteristics	TSD	RBD	Nightmare disorder
Onset/precipitating factors	Following traumatic experience Associated sleep deprivation or disturbance Rapid onset (weeks to months)	No specific precipitating factors Insidious onset	May be reactive to life stressors, but generally ubiquitous in general population Variable onset
Patient demographic (typical)	Young adults	Older males	May be seen in any age or gender
Nightmares	Related to prior trauma	Defense of sleeper against attack	Content may be stereotyped, but often random
Disruptive nocturnal behaviors	Gross body movements, defensive posturing Vocalizations Recorded in REM and NREM Rarely recorded in sleep lab	Dream enactment with combative, injurious behaviors Exclusive to REM Frequently recorded in sleep lab	Absent
Autonomic hyperarousal	Profound and concordant with dream content	Uncommon	Minor, even in highly disturbing dreams
REM sleep without atonia	Present, but "any" EMG index often normal	Present and "any" EMG activity index >18.2%	Absent
Associated illnesses	Posttraumatic stress disorder	Alpha synucleinopathies (Parkinson's disease, Lewy body dementia, multiple system atrophy) Narcolepsy	Anxiety PTSD Personality disorders
Comorbid sleep disorders	Insomnia and OSA frequent	Periodic limb movements	Insomnia
Therapy	Prazosin	Clonazepam Melatonin	Prazosin Imagery rehearsal therapy Lucid dreaming
Clinical course	Frequency and severity of symptoms diminish over time	Dependent upon underlying etiology, but typically slowly progressive	Frequency and severity of nightmares diminish over time

Abbreviations: *EMG* electromyogram, *OSA* obstructive sleep apnea, *PTSD* posttraumatic stress disorder, *RBD* REM sleep behavior disorder, *TSD* trauma associated sleep disorder

choice for RBD, does not have any efficacy in treating either the nightmares or DNB associated with TSD. In our experience, prazosin results in clinical improvement in >50% of patients with TSD.

The possibility that RBD could be precipitated by trauma was first posited by Husain et al. [46]. In their study of male veterans with ages ranging from 46 to 78 years, of 22 patients with PTSD, 15 also had RBD. The nightmare content of all 22 patients was trauma related. Notably, none of the patients with RBD had either Parkinson's disease or dementia with Lewy bodies. Dallam et al. conducted a retrospective review of elderly military veterans [47] and found 16 of 197 (8%) patients, all of whom had PTSD and dementia, reported war-related nocturnal vocalizations. Seven of their patients reported combative nocturnal behaviors. Another study assessed 12 patients with PTSD, 10 of whom had DEB [48]. In this study, phasic RWA on PSG was reported in 80%. The absence of a clinical course describing the onset of symptoms after trauma in these studies leaves open the question as to whether these patients initially had unrecognized TSD, although it appears more likely that the patients in these reports developed RBD with some incorporation of PTSD symptoms later in life.

Medication-associated RWA and cases of secondary RBD are reported with the use of antidepressants, specifically serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRI), and tricyclic antidepressants (TCA) [49, 50]. As with classic RBD, one study postulated that antidepressants may expose an impending neurodegenerative disorder [51]. Yet, there is a different hypothesis which is supported by more robust research suggesting that psychiatric disease itself may increase the risk of RBD independent of antidepressant usage [50]. Additionally, a recent study reported that while RWA was significantly increased in patients taking SSRI or SNRI, patients on these medications were not at increased risk for RBD [52]. In our initial report of TSD, two patients were taking SSRIs. Notably, in both cases, the patients reported DNB and nightmares prior to initiating therapy. In another study, which assessed combat veterans with an average age of 30 years, Wallace et al. reported four patients with RWA, DEB, and sleep-related injury. All of these patients were taking SSRIs and were classified as having secondary RBD [9]. Given their young age and symptom onset after combat exposure, it is possible these patients had TSD. Ultimately, the use of antidepressants, which is fre-

quent in trauma survivors, could confound or potentially exacerbate the underlying diagnosis of TSD.

Nightmare Disorder

Nightmare disorder is a REM-related parasomnia characterized by recurrent disturbing dreams that generally involve a threat to an individual's safety and often result in awakening with the ability to recall the nightmare's contents. Nightmares may be reactive to life stressors but are rather ubiquitous in the general population, affecting males and females of any age [12]. TSD is primarily distinguishable from nightmare disorder by the symptoms of excessive nocturnal movements and DNB, which do not occur with this established parasomnia. In nightmare disorder, autonomic hyperarousal is nearly always absent or at most minor, even in highly disturbing dreams [12]. This contrasts sharply with the profound sympathetic output experienced by TSD patients. Further, although nightmares in TSD are hypothesized to occur primarily in REM sleep [24], they have been reported in NREM [23]. An additional aspect is that TSD patients may not recall their nightmares; this finding has also been reported in PTSD patients with TRN [53]. However, as nightmares are a core symptom of TSD, a better understanding of this component of TSD is required.

Dream content can be classified as replicative/replay, non-replicative/symbolic, or mixed [53]. The nightmares of TSD tend to be replicative of the patient's traumatic experience. Studies evaluating combat veterans and survivors of World War II Japanese prison camps and the Holocaust indicate TRN can persist for more than 40 years [23, 25]. While nightmares tend to decrease in frequency and intensity over time, a study which evaluated Vietnam veterans demonstrated a relationship between the frequency of daytime stressors and increased nightmares as well as nightmare-related distress [39]. The clinical course of TSD is not yet well established; it is likely that the symptoms persist in a manner similar to the aforementioned studies on nightmares.

Other Sleep Disorders

There are several other disorders which may present with symptoms potentially suggestive of TSD. Severe OSA has been reported to mimic RBD with symptoms of DEB, nightmares, and vocalizations [54]. These patients were not reported to have RWA and sleep-disordered breathing preceded the onset of DNB. Further, treatment with CPAP resolved their RBD-like symptoms [54]. While some patients with TSD have OSA, we have not observed DNB emanating from arousals due to sleep-disordered breathing. Periodic limb movement disorder (PLM) is frequently reported in patients with PTSD, and the movements of either the arms or legs could be interpreted by a bed partner as DNB. In our experience, the palpable rage and graphic vocalization of TSD make it clinically distinguishable from PLM. Nocturnal epilepsy can present with DEB which are at times violent; however, the DNB in nocturnal epilepsy are stereotypical and an EEG would document epileptic activity [55]. Polysomnography, potentially on several nights, may be required to differentiate these sleep disorders from TSD. This could also acclimate the patient to the lab environment and potentially increase the likelihood of a patient exhibiting DNB.

Neurobiological Hypothesis of TSD

The neurobiological correlates of TSD remain largely unexplored [56]. However, the growing body of preclinical and clinical research on trauma and PTSD provides insight into how traumatic experiences and disrupted sleep may trigger TSD. The stress of trauma leads to metabolic and structural changes in the brain that can be demonstrated with functional neuroimaging [57, 58]. Sleep deprivation and disruption appear to be priming factors for these changes and the development of TSD.

There is substantial evidence that REM and NREM sleep are dysregulated following trauma (see review by Germain [4]), which is consistent with observations that TSD symptoms can occur in both REM and NREM [9, 50, 65]. However, disturbances in REM sleep physiology, in particular, appear crucial in the development of TSD. Additionally, the characteristic features of TSD, including phasic RWA, occur in REM. In trauma survivors, disturbed REM sleep portends a higher risk for developing PTSD [92] as resilience is compromised and emotional reactivity is amplified [51]. Individual variability in REM sleep propensity and childhood exposure to stressors or trauma may impact REM physiology [57]. Insana et al. showed in combat veterans that REM sleep fragmentation and DNB were associated with adverse childhood experiences [59]. Similar findings were reported by Thordardottir et al. who reported that childhood trauma exposure was associated with DNB later in life [2]. Thus, trauma, particularly at a young age, may affect the development of CNS structures that control REM sleep, particularly those responsible for atonia.

In normal sleep, neurons in the laterodorsal and pedunculopontine tegmental nuclei (LDT/PPT) excite neurons of the nucleus reticularis magnocellularis in the medulla, which in turn hyperpolarize spinal and brainstem motor neurons producing skeletal muscle atonia, a REM defining feature [60, 61]. Another characteristic of REM sleep is that sympathetic tone is markedly reduced [62, 63] as monoaminergic nuclei, including the locus coeruleus (LC) and dorsal

raphe (DR), are silent [64]. The suppression of central adrenergic neurotransmitters such as norepinephrine (NE) during REM "may be one of the most fundamental and functionally important aspects of this state" [65]. Monoamine nuclei inactivity also contributes to muscle atonia as NE and serotonin, the products of the LC and DR, respectively, excite motor neurons to increase muscle tone [66, 67]. Following trauma, hyperadrenergic activity can be visualized on functional neuroimaging as increased cerebral blood flow and hypermetabolism in the LC [7, 17, 58, 68]. Excess NE creates a nocturnal state of sympathetic hyperactivity that can cause symptoms of tachycardia and DNB as well as objective PSG findings of RWA that are characteristic of TSD [58, 69, 70].

Traumatic nightmares, a hallmark of TSD, likely occur during both NREM [17] and REM sleep, but are conceptualized as exclusively REM phenomena [12]. Despite the emotional and distressing content of nightmares, autonomic activation, as measured by heart rate and respiratory rate, is low or absent during a nightmare [71]. Based on the less than expected sympathetic activity during nightmares, Fisher and colleagues postulated dreaming possessed a mechanism for modulating anxiety and "desomatizing the physiologic response to it" in order to emotionally cope with traumatic experiences [27]. Along these lines, a recent neurocognitive model for nightmares proposed by Nielsen et al. [72] suggests the purpose of dreaming is to facilitate extinction of fearful memories. During normal dreaming there are four regions of the brain [amygdala, medial prefrontal cortex (mPFC), hippocampus complex, and anterior cingulate cortex (ACC)] that synergistically control emotional processes [72]. Stress precipitates dysfunction in this interactive network which can result in nightmares. Supporting this model is research demonstrating high activity levels in these structures during REM sleep and dreaming [73, 74]. Further, lesioning these structures or their connections results in frequent nightmares [75].

The amygdala is active during REM sleep and processes fearful experiences, decreasing their disturbing nature [73, 76–78]. Amygdalar projections are responsible for sympathetic nervous system activation leading to hyperarousal and abnormal motor activity during REM [79–81]. Additional projections to the trigeminal and facial motor nuclei facilitate fearful expressions, and connections with the nucleus reticularis pontis caudalis are involved in the startle reflex. Based on animal studies, stimulation of the amygdala results in locomotor activity [82], whereas amygdala outputs to the striatum may mediate escape behavior [83] and projections to the central gray facilitate freezing and vocalizations associated with fear [80, 84]. Trauma, especially when associated with sleep disturbances, increases amygdalar activity [58]. Increased output to its many projections substantiates the role of the amygdala in generating DNB and vocalizations in patients with TSD.

Sleep deprivation is hypothesized as a predisposing factor to the development of TSD in adults. Some CNS structures are uniquely vulnerable to the effects of sleep deprivation, and the associated dysfunction likely contributes to the development of TSD. The mPFC within the frontal lobes controls fear extinction during dreaming and regulates the amygdala [85]. Impairment of the dorsal mPFC following trauma is linked to nightmare generation. Additionally, sleep deprivation can contribute to nightmares by causing mPFC hypoactivity and increasing amygdala activation [56, 57]. Frontal lobe impairment results in an uninhibited limbic system that may trigger violent/aggressive impulses manifesting as DNB [86]. Another key structure in dreaming as well as the consolidation of memories is the hippocampus, which regulates fear expression and the extinction of fearful memories [87]. The ACC is integral in the neural circuitry of pain [88], including emotional pain [89], and likely mediates affect distress, whereas the insular cortex processes emotions and is involved in autonomic control [77]. Sleep deprivation/disturbances and trauma result in volume loss in all of these structures [90–92] which can result in persistent fear, REM sleep disruption, and TRN [74]. Innovative clinical and preclinical models are required to ferret out the effects of trauma on these CNS structures and their contribution to TSD [93].

Conclusion

Trauma and sleep deprivation/disturbance result in complex physiologic changes in CNS structures that are integral to dream processing and REM sleep. These changes result in autonomic hyperactivity and DNB, the defining characteristics of TSD. Current clinical guidelines do not suggest that sleep disturbances, most notably nightmares, should necessarily be considered a distinct disorder in patients with PTSD. TSD represents a unique parasomnia, distinct from PTSD as well as other established sleep disorders (i.e., parasomnias) based on etiological, clinical, and treatment-based responses. While both PTSD and TSD are incited by trauma, TSD is exclusively a nocturnal disorder. Trauma-related nightmares, which are found in up to 80% of patients with PTSD, transcend the established nightmare definition when they have autonomic hyperactivity and disruptive nocturnal behaviors to include REM without atonia. REM sleep behavior disorder which also has nightmares and dream enactment behaviors is not incited by trauma, nor does it have the symptoms of autonomic hyperactivity or disturbed sleep present in patients with TSD. Treatment regimens for PTSD typically consist of SSRIs and prazosin and clonazepam for RBD. The treatment of TSD remains anecdotal, with a lack of response to clonazepam but clinical improvement with prazosin, noting that RWA may be exacerbated by SSRIs.

Recognizing that TSD has these distinct features and classifying it as a unique parasomnia are paramount to treating the extreme nocturnal distress associated with this disorder.

To date the understanding of TSD is based on limited scientific literature. Given the frequent occurrence of sleep disturbances after trauma and their multifactorial nature, trauma survivors should be specifically asked about TRN and DNB. For those with symptoms suggestive of TSD, a clinical evaluation and PSG are recommended. This could facilitate characterization of this novel disorder to include aspects such as the occurrence of DNB during PSG and RWA. Longitudinal evaluation of patients is needed to thoroughly characterize symptom persistence and the impact of confounding variables such as medications, stress, or recurrent trauma. Therapeutic options for TSD are limited at this time, and randomized controlled trials are required to determine optimal pharmacologic and behavioral interventions. Additionally, understanding how sleep deprivation/disturbances in the peri-traumatic period contributes to the development of TSD may lead to policies that make sleep a priority in professions such as military service or first responders.

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