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SLEEP DISORDERS (P GEHRMAN, SECTION EDITOR)

Trauma Associated Sleep Disorder: Clinical Developments 5 Years After Discovery

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Abstract

Purpose of Review We review recent and growing evidence that provides support for a novel parasomnia, trauma associated sleep disorder (TASD). Based on these findings, we further develop the clinical and polysomnographic (PSG) characteristics of TASD. We also address factors that precipitate TASD, develop a differential diagnosis, discuss therapy, and propose future directions for research.

Recent Findings Nightmares, classically a REM phenomenon, are prevalent and underreported, even in individuals with trauma exposure. When specifically queried, trauma-related nightmares (TRN) are frequently associated with disruptive nocturnal behaviors (DNB), consistent with TASD. Capture of DNB in the lab is rare but ambulatory monitoring reveals dynamic autonomic concomitants associated with disturbed dreaming. TRN may be reported in NREM as well as REM sleep, though associated respiratory events may confound this finding. Further, dream content is more distressing in REM. Therapy for this complex disorder likely requires addressing not only the specific TASD components of TRN and DNB but comorbid sleep disorders.

Summary TASD is a unique parasomnia developing after trauma. Trauma-exposed individuals should be specifically asked about their sleep and if they have nightmares with or without DNB. Patients who report TRN warrant in-lab PSG as part of their evaluation.

Keywords Trauma associated sleep disorder · Trauma-related nightmares · Disruptive nocturnal behaviors · Nightmares

Introduction

Descriptions of disturbed sleep following trauma exposure date back millennia. Around 50 BC, in his poem De Rerum Natura, Lucretius described that "mortals…Often in sleep… take the towns by storm, Succumb to capture, battle on the field, Raise a wild cry as if their throats were cut…And many wrestle on And groan with pains…Many amid their slumbers…meet death…frenzied in their fright." [1] In Plutarch's *Parallel Lives*, probably written at the beginning of the second century AD, he describes the Roman general Gaius Marius at the end of his life suffering from "nightly terrors and harassing dreams… and flashbacks to previous battles." [2, 3] Descriptions of trauma-related nightmares (TRN) with disruptive nocturnal behaviors (DNB; e.g., combative motor behaviors, thrashing, vocalizations, defensive posturing) have been described in a Civil War soldier imprisoned at Andersonville [4], in descriptions of "combat exhaustion" after the World Wars [5], and in Holocaust survivors, with one concentration camp survivor reporting "Ever since the war is over, those things come back to me when I dream…people are after me…I used to dream and shout." [6] More recently, the Vietnam War and wars in Iraq and Afghanistan have led to intense research into the psychological aftermath of trauma. Descriptions from soldiers of TRN with associated DNB and

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sympathetic surges defied diagnostic criteria for existing parasomnias, leading to the proposal of trauma associated sleep disorder (TASD) as a unique REM-related parasomnia in 2014 [7••]. Since that time, a growing body of literature has expanded our understanding of TASD and further solidified it as a distinct disorder that can occur after combat or non-combat trauma exposure.

Clinical and Polysomnographic Features of TASD

The presentation of TASD can be variable and may depend on the nature of the inciting traumatic event and individual factors unique to the trauma survivor [8]. Table 1 lists the proposed diagnostic criteria for TASD. Until recently, there has been a relative paucity of objective PSG data on nightmares in trauma survivors because they are notoriously difficult to capture in the lab. In fact, lab studies of posttraumatic stress disorder (PTSD) patients capture nightmares on less than 1% of nights [9]. For this reason, subjective reports of the severity and frequency of sleep disturbances reported in trauma survivors far exceed the objective sleep disturbances measured in the lab [10, 11]. It has been postulated that the monitored lab environment imparts a sense of safety and disturbed sleep and nightmare frequency are therefore reduced [12•]. The low capture rate of nightmares and other DNB following trauma in the lab may be one reason for the delay in recognition of TASD as a distinct parasomnia. Despite this, new research is providing additional insight into the clinical characteristics and PSG findings of TASD and TRN.

Table 1 Diagnostic criteria for trauma associated sleep disorder (TASD)

Diagnostic criteria
Criteria A–E must be met
A. Onset of symptoms after combat or other traumatic experience
B. A history of altered dream mentation that is related to prior traumatic experience
C. Self or witnessed reports of disruptive nocturnal behaviors to include at least one of the following:
1. Abnormal vocalizations
a. Moaning, screaming, or yelling
2. Abnormal motor behaviors in sleep
a. Tossing, turning, or thrashing
b. Combative behaviors such as striking bedpartner
D. Symptoms of autonomic hyperarousal or PSG monitoring demonstrates one or more of the following associated with dream mentation:
1. Tachycardia
2. Tachypnea
3. Diaphoresis
E. There is an absence of EEG epileptiform activity on PSG and the disturbance is not better explained by another sleep disorder, mental disorder, medical disorder, medication, or substance use
Notes:
1. PSG may demonstrate:
a. Variable amounts of REM sleep without atonia
b. Dream enactment behavior in REM sleep
2. Onset is typically in close temporal proximity to trauma exposure, often in the setting of sleep deprivation/disruption
3. Patients with TASD frequently have comorbid insomnia and/or obstructive sleep apnea

Altered Dream Mentation Related to Prior Trauma

Nightmares in TASD develop after the inciting traumatic event and are typically related to the specific trauma the patient experienced. A recent report of a case of TASD by Feemster et al. described a veteran who reported nightmare themes which "involved dismantling cars hit by improvised explosive devices, gathering personal belongings of soldiers who had been killed, and witnessing several young soldiers sent into the field who never returned." [13•] This case is similar to our previous reports as dream content is related to multiple traumatic events experienced by the patient and typically includes elements of death, dying, violence, or threats to the safety and well-being of the patient or their colleagues [14–16, 17••]. In some cases of TASD, the patient has a lack of dream recall, and only when the bedpartner describes yelling, grunting, or other associated distress in the patient is the occurrence of TRN reported [7••, 18].

While nightmares are considered a REM parasomnia, TRN have been reported in both rapid eye movement (REM) and non-rapid eye movement (NREM) sleep [17••, 19, 20, 21•]. However, greater dream content recall and increased nightmare distress predominate from TRN preceded by REM sleep [21•]. Additionally, in the most recent report by Phelps et al., the majority of patients that reported DNB had sleep disordered breathing [17••]. Thus, it is unclear if the previous reports of NREM "nightmares" would fulfill the diagnostic criteria for this disorder, as the associated awakening could be from sleep disordered breathing. Clinically, these may be distinguished by the fact that nightmare-related awakenings are more often associated with vivid dream recall than awakenings from other causes such as sleep disordered breathing.

Disruptive Nocturnal Behaviors and REM Sleep Without Atonia

The most pronounced aspect of TASD are the DNB, which are often violent in nature. They consist of vocalizations such as moaning, cursing, or screaming and motor behaviors which can be combative or thrashing. Early reports of trauma survivors with symptoms consistent with TASD who were evaluated with PSG identified violent body movements, bursts of tachycardia, vocalizations, and elevated EMG tone in NREM and REM [19, 20, 22]. Mellman and colleagues recorded recurrent startle-panic awakenings with associated increase in heart rate and respiratory rate as well as thrashing, violent movements in Vietnam Veterans with PTSD [1, 23]. In the case described by Feemster, the patient had "violent sleep movements, yelling, or jerking in his sleep, about once or

twice per night." [13•] While these pronounced DNB did decrease over time, they persisted for many years but were not documented on PSG. Intriguingly, the amount of movement time during sleep in PTSD patients has been positively correlated with sleep efficiency [24, 25]. It has been postulated that increased movement may be protective against nocturnal panic to oppose a lack of movement or "freezing" motor response to fear [26, 27]. In TASD, when an event consisting of TRN and DNB occurs, motor and autonomic quiescence appear to be overridden by a state of central nervous system (CNS) hyperarousal. Briefly, trauma results in changes in the volume, activity, and function of multiple CNS structures, including hyperactivity of the amygdala that results in fear and many accompanying downstream effects [28•, 29]. Direct stimulation of the hypothalamic-pituitary-adrenal (HPA) axis by the amygdala perpetuates hyperarousal in sleep and can result in physical expressions of fear such as nocturnal vocalizations and DNB [30–33]. This is further compounded by hyperadrenergic activity of the locus coeruleus (LC) and peri-locus coeruleus that is observed in trauma-exposed individuals, promoting the "fight or flight" response described by TASD patients [18, 34, 35].

There is recent evidence that DNB consistent with TASD are in fact quite prevalent when specifically queried. In an evaluation of Vietnam Veterans with and without PTSD using the Mayo Questionnaire and self-report, Baird et al. found that 78% of veterans with PTSD and 11.8% without PTSD reported these symptoms [36•]. A potential reason why DNB are not more thoroughly evaluated is that they are rarely captured in the lab, which is likely due to the decreased nocturnal arousal patients experience in this monitored environment that they perceive as safe [17••, 21•, 37]. In an illustrative case, a 39-year-old female US soldier with previous deployments to Iraq and Afghanistan reported replicative TRN that consisted of mutilated bodies. On her in-lab video PSG, DNB consisting of kicking and vocalizations in conjunction with a TRN were captured (Video 1 in the Electronic Supplementary Material). Based on her symptoms and PSG findings, she was diagnosed with TASD.

In addition to DNB, phasic EMG abnormalities in REM can be seen on PSG in TASD patients. Previous reports have noted REM sleep without atonia (RWA) in TASD patients using "any" EMG activity index on mentalis EMG according to previously established methods by the SINBAR group [38] as well as the use of the montage described by the AASM Scoring Manual with the submentalis and anterior tibialis muscles [39, 40]. However, not all TASD patients have elevated "any" EMG activity, which may reflect that RWA is only present when the patient is experiencing a nightmare [7••]. Further studies are needed to create a unified scoring criterion for RWA observed in TASD [41] and to determine if RWA and DNB represent two points on a spectrum of motor pathology severity in TASD. Additionally, while the exact neurobiologic mechanisms for fulminant DNB, as opposed to RWA, have not yet been determined, findings of increased RWA in a patient with a history of trauma exposure should prompt a thorough investigation of the video PSG for DNB.

Autonomic Hyperarousal

Patients with TASD describe symptoms of increased sympathetic activation to include increased heart rate, rapid breathing, and night sweats [28•]. Disturbed dreaming has been linked to excessive physiologic activation [18] and studies on patients with PTSD have detected autonomic imbalance and heightened autonomic arousal in sleep by measuring heart rate variability [42–44]. Patients with PTSD who report nightmares may also demonstrate faster respiratory rates during sleep than those without nightmares [45]. In an early study on nightmares that were captured, Fisher et al. reported that nightmares arising from REM are anticipated by a gradual increase in anxiety, instability, and autonomic arousal including increasing heart rate prior to awakening [37]. It is, however, unclear if the participants in this study met criteria for PTSD [37]. Patients with PTSD have a higher resting heart rate and greater blood pressure reactivity during distress than non-PTSD patients [46]. Figure 1 is a 30-second epoch of REM sleep from a 24-year-old US Marine with TASD who experienced a TRN during an attended PSG. The epoch demonstrates a profound increase in heart rate preceding arousal from the nightmare with associated tachypnea. The patient suffered from his nightmares on a nightly basis after witnessing the aftermath of a bombing in Africa that claimed the lives of fellow service members. His autonomic surges were so distressing that he slept sitting up in bed so he could catch his breath upon awakening from his replicative nightmares. The epoch does not demonstrate the DNB he described occurring at home. Importantly, DNB can cause significant artifact and epochs containing DNB must be interpreted carefully in patients with TASD to avoid scoring an epoch of REM sleep as wake.

Recent reports found elevated heart rates occurring during or after nightmare awakening but not preceding the arousal [17••, 21•]. A potential reason for this is that the dream content may not have been as distressing as the TRN observed in TASD. Another possible explanation is that sleep disordered breathing was frequently associated with awakenings attributed to nightmares [17••]. Obstructive sleep apnea (OSA) is frequently comorbid with TASD [7••] and PTSD [47, 48]. Baird and colleagues reported increased rates of OSA in PTSD patients versus trauma-exposed controls and Miller et al. found that an elevated respiratory event index predicted morning endorsement of nightmares [36•, 49•]. Thus, respiratory events, rather than nightmares per se, may cause arousals not preceded by enhanced sympathetic activity. Regardless of when it occurs in relation to a nightmare, an increased heart rate and/or arousal in sleep may replicate the physiological

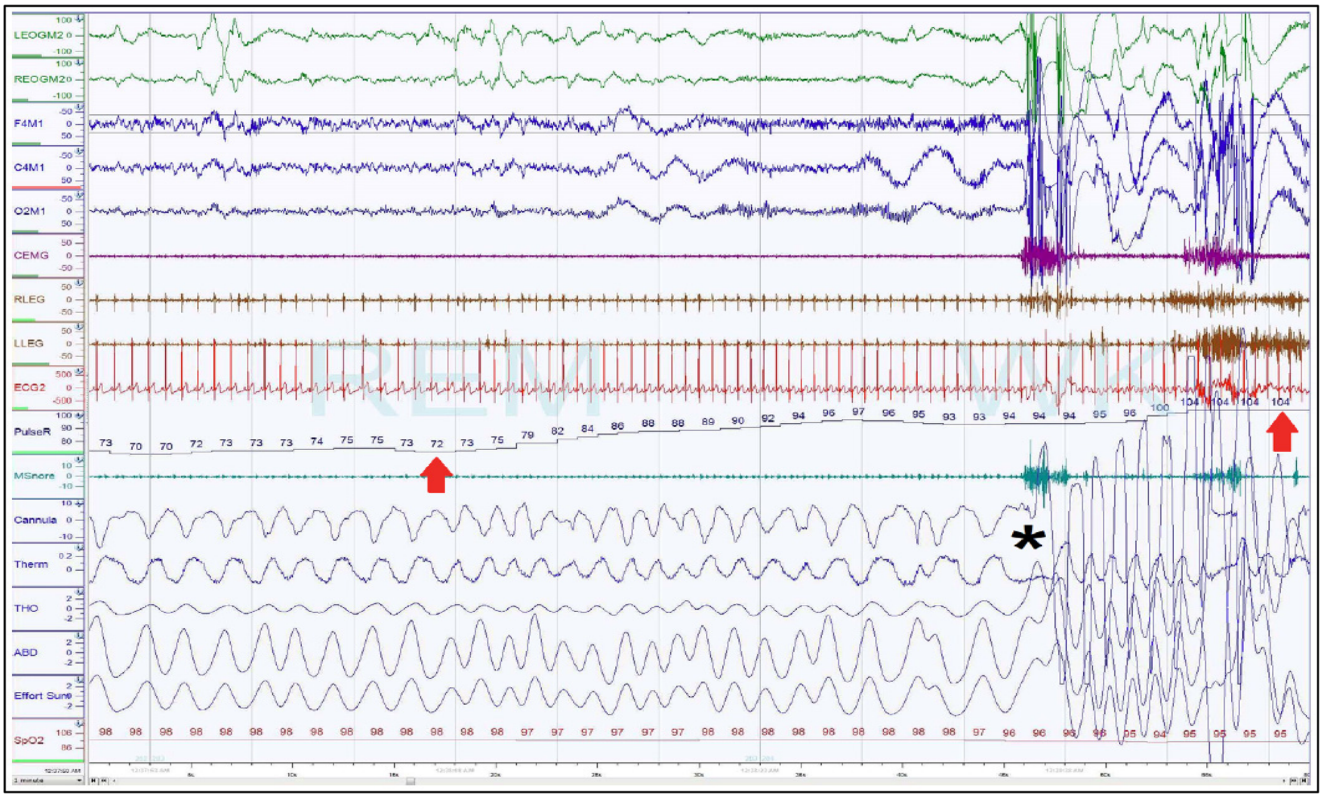

Fig. 1 Two 30-s epochs of sleep (REM then wake), in a 24-year-old, male, US Marine, capturing the autonomic hyperactivity that is characteristically associated with trauma-related nightmares (TRN) in patients with TASD. The epochs demonstrates a dramatic increase in heart rate (red arrows) prior to an abrupt arousal with associated tachypnea (asterisk). The patient described a replicative TRN involving the aftermath of a bombing with loss of life he witnessed during a tour in Africa

responses associated with the patient's trauma experience and activate the trauma memory network, including memories of the traumatic event [17••]. The finding by Miller et al. that a lower prior-night sleep respiratory sinus arrhythmia (a noninvasive index of parasympathetic tone) predicted morning endorsement of nightmare occurrence in patients with PTSD provides further evidence of nocturnal autonomic disturbance in these patients [49•]. While OSA does not necessarily appear to alter dream content [50], apneas and hypopneas can result in sympathetic activation, which can cause an increase in heart rate and arousal. The mechanism by which OSA is linked to nightmares, be it through sympathetic activation contributing to nightmare generation or enhanced nightmare recall due to an associated awakening with the arousal, or the co-occurrence of OSA and PTSD [51], is unknown. However, in patients with OSA and nightmares, positive airway pressure therapy treating the patient's OSA has been associated with decreased nightmare frequency [52, 53].

Additional PSG Findings in TASD

Studies reporting on other PSG variables in subjects with PTSD or DNB have been mixed, with some supporting no consistent objective findings [24, 54, 55] and others associating PTSD with increased REM sleep, increased REM density, increased N1 sleep, and reductions in slow wave sleep [56, 57], the latter two findings which result in a lower arousal threshold across the night. Reports on differences in quantitative EEG suggesting alterations in central arousal have also been inconsistent [58–60]. The variation in findings may be due to the heterogeneity of PTSD and trauma [27]. Another difficulty that arises in characterizing PSG variables in this patient population is the impact of pharmacotherapy on sleep, particularly antidepressants, which are prescribed to many trauma survivors.

In their cohort of PTSD patients with DNB, Phelps and colleagues reported increased sleep onset latency (SOL), wake after sleep onset (WASO), and REM latency and reduced sleep efficiency and overall REM percentage. In our study of nightmares in active duty military personnel, patients with nightmare disorder had longer SOL and REM latency on PSG than controls. Interestingly, those patients with DNB had significantly higher stage N3 percentage and lower WASO than subjects with nightmare disorder not related to trauma [12•]. This finding further supports the notion that TRN sufferers may sleep better in a monitored environment in which they feel safe.

Factors Precipitating TASD

Severity of Trauma

Symptoms of TASD develop in individuals after a traumatic experience. The onset of nightmares and DNB is typically within weeks to months of the inciting trauma [7••, 13•, 19, 22, 28•]. However, as most trauma-exposed individuals do not develop TASD, it is likely there are factors besides traumatic exposure itself which result in TASD. Most prominent of these features appears to be the nature of the traumatic experience. Neurocognitive models of nightmares have previously found that increasing trauma severity leads to more intense and replicative nightmares [61, 62]. Similarly, it appears that the development of TASD is associated with more personal and severe traumatic experiences. The majority of reports are in combat veterans [7••, 13•, 20, 22], which is likely related to the severity of their traumatic experiences. However, DNB and TRN, consistent with TASD, have been reported after other intense traumatic experiences including maritime disasters, sexual assault, and burn injuries [19, 63]. In contrast, college students who experienced an earthquake had more frequent earthquake-related nightmares, but the nightmares were only mild and without other features of TASD [64].

Sleep Deprivation and Disruption

It appears that suboptimal sleep, both duration and quality, preceding and following a traumatic experience contribute to the development of TASD. Acute and chronic sleep deprivation is inherent to military service, occurring during regular military duty in garrison and during deployment [3, 28•, 65]. Short sleep duration is common in the months following combat deployment, with one study showing 72% of redeploying soldiers sleeping less than 6 h per night (mean sleep duration 5.8 h) in the 6 months after returning [23]. Notably, the patient whose epoch of sleep is featured in Fig. 1 suffered from insufficient sleep at the time of his trauma in Africa and never achieved normal sleep before being deployed again to Afghanistan.

Sleep disruption and short sleep duration have been increasingly associated with the development of PTSD [23, 66, 67]. The relationship between sleep disturbance and PTSD symptoms appears to be bidirectional. A recent study by Kanady et al. demonstrated that "fear of sleep" after trauma is associated with reduced total sleep time as well as greater nightmare frequency and increased DNB. [68]. Chronic sleep deprivation is also well-recognized in military personnel with one study showing an average sleep duration of 6.3 h, a finding consistent across both previously deployed and non-deployed individuals [69]. The frequent and habitual disruption of sleep may be one of the reasons that TASD is more commonly reported in military personnel and veterans.

Poor sleep quality surrounding a traumatic experience likely contributes in a similar manner to the development of TASD. Recent studies support an elevated prevalence of OSA in military personnel and high comorbidity between TASD and sleep disordered breathing [7••, 65, 70]. Dysfunctional REM sleep may be the link between OSA and TASD. Supporting this idea is a study involving postpartum mothers, a population known to experience significant curtailment and fragmentation of sleep. In this study, the women interviewed endorsed an increased prevalence of dream associated motor activity compared to controls in the months following delivery (57% vs. 25%, $p < .001$) [71]. Prior traumatic experiences may potentiate this REM sleep dysfunction and increase the risk of developing TASD with subsequent trauma. This idea is supported by a report showing early-life trauma was associated with fragmented REM sleep in military veterans [72].

Specifically regarding cases consistent with TASD, Schlosberg et al. reported in their cohort that individuals who had suffered from sleep deprivation and disruption subsequently developed symptoms consistent with this parasomnia [22]. In their case series of acute combat fatigue patients, nightly sleep averaged only 129 to 150 min in the days preceding symptom development. The patients reported nightmares as well as PSG findings of "high EMG tone, numerous body movements, and bursts of tachycardia" suggestive of TASD. Although not explicitly reported, it is more than likely that these sleep disturbances were present in previous cases described in maritime disaster and Holocaust survivors [19]. Given the postulate that REM dreaming functions in normal emotional memory consolidation and stress adaptation, acute and chronic sleep curtailment likely impairs this adaptive response [14, 73, 74]. This concept is further supported by a study showing that sleep deprivation, specifically REM sleep, following viewing a traumatic film scene leads to more frequent and distressing trauma memories and anxiety [14, 75]. Improving sleep in the peri-traumatic period may reduce the likelihood of developing TASD.

Individual Factors

Factors specific to the trauma victim including genetic susceptibility and age at the time of trauma exposure may influence TASD development. Some individuals may be more prone to developing a pathologic response to trauma based on a genetic predilection [76, 77]. Family [78] and twin [79, 80] studies have identified an underlying genetic vulnerability for developing PTSD. Additionally, gene-environment interactions have been studied in PTSD patients with neurobiological abnormalities noted in genes regulating areas thought to be involved in the pathogenesis of TASD [28•] including the HPA axis [81], the Locus Coeruleus (LC)-Noradrenergic System [82], and various neurotransmitters involved in the Limbic-

Frontal System [83, 84]. In fact, it is estimated that more than 30% of the variance associated with PTSD is attributable to a heritable component [85, 86].

There is also evidence that a patient's age at the time of trauma exposure may impact the development of TASD. In a recent study by Thordardottir et al., age at the time of a trauma exposure led to differences in nocturnal symptoms [87•]. They found avalanche survivors who were children (ages 2–12) at the time of trauma exposure were significantly more likely to endorse dream enactment behavior than their non-exposed peers sixteen years later (relative risk 3.54). However, those who were adults at the time of the traumatic exposure reported increased nightmares associated with the trauma (relative risk 2.69) but no increase in dream enactment behavior [87•]. This provocative finding suggests that an immature brain may be particularly susceptible to the development of trauma-related motor pathologies.

Differential Diagnosis of TASD

TASD has been proposed as a mash-up disorder of PTSD and REM sleep behavior disorder (RBD) [13•]. The criteria of TASD include features from nightmare disorder, PTSD, and RBD; although when diagnostic criteria are applied, TASD is a distinct disorder. Nightmare disorder is a REM parasomnia defined by repeated, dysphoric, well-remembered dreams with an alert awakening from the dream and concomitant day or nighttime disturbances [88]. In TASD, the patient may experience a variety of distressing symptoms including DNB and autonomic surges without consistent dream recall [7••]. For patients without distinct dream recall, corroborating history from the bedpartner is critical in making the diagnosis. Nightmares are central to both TASD and PTSD and are considered the "hallmark of PTSD." [89] Dream content in both TASD and PTSD disorders is related to a prior traumatic experience [7••, 18]. However, whereas PTSD has symptom burden in both the wake and sleeping states, TASD is a parasomnia with symptomatology restricted to sleep. Additionally, cases of TASD have been described in patients without PTSD [7••]. Motor activity, to include "thrashing, violent movements," have been linked to PTSD nightmares [18, 90]; however, Woodward showed PTSD patients both with and without panic disorder had reduced movement time compared to controls [26]. The key distinguishing feature between nightmare disorder, PTSD nightmares, and TASD is the DNB and associated RWA observed in TASD [41]. Importantly, review of the video PSG is required to accurately characterize the findings [91, 92].

RBD is characterized by dream enactment behavior and RWA but has several distinctive differences from TASD. Predisposing factors for RBD include male gender, age 50 or greater, and an underlying neurological disorder, especially synucleinopathies [93]. While more longitudinal studies in TASD are needed, no reports to date, to include a 53-year-old patient with a > 10-year history of TASD, have shown progression to a neurogenerative disorder [13•]. Younger patients diagnosed with RBD have shown a more equal gender distribution as well as association with antidepressant use and autoimmune disorders in women [94]. However, while antidepressants can increase RWA, recent evidence does not support it causes DNB or increase the likelihood of diagnosing RBD [95]. Additionally, in patient reports with TASD, DNB predated the use of an antidepressant [28•]. Pseudo-RBD has been described in patients with OSA [96], which is frequently comorbid with TASD [7••]; however, multiple cases of TASD have described persistent complex motor behaviors in the setting of treated OSA, both in the laboratory and at home [13•, 28•].

One of the key distinguishing features of TASD is the onset of symptoms in close temporal proximity to a traumatic experience [19], as opposed to the onset in RBD that tends to be insidious. The majority of TASD cases are described in young male combat veterans, although as noted, TASD does occur in women. While combat appears to be the most common inciting event, previous cases have been reported after other traumatic events to include Holocaust survivors, sea disasters, and avalanches [20, 87•]. Dream content in TASD is related to the inciting trauma, unlike RBD in which dreams can be violent and distressful but not related to a specific event and can, in fact, be similar to dreams in the general population [97]. Lastly, clonazepam, a drug of choice for RBD [98], does not have any known efficacy in treating either the DNB or nightmares of TASD [7••].

Therapeutic Considerations for TASD

Evidence supporting pharmacologic treatment of TASD is limited and involves substantial extrapolation from TRN. In the initial TASD case series, prazosin led to improvement in both DNB and nightmares in all four patients, with two individuals experiencing return of DNB and TRN with discontinuation [7••]. Prior animal research has supported that trauma exposure may result in persistent nocturnal elevation in noradrenergic activity in the amygdala, potentially contributing to recurrent TRN [99]. Prazosin, a central-acting α-1 adrenergic receptor antagonist, likely blunts this pathologic noradrenergic response leading to a reduction in nightmare frequency. Initial studies of this medication for DNB were promising, with improvements in subjective sleep quality and nightmare frequency [90, 100].

However, the effectiveness of prazosin has recently been challenged in a placebo-controlled study by Raskind et al. who studied veterans with PTSD and frequent nightmares [101]. In this study, the authors found no significant difference in PTSD symptoms or nightmare frequency with prazosin compared to placebo. A potential reason the authors cited for this unexpected finding was that patients in the study were not

evaluated for OSA. Similarly, in the TASD case reported by Feemster et al., their patient also did not have improvement with prazosin [13•]. This patient was only titrated to 4 mg prior to discontinuation of prazosin and also had untreated OSA [13•]. Potentially supporting the premise that untreated OSA is a reason that patients may not respond to prazosin is that in the original TASD case series, patients received prazosin in combination with PAP therapy for their comorbid OSA [7••]. As previously mentioned, patients with TASD and PTSD have high rates of comorbid OSA. Further supporting the role of OSA treatment in the amelioration of TASD symptoms is a study by Tamanna et al. that reported treatment of OSA with PAP in PTSD patients decreased nightmare frequency [52]. In this study, for each 10% increase in PAP compliance, there was an associated decrease of one nightmare per week [52]. Unfortunately, PAP compliance in patients with PTSD is known to be poor [102]. The relationship between OSA and TASD is likely multifaceted with PAP therapy improving sleep quality, decreasing nocturnal noradrenergic output, and potentially normalizing REM sleep and dreaming.

Specific to TASD, prazosin may have a novel benefit in treating DNB. The noradrenergic output from the LC plays a complex inhibitory role in the pontine-originating REM atonia pathway and previous studies have shown abnormal LC neurons in individuals with PTSD [103–105]. Prazosin may normalize this noradrenergic input and restore appropriate REM sleep atonia. Additionally, we have previously suggested that there may be a unique TRN phenotype (i.e., TASD), characterized by noradrenergic hyperarousal on polysomnography, which is more likely to benefit from prazosin [92]. This is supported by a previous study of prazosin in PTSD which showed that a higher pretreatment blood pressure was associated with improved PTSD symptom response [106]. In our clinical practice, we continue to prescribe prazosin to our TASD patients with generally good results. Unfortunately, research supporting alternative pharmacotherapies is lacking. Melatonin, which has shown efficacy in RBD, is thought to support REM atonia through potentiation of spinal motor neuron inhibitory input. This mechanism could improve DNB, although in the report by Feemster et al. melatonin was also ineffective, but further study in TASD [107] is warranted [13•].

Non-pharmacologic treatment of TASD remains mostly speculative. Imagery rehearsal therapy for the treatment of TRN appears to be the most useful cognitive behavioral psychotherapy [108, 109]. The landmark study by Krakow et al. reported a reduction in nightmare frequency from 6 to 2 per week (vs. no change in controls) and improvement in CAPS PTSD scores from 81 to 49 (vs. 79 to 68 in controls) after 6 months of therapy [110]. Anecdotally, we find that TASD patients who are able to both report and visualize their nightmares are most likely to benefit from this form of therapy. Improving sleep duration and quality and addressing comorbid sleep disorders to include insomnia appears to be crucial in treating TASD. There is likely a distinct role for cognitive behavioral therapy for insomnia (CBT-I) in treating TASD as nearly all patients with this disorder have comorbid insomnia. In a recent study, individuals with PTSD treated with CBT-I reduced their "fear of sleep," an effect that persisted 6 months after therapy. This sleep disturbance, fear of sleep, appears to be specific to trauma and warrants attention given its association with greater nightmare frequency, DNB, PTSD severity, increased hypervigilance, and reduced total sleep time [68]. There is also recent evidence, albeit limited, that the combination of CBT-I and IRT can improve both sleep and PTSD symptoms to include TRN [111].

Conclusions

Trauma and disturbed sleep can lead to the development of TASD, a unique parasomnia that is distinct from the currently established parasomnias and PTSD. The TRN, DNB, and autonomic hyperactivity that are characteristic of TASD are frequently reported in survivors of traumatic experiences, but rare capture in the lab limits our understanding of this disease and its neurobiological underpinnings. Reducing the gap between subjective reports and objective evidence of TASD is paramount. As nightmares are infrequently self-reported, even in trauma survivors, all patients with a history of trauma should be queried about symptoms consistent with TASD. When TASD is suspected, a full clinical evaluation and PSG are recommended. As few objective PSG anomalies have been consistently reported after trauma, research using functional neuroimaging may be helpful in distinguishing sleep disturbances in this population by capturing subcortical metabolic and blood flow changes that can distinguish between healthy and clinical samples with poor sleep [112–114]. Neuroimaging will also be crucial in advancing the proposed neurobiological hypothesis of TASD [28•]. Perhaps of equal importance in understanding TASD is elucidating the genetic and epigenetic factors that may predispose an individual to develop this profound nocturnal disorder. Knowledge of the genetics of TASD and the neuronal pathways involved in symptom development and maintenance may lead to the development of preventative strategies in vulnerable individuals and guide targeted therapy.

DNB and nightmare severity tend to be more intense in close proximity to the inciting trauma; yet, persistent evidence of TASD has been observed more than 10 years after the inciting traumatic event [13•, 87•]. Further longitudinal studies are needed to fully elucidate the clinical course of TASD, including the impact of treatment, comorbid disorders, and recurrent trauma. Characterization of RWA in TASD is also needed, particularly in the absence of confounding factors such as medications. Studying patients with TASD in the home using video monitoring or on multiple consecutive

nights in the lab or at home may aid in capturing objective findings. In our experience, patients with TASD have increased symptomatology in the lab on the second or third consecutive night, possibly due to acclimatization to the lab environment.

To date, pharmacologic therapy for TASD has largely been confined to the use of prazosin to reduce the autonomic hyperactivity characteristic of this disorder. From our clinical experience, it appears that treating all the sleep disorders present concomitantly is what is required for an optimal therapeutic response. Further research is needed to determine which treatment regimen is ideal, be it pharmacologic, cognitive/behavioral, or in combination with PAP therapy in patients with comorbid OSA. Additional knowledge of how disturbed sleep or sleep deprivation at the time of trauma influences the development of TASD may also impact therapy as the restoration of sleep duration and quality following trauma is one potential preventative measure that could mitigate the development of this parasomnia.

Compliance with Ethical Standards

Disclaimer The opinions and assertions in this manuscript are those of the authors and do not represent those of the Department of the Air Force, Department of the Army, Department of Defense, or the US government.

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

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Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

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