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SCIENTIFIC INVESTIGATIONS

Sleep disturbances following traumatic brain injury are associated with poor neurobehavioral outcomes in US military service members and veterans

Cassandra L. Pattinson, PhD[1]; Tracey A. Brickell, DPsych[2,3,4,5,6,7]; Jason Bailie, PhD[2,6,8]; Lars Hungerford, PhD[2,6,9]; Sara. M. Lippa, PhD[3,4]; Louis M. French, PsyD[2,3,4,5]; Rael T. Lange, PhD[2,3,4,6,7,10]

[1]University of Queensland, Institute for Social Science Research, Brisbane, Queensland, Australia; [2]Defense and Veterans Brain Injury Center, Silver Spring, Maryland; [3]Walter Reed National Military Medical Center, Bethesda, Maryland; [4]National Intrepid Center of Excellence, Bethesda, Maryland; [5]Uniformed Services University of the Health Sciences, Bethesda, Maryland; [6]General Dynamics Information Technology, Falls Church, Virginia; [7]Centre of Excellence on Post-Traumatic Stress Disorder, Ottawa, Ontario, Canada; [8]Naval Hospital Camp Pendleton, Oceanside, California; [9]Naval Medical Center, San Diego, California; [10]University of British Columbia, Vancouver, Canada

Study Objectives: This study examined whether sleep disturbances were associated with neurobehavioral outcome following a traumatic brain injury (TBI) in a well characterized group of service members and veterans.

Methods: Six hundred and six participants were enrolled into the Defense and Veterans Brain Injury Center, 15-Year Longitudinal TBI study. All participants completed a battery of tests measuring self-reported sleep disturbances, neurobehavioral symptoms, and posttraumatic stress disorder symptoms. Data were analyzed using analysis of variance with post hoc comparisons. Four groups were analyzed separately: uncomplicated mild TBI; complicated mild, moderate, severe, or penetrating combined TBI; injured controls (ie, orthopedic or soft-tissue injury without TBI); and noninjured controls.

Results: A higher proportion of the mild TBI group reported moderate-severe sleep disturbances (66.5%) compared to the injured control group (54.9%), combined TBI (47.5%), and noninjured control groups (34.3%). Participants classified as having Poor Sleep had significantly worse scores on the majority of TBI-Quality of Life scales compared to those classified as having Good Sleep, regardless of TBI severity or the presence of TBI. There was a significant interaction between sleep disturbances and posttraumatic stress disorder. While sleep disturbances and posttraumatic stress disorder by themselves were significant factors associated with worse outcome, both factors combined resulted in worse outcome than either singularly.

Conclusions: Regardless of group (injured or noninjured control), sleep disturbances were common and were associated with significantly worse neurobehavioral functioning. When experienced concurrently with posttraumatic stress disorder, sleep disturbances pose significant burden to service members and veterans.

Keywords: TBI, military, veterans, sleep disturbances, posttraumatic stress disorder, PTSD

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Current evidence indicates that sleep disturbances are a significant problem following traumatic brain injury, particularly for service members and veterans. As such, this study sought to understand the effects of sleep disturbances following traumatic brain injury on neurobehavioral ratings in 606 service members and veterans.

Study Impact: This study reports that sleep disturbances are prevalent and debilitating. The results suggest that sleep disturbances are important to consider when assessing and treating neurobehavioral symptoms, especially in service member and veteran populations.

INTRODUCTION

Traumatic brain injuries (TBI) are prevalent in US military service members and veterans. The majority (~80%) of these injuries are typically classified as mild. Regardless of TBI severity, most people who sustain a TBI have good neurobehavioral recovery.[1] However, there is also a large minority who report a variety of negative health and psychosocial symptoms many weeks, months, or even years postinjury.[2,3] One of the most prevalent, debilitating, and persistent comorbidities following TBI is sleep disturbance.[4,5]

Sleep disturbances are estimated to occur in approximately 20–25% of service members and veterans.[6,7] These high rates of sleep disturbances may be exacerbated by a multitude of military-related factors, including shift work, stress of deployment, deployment across time zones,[8] and/or may be a direct consequence of TBI and/or posttraumatic stress disorder (PTSD). Indeed, the incidences of sleep disturbances increase significantly if military personnel and veterans are diagnosed with either co-occurring PTSD or TBI.[9] Sleep disturbances most commonly reported following TBI include a longer sleep onset, more frequent periods of wake after sleep onset, and shorter total sleep duration.[4,10] Furthermore, sleep disturbances that co-occur with TBI may be chronic and have been associated with prolonged recovery, increased risk of poor quality of life, declines in job performance, and may contribute to degradation of mental and physical health.[4,11–13]

Sleep disturbances are a clinical symptom of PTSD.[14] However, sleep disturbances are also a significant risk factor

for developing PTSD[15,16] and have been shown to affect PTSD maintenance and increase symptom severity.[17–19] Furthermore, sleep disturbances and PTSD individually have each been associated with poorer neurobehavioral functioning. A recent study from our research group reported that PTSD was a stronger predictor of neurobehavioral functioning than TBI (of all severities) alone.[1] Similarly, another study indicated that self-reported sleep disturbances partially mediated the association between increased PTSD and declines in cognitive outcomes in blast-exposed veterans.[20] As such, identifying the relative effect of sleep, TBI and PTSD, as well as the combination of these factors on neurobehavioral functioning in service members and veterans is vital.

The purpose of this study was to examine the association between sleep disturbance and neurobehavioral outcomes in a well characterized group of service members and veterans, 1–10 years post-TBI. There were 2 broad TBI groups examined; uncomplicated mild TBI (MTBI) and the combined TBI (CTBI) group comprising of complicated mild, moderate, severe, and penetrating. In addition, we also included 2 control groups of service members and veterans without a history of TBI, with or without a soft-tissue or orthopedic injury (ie, injured controls [IC] and noninjured controls [NIC], respectively). Furthermore, PTSD has been shown to be a strong predictor of neurobehavioral outcomes;[1] veterans with comorbid TBI and PTSD have been shown to report higher sleep disturbances.[9] As such, exploratory analysis was conducted to examine the effects of PTSD and sleep, singularly and combined, on neurobehavioral functioning.

METHODS

Participants

Participants were 606 US military service members and veterans prospectively enrolled in a larger study designed to examine the natural history of recovery from TBI (ie, 15-Year Longitudinal TBI Study, Defense and Veterans Brain Injury Center [DVBIC]: Sec721 NDAA FY2007). Participants were recruited into 4 broad groups: uncomplicated MTBI (n = 218); complicated mild, moderate, severe, and penetrating TBI (CTBI; n = 118); IC, n = 162); and NIC (n = 108).

Participants were targeted for recruitment using hospital-based and community-based recruitment strategies. Hospital-based strategies included recruitment from 3 US medical treatment facilities: Walter Reed National Military Medical Center, Naval Hospital Camp Pendleton, and Naval Medical Center San Diego. Recruitment sources included hospital inpatient wards, DVBIC outpatient TBI clinics, and other inpatient and outpatient TBI programs at these facilities. Community-based strategies included recruitment via a number of nationwide community outreach initiatives, such as attendance at military events (eg, Yellow-ribbon events), social media (eg, Facebook), and a third party posting/forwarding of flyers or business cards (eg, brain injury/military organization, acquaintance, DVBIC network).

Participants were enrolled in the study if they were male or female, 18 years of age or older, and able to read and understand English. Participants were excluded if they had a history of significant neurological or psychiatric conditions unrelated to the injury event or deployment (eg, meningioma, bipolar disorder).

Participants were included in 1 of the 2 TBI groups if they had sustained a brain injury as indicated by 1 or more of the following: 1) period of alteration of consciousness, loss of consciousness, or posttraumatic amnesia that was directly attributable to head trauma; 2) trauma-related intracranial abnormalities as indicated by neuroradiological scans; and/or 3) Glasgow Coma Scale < 15 (if available). Participants were included in the IC group if they had sustained an orthopedic and/or soft tissue injury; there was no evidence of intracranial abnormality or an altered state of consciousness (eg, Glasgow Coma Scale < 15, alteration of consciousness, loss of consciousness, or posttraumatic amnesia) as a result of the injury; the presenting complaint was not due to a neurological condition/disorder (eg, cerebrovascular accident); and they had no history of TBI. Participants were included in the NIC group if they had no history of an orthopedic and/or soft-tissue injury and no history of TBI.

For the purposes of this study, participants were selected from the larger study if 1) they had been evaluated 1-year or more postinjury but not greater than 10 years (for the TBI and IC groups only), 2) they had completed the target battery of neurobehavioral measures with no missing data, 3) the severity of TBI could be confidently determined and classified (for the TBI group only; see section below for details], and 3) they had scored below the recommended cutoff on the Validity-10[21], a measure designed to evaluate symptom exaggeration.

TBI evaluation and severity classification

Diagnosis and classification of TBI was based on a medical record review and a comprehensive lifetime TBI history interview. The lifetime TBI history interview was completed by Masters-level clinical research personnel who were specifically trained (by RTL and SML) to evaluate the presence and severity of TBI. The TBI history interview consisted of the Ohio State University TBI identification method[22] and an extended semistructured clinical interview designed to 1) extract more detailed information to estimate the presence/duration of loss of consciousness, post-traumatic amnesia, alteration of consciousness, and retrograde amnesia and 2) gather military-specific information regarding injury circumstances (eg, type of blast, protection worn, etc.). Final determination and classification of TBI severity was undertaken by consensus, considering all information, during case conferencing with the interviewer and a PhD-level clinician/scientist trained in neuropsychology and TBI diagnostic interviewing (RTL and SML). Participants were included in the MTBI group (n = 218) if they met the following criteria: uncomplicated MTBI 1) Glasgow Coma Scale =13–15, post-traumatic amnesia < 24 hours, loss of consciousness < 30 minutes, and/or alteration of consciousness present and 2) no trauma-related intracranial abnormality on CT or MRI. In accordance with prior studies,[2] participants were included in the CTBI group (n = 118) if they met criteria that exceeded the severity of uncomplicated mild TBI. This included, complicated mild TBI (n = 29; ie, presence of trauma-related intracranial abnormality on computed tomography or magnetic resonance imaging),

moderate TBI (n = 25), and severe TBI (n = 30). Also included in the CTBI group were participants with penetrating TBI (n = 34), which is a breach of the cranial vault and/or dura mater by an external object (eg, bullet, shrapnel) and/or skull fragment.[2]

Measures and procedure

Participants completed a 2.5-hour battery of self-report neurobehavioral measures that included the Sleep Disturbance scale from the Patient-Reported Outcomes Measurement Information System (PROMIS), PTSD Checklist-Civilian version (PCLC),[23] Neurobehavioral Symptom Inventory (NSI),[24] and the Traumatic Brain Injury Quality of Life (TBI-QOL).[25]

The PROMIS Sleep Disturbance short form 8A[26] scale is a measure designed to assess self-reported sleep quality, sleep depth, and restoration associated with sleep (eg, difficulties getting to sleep or staying asleep, adequacy of and satisfaction with sleep). The Sleep Disturbance scale was administered using an 8-item static short form that requires the test taker to respond to each item on a 5-point scale. A total raw score was calculated by summing the responses to all items and converted to T-scores (mean = 50, standard deviation = 10). High T-scores reflect worse functioning. Distribution of *t*-scores on the Sleep Disturbance scale were used to classify 3 sleep categories as follows: No Sleep Disturbance (50T or less), Mild Sleep Disturbance (> 50T to 55T), and Moderate-Severe Sleep Disturbance (> 55T).

The PCLC is a 17-item measure designed to evaluate self-reported PTSD symptoms. The PCLC requires the test taker to rate the presence/severity of each symptom on a 5-point scale. A total score was obtained by summing the ratings for the 17 items (range = 17–85). Participants were classified as PTSD-Present in accordance with the DSM-IV-TR criteria[14]; moderate or higher symptoms for 1) 1 or more Criterion B symptoms (ie, re-experiencing or being repeatedly triggered, emotionally and physically), 2) 3 or more Criterion C symptoms (ie, avoidance of thoughts or activities that remind you of your stressful experience), and 3) 2 or more Criterion D symptoms (ie, increased arousal, feeling jumpy, super alert, and/or having trouble concentrating).

The NSI is a 22-item measure designed to evaluate self-reported postconcussion symptoms (eg, headache, balance, nausea, etc.) rated on a 5-point scale. A total score was obtained by summing the ratings for the 22 items (range = 0–88).

The Validity-10[21] is a symptom validity test designed to detect symptom exaggeration when administering the NSI. Clinical validation studies have supported its use for this purpose.[27–31] The Validity-10 scale consists of 10 items from the NSI that are considered atypical and infrequently endorsed by individuals following TBI. As recommended by Vanderploeg and colleagues,[21] a cutoff score of > 22 was used to classify symptom exaggeration.

The TBI-QOL is a measure designed to provide a comprehensive evaluation of health-related quality of life for persons following TBI. For the purposes of this study, 13 of the 20 TBI-QOL scales were administered. The TBI-QOL was administered using static short forms that consisted of 8–10 items for each subscale, rated on a 5-point scale. Raw scores for each scale were calculated by summing all items within each scale and then converted to T-scores (mean = 50, standard deviation = 10). For the majority of scales, high T-scores reflect worse functioning (ie, Anger, Anxiety, Depression, Emotional and Behavioral Dyscontrol, Grief/Loss, Fatigue, Headaches, Pain Interference). However, for 5 scales, high T-scores reflect better functioning (ie, Cognitive Concerns-Executive Functioning, Cognitive Concerns-General, Ability to Participate in Social Roles and Activities, Positive Affect and Well-being, and Self Evaluation). Using scores from all 13 TBI-QOL scales, the number of scales with "abnormal scores" was also calculated. An abnormal score was defined as a T-score greater than 1 standard deviation (ie, 10) from the mean (ie, 50) that is reflective of poor functioning (eg, Anxiety > 60T; Cognitive Concerns-General < 40T).

The protocol under which these data were collected was approved by the Institutional Review Board of Walter Reed National Military Medical Center, Bethesda, MD. This study was completed in accordance with the guidelines of the Declaration of Helsinki.

Statistical analysis

Analyses were conducted using SPSS 24.0. First, prevalence of sleep disturbances for each of the injured and NIC groups was reported. To examine the influence of sleep disturbance on neurobehavioral functioning, 2 distinct sleep subgroups were created using the Sleep Disturbance scale categories (n = 509): 1) Good Sleep (50T or less; ie, No Sleep Disturbance) and 2) Poor Sleep (Greater than 55T; ie, Moderate-Severe Sleep Disturbance). To ensure that the control "Good Sleep" group only had those participants who reported no sleep problems, participants with scores ranging from 51T to 55T on the Sleep Disturbance scale (n = 97; ie, Mild Sleep Disturbance) were excluded from these analyses. Analysis of variance with pairwise comparisons was used to assess differences between the sleep subgroups across each of the injury severities. Bonferroni correction (α[.05]/[number of tests;16]) was used to adjust for multiple comparisons, as such $P < .0031$ was deemed significant for these analyses. Then, to examine if poor sleep was associated with poorer neurocognitive functioning cumulative percent of the number of abnormal scores was assessed for each of the injury severity and noninjury control groups.

Finally, to examine the interaction between sleep and PTSD in the entire sample (ie, MTBI, CTBI, IC, and NIC combined), exploratory analyses were undertaken. The sample was divided into 4 PTSD/sleep groups based on DSM-IV-TR symptom criteria for PTSD and the 2 sleep subgroups as follows: PTSD-Present/Good Sleep (n = 27), PTSD-Present/Poor Sleep (n = 201), PTSD-Absent/Good Sleep (n = 155), and PTSD-Absent/Poor Sleep (n = 126). The entire sample was used for these analyses, instead of using the 4 groups separately, because 1) there is a naturally low prevalence of participants in the PTSD-Present/Good Sleep subgroup (n = 27) that would not allow for such comparisons in a smaller sample and 2) neurobehavioral functioning was similar across each of the 4 groups.

RESULTS

Prevalence of sleep disturbances

In the total sample, approximately half of the sample (54.0%) was classified as having moderate-severe sleep disturbance (n = 327)

and 16.0% classified as having mild sleep disturbance (n = 97). Approximately one-third of the sample (30.0%) was classified as having no sleep disturbance (n = 182).

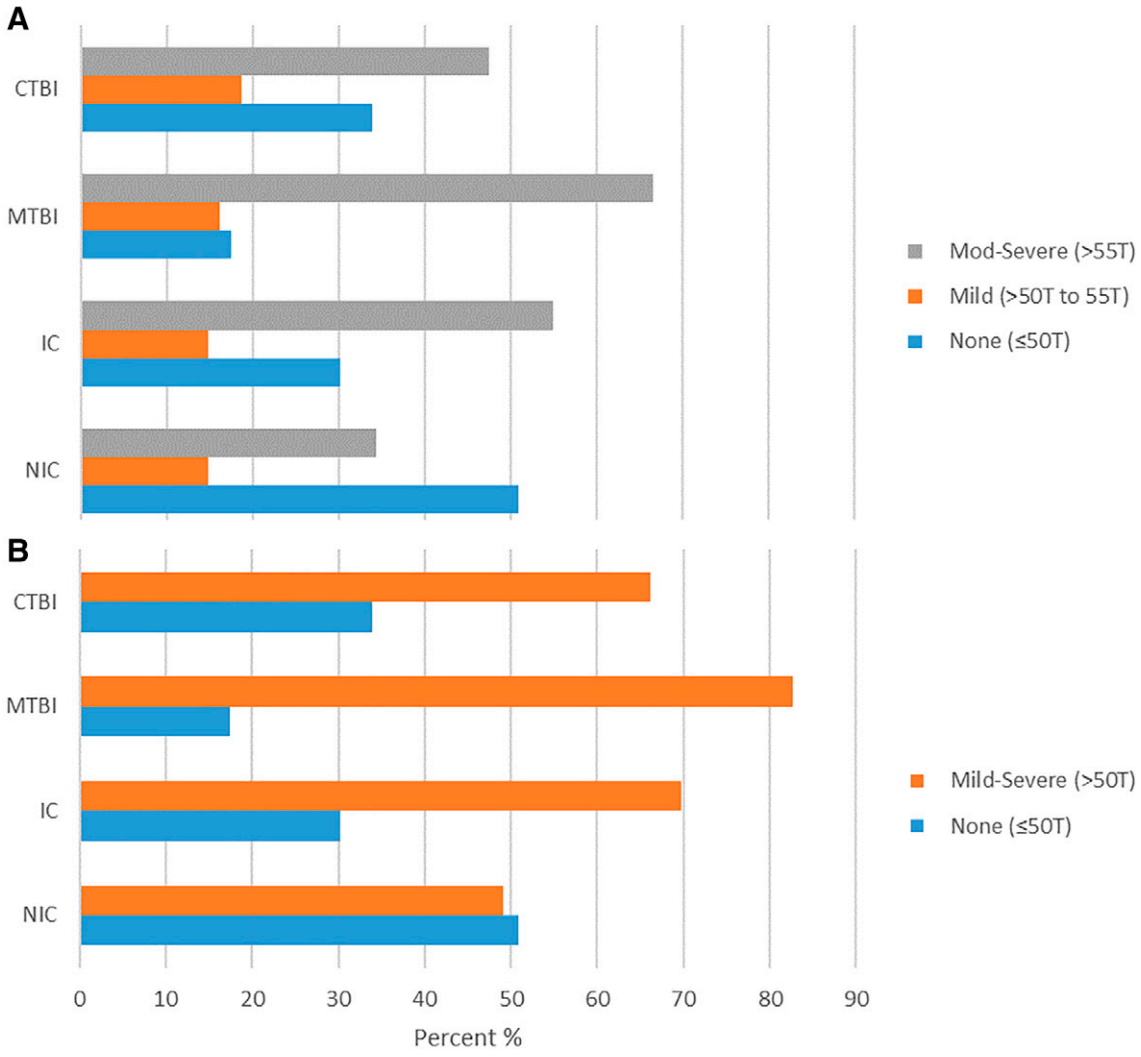
The prevalence of sleep disturbance was further examined across the 4 groups (ie, MTBI, CTBI, IC, and NIC). Moderate-severe sleep disturbance was most prevalent in the MTBI group (66.5%), followed by the IC (54.9%), CTBI (47.5%), and NIC (34.3%) groups, see **Figure 1A**. Pairwise comparisons revealed that there was a significantly higher proportion of the MTBI group classified with moderate-severe sleep disturbance compared to the IC ($P = .022$, H = .25, small effect size), CTBI ($P = .001$, H = .39, small-medium effect size), and NIC groups ($P < .001$, H = .65, medium-large effect size). In addition, there was a higher proportion of the IC group ($P = .001$, H= .42, medium effect size) and CTBI ($P = .044$, H = .27, small effect size) group classified with moderate-severe sleep disturbance compared to the NIC group (ie, MTBI > IC and CTBI > NIC).

The prevalence of any sleep disturbance (ie, mild, moderate, or severe) was highest in the MTBI group (82.6%), followed by the IC (69.8%), CTBI (66.1%), and NIC (49.1%) groups, see **Figure 1B**. Pairwise comparisons revealed that there was a significantly higher proportion of the MTBI group classified as having any sleep disturbance compared to the IC ($P = .003$, H = .30, small effect size), CTBI ($P = .001$, H = .38, small-medium effect size), and NIC groups ($P < .001$, H = .73, large effect size). In addition, there was a higher proportion of the IC group ($P = .001$, H = .43, medium effect size) and CTBI ($P = .010$, H =.35, small-medium effect size) group classified as having any sleep disturbance compared to the NIC group (ie, MTBI > IC and CTBI > NIC).

Poor Sleep and neurobehavioral functioning

The influence of sleep disturbance on neurobehavioral functioning was examined in each of the 4 groups separately (ie, MTBI,

Figure 1—Proportion of study population reporting presence and severity of sleep disturbances.



(**A**) Illustrates the proportion of service members and veterans reporting no, mild, and moderate-severe sleep disturbances across each of the 3 injury groups and the noninjured controls. (**B**) Illustrates the proportion of service members and veterans reporting any sleep disturbances vs no sleep disturbances across each of the 3 injury groups and the noninjured controls. CTBI = combined traumatic brain injury; complicated mild, moderate, severe and penetrating brain injury, IC = injured controls, NIC = noninjured controls, MTBI = mild traumatic brain injury.

Table 1—Descriptive statistics and group comparisons of demographic and neurobehavioral measures by sleep category: uncomplicated mild TBI group.

Measures	Uncomplicated MTBI				*P*	d[c]	Summary (d ≥ .40)
	Poor Sleep (n = 145)		Good Sleep (n = 38)				
	M	SD	M	SD			
Demographics							
Age (in years)	39.7	9.1	38.8	9.9	.560	.11	–
Education (in years)	15.0	2.2	15.2	2.5	.636	.09	–
# Combat Deploy	4.1	4.5	3.0	2.9	.175	.25	–
# Lifetime Blasts	44.3	70.6	46.0	72.2	.897	.02	–
Time Since Injury	133.9	84.9	124.7	106.5	.572	.10	–
Neurobehavioral							
PCLC Total	40.2	13.6	25.0	9.7	< .001	1.19	Poor > Good
PCLC Total-Mod[b]	22.5	9.3	14.1	5.9	< .001	.98	Poor > Good
NSI Total	32.2	14.5	12.0	12.0	< .001	1.44	Poor > Good
TBI-QOL Anger	55.0	10.6	44.3	8.0	< .001	1.07	Poor > Good
TBI-QOL Anxiety	57.3	8.6	46.2	9.3	< .001	1.27	Poor > Good
TBI-QOL Depression	50.6	7.9	43.6	7.6	< .001	.89	Poor > Good
TBI-QOL EBDYS	49.3	9.1	40.1	7.5	< .001	1.05	Poor > Good
TBI-QOL Grief	45.6	9.7	37.7	9.1	< .001	.82	Poor > Good
TBI-QOL PAWB[a]	51.6	7.9	57.0	8.9	< .001	.68	Poor < Good
TBI-QOL Fatigue	57.4	8.3	46.9	9.4	< .001	1.22	Poor > Good
TBI-QOL Headache	53.3	7.0	45.1	8.2	< .001	1.13	Poor > Good
TBI-QOL Pain	58.8	7.1	51.2	8.3	< .001	1.02	Poor > Good
TBI-QOL Cogn-EF[a]	36.0	7.0	44.3	8.6	< .001	1.14	Poor < Good
TBI-QOL Cogn-Gen[a]	33.9	7.6	42.7	9.8	< .001	1.09	Poor < Good
TBI-QOL Social-Int[a]	44.5	6.1	47.8	9.7	.011	.48	Poor < Good
TBI-QOL Self-Eval[a]	51.4	7.9	58.9	8.2	< .001	.94	Poor < Good

[a]For the majority of measures, high scores reflect worse functioning, with the exception of the measures indicated. For these measures, low scores reflect worse functioning. [b]Modified PCL-C total score summing items 1 through 8, 16, and 17. [c]Cohen's effect size: Small (0.2), Medium (0.5), Large (0.8). Sex comparisons: Female Poor Sleep=10.3%, Female Good Sleep=15.8% (*P* = .349). Cogn-EF = Cognitive Complaints-Executive Functioning, Cogn-Gen = Cognitive Complaints-General Concerns, EBDYS = Emotional and Behavioral Dyscontrol, MTBI = mild traumatic brain injury, NSI = Neurobehavioral Symptom Inventory, PAWB = Positive Affect and Well Being, PCLC = posttraumatic stress disorder (PTSD) Checklist-Civilian version, Self-Eval = Self Evaluation, Social-Int = Social Interaction, TBI-QOL = Traumatic Brain Injury Quality of Life.

CTBI, IC, NIC). Descriptive statistics and group comparisons for the neurobehavioral measures and select demographic variables by Sleep subgroup (Poor Sleep vs Good Sleep) in each of the 4 groups is presented in **Table 1**, **Table 2**, **Table 3**, and **Table 4**.

In the MTBI group, there were no significant group differences for all demographic variables. There were however significant group differences for all neurobehavioral measures, except for the Social Interaction domain (*P* = .011; d = .48, medium effect size). The Poor Sleep subgroup consistently had worse scores on all measures compared to the Good Sleep subgroup. The effect sizes ranged from large to very large (d = .82 to d = 1.44) with the exception of the TBI-QOL Positive Affect and Well-being (d = .68, medium-large).

In the CTBI group, there were no significant group differences for demographic variables, except for the number of lifetime blasts (Poor Sleep > Good Sleep; *P* = .032, d = .50, medium effect size). For the neurobehavioral measures, the Poor Sleep group consistently had significantly worse scores on all measures compared to the Good Sleep subgroup. The effect sizes ranged from large to very large (d = .75 to d = 1.39) for the majority of

Table 2—Descriptive statistics and group comparisons of demographic and neurobehavioral measures by sleep category: complicated mild, moderate, severe, and penetrating, combined TBI group.

Measures	CTBI				*P*	d[c]	Summary (d ≥ .40)
	Poor Sleep (n = 56)		Good Sleep (n = 40)				
	M	SD	M	SD			
Demographics							
Age (in years)	38.2	8.6	37.5	9.4	.712	.08	–
Education (in years)	14.4	2.1	14.8	2.4	.485	.15	–
# Combat Deploy	2.3	2.3	2.1	1.8	.554	.12	–
# Lifetime Blasts	28.8	55.6	9.0	16.7	.032	.50	Poor > Good
Time Since Injury	115.2	50.0	112.0	48.0	.753	.07	–
Neurobehavioral							
PCLC Total	38.8	12.6	24.4	7.3	< .001	1.39	Poor > Good
PCLC Total-Mod[b]	20.6	8.1	14.1	5.5	< .001	.93	Poor > Good
NSI Total	33.9	15.4	13.7	10.7	< .001	1.51	Poor > Good
TBI-QOL Anger	54.9	11.0	46.8	9.2	< .001	.79	Poor > Good
TBI-QOL Anxiety	56.3	7.5	46.8	7.1	< .001	1.30	Poor > Good
TBI-QOL Depression	52.8	9.1	45.2	7.5	< .001	.90	Poor > Good
TBI-QOL EBDYS	51.0	10.1	42.0	8.6	< .001	.95	Poor > Good
TBI-QOL Grief	50.4	11.5	43.3	9.9	.002	.65	Poor > Good
TBI-QOL PAWB[a]	50.3	9.2	56.7	7.8	< .001	.75	Poor < Good
TBI-QOL Fatigue	58.2	8.3	47.1	8.7	< .001	1.31	Poor > Good
TBI-QOL Headache	53.0	7.5	44.5	7.0	< .001	1.16	Poor > Good
TBI-QOL Pain	58.2	7.7	48.1	6.8	< .001	1.39	Poor > Good
TBI-QOL Cogn-EF[a]	36.0	7.8	41.8	7.1	< .001	.76	Poor < Good
TBI-QOL Cogn-Gen[a]	34.2	8.5	40.7	8.9	< .001	.75	Poor < Good
TBI-QOL Social-Int[a]	44.0	6.0	48.8	7.9	.001	.69	Poor < Good
TBI-QOL Self-Eval[a]	49.3	9.2	57.0	8.6	< .001	.86	Poor < Good

[a]For the majority of measures, high scores reflect worse functioning, with the exception of the measures indicated. For these measures, low scores reflect worse functioning. [b]Modified PCL-C total score summing items 1 through 8, 16, and 17. [c]Cohen's effect size: Small (0.2), Medium (0.5), Large (0.8). Sex comparisons: Female Poor Sleep=5.4%, Female Good Sleep=2.5% (*P* = .490). Cogn-EF = Cognitive Complaints-Executive Functioning, Cogn-Gen = Cognitive Complaints-General Concerns, CTBI = combined traumatic brain injury, EBDYS = Emotional and Behavioral Dyscontrol, NSI = Neurobehavioral Symptom Inventory, PAWB = Positive Affect and Well Being, PCLC = posttraumatic stress disorder (PTSD) Checklist-Civilian version, Self-Eval = Self Evaluation, Social-Int = Social Interaction, TBI-QOL = Traumatic Brain Injury Quality of Life.

measures. Medium-large effect sizes were found for the TBI-QOL Grief (d = .66) and Social Interaction (d = .69) scales.

In the IC group, there were no significant group differences for all demographic variables. There were significant group differences for all neurobehavioral measures with the exception of the TBI-QOL Social Interaction scale (*P* = .101, d = .30, small effect size). For these measures, the Poor Sleep subgroup consistently had significantly worse scores compared to the Good Sleep subgroup, with effect sizes ranging from large to very large (d = .89 to d = 1.58). A medium-large effect size was found for the TBI-QOL Emotional and Behavioral Dyscontrol scale (d = .62).

In the NIC group, there were no significant group differences for the majority of demographic variables. However, the Poor Sleep subgroup did report having been exposed to a significantly larger number of lifetime blasts compared to the Good Sleep subgroup (*P* = .015, d = .55, medium effect size). There were significant group differences for all neurobehavioral measures, with the exception of the TBI-QOL Social Interaction scale (*P* = .063, d = .40, small-medium effect size). For the majority of measures, the Poor Sleep subgroup consistently had significantly worse scores compared to the Good Sleep subgroup; effect sizes ranged from large to very large (d = .77 to d = 1.98).

Table 3—Descriptive statistics and group comparisons of demographic and neurobehavioral measures by sleep category: injured control group.

Measures	Injured Controls				*P*	d[c]	Summary (d ≥ .40)
	Poor Sleep (n = 89)		Good Sleep (n = 49)				
	M	SD	M	SD			
Demographics							
Age (in years)	40.4	8.6	41.5	10.5	.508	.12	–
Education (in years)	15.1	2.2	15.6	2.6	.232	.21	–
# Combat Deploy	4.3	4.0	3.6	4.0	.351	.17	–
# Lifetime Blasts	46.7	73.9	42.0	78.1	.729	.06	–
Time Since Injury	101.3	47.9	97.9	53.0	.700	.07	–
Neurobehavioral							
PCLC Total	35.4	12.3	22.0	8.0	< .001	1.25	Poor > Good
PCLC Total-Mod[b]	19.4	8.4	12.4	4.9	< .001	.98	Poor > Good
NSI Total	27.8	14.8	7.8	8.8	< .001	1.58	Poor > Good
TBI-QOL Anger	51.7	9.7	43.1	7.5	< .001	.97	Poor > Good
TBI-QOL Anxiety	54.5	8.7	45.3	8.7	< .001	1.07	Poor > Good
TBI-QOL Depression	49.4	8.5	42.4	6.4	< .001	.91	Poor > Good
TBI-QOL EBDYS	45.5	8.4	40.6	6.9	.001	.62	Poor > Good
TBI-QOL Grief	42.5	9.4	35.6	5.6	< .001	.85	Poor > Good
TBI-QOL PAWB[a]	51.5	7.3	59.2	7.4	< .001	1.04	Poor < Good
TBI-QOL Fatigue	57.1	7.9	45.7	8.5	< .001	1.39	Poor > Good
TBI-QOL Headache	52.4	7.1	42.3	5.8	< .001	1.51	Poor > Good
TBI-QOL Pain	56.4	8.2	46.4	7.5	< .001	1.25	Poor > Good
TBI-QOL Cogn-EF[a]	37.5	7.8	45.1	8.7	< .001	.94	Poor < Good
TBI-QOL Cogn-Gen[a]	36.1	8.8	45.5	8.2	< .001	1.08	Poor < Good
TBI-QOL Social-Int[a]	43.7	6.6	46.1	10.6	.101	.30	–
TBI-QOL Self-Eval[a]	53.4	8.5	60.4	6.8	< .001	.89	Poor < Good

[a]For the majority of measures, high scores reflect worse functioning, with the exception of the measures indicated. For these measures, low scores reflect worse functioning. [b]Modified PCL-C total score summing items 1 through 8, 16, and 17. [c]Cohen's effect size: Small (0.2), Medium (0.5), Large (0.8). Sex Comparisons: Female Poor Sleep=6.7%, Female Good Sleep=16.3% (*P* = .074). Cogn-EF = Cognitive Complaints-Executive Functioning, Cogn-Gen = Cognitive Complaints-General Concerns, EBDYS = Emotional and Behavioral Dyscontrol, M = mean, NSI = Neurobehavioral Symptom Inventory, PAWB = Positive Affect and Well Being, PCLC = posttraumatic stress disorder (PTSD) Checklist-Civilian version, SD = standard deviation, Self-Eval = Self Evaluation, Social-Int = Social Interaction, TBI-QOL = Traumatic Brain Injury Quality of Life.

Good/Poor Sleep and TBI-QOL score

The cumulative percentage of the number of abnormal TBI-QOL scales (13 maximum) by sleep subgroup in each of the 4 groups is presented in **Table 5**. In all 4 groups, the Poor Sleep subgroup consistently had a higher number of abnormal TBI-QOL scales compared to the Good Sleep subgroup for the vast majority of comparisons (**Table 5**). For example, in the MTBI group, 51.5% of the Poor Sleep subgroup had 4 or more abnormal TBI-QOL scales compared to 10.8% of the Good Sleep subgroup.

PTSD (Presence/Absence) combined with Sleep (Good/Poor) on TBI-QOL score

The cumulative percentage of the number of abnormal TBI-QOL scales across the 4 PTSD/Sleep subgroups in the entire sample is presented in **Table 6** and **Figure 2**. Select pairwise comparisons designed to examine the influence of Sleep within the same PTSD categories (ie, PTSD-Present/Good vs Poor Sleep; PTSD-Absent/Good vs Poor Sleep) revealed that the Poor Sleep subgroup had a higher number of abnormal TBI-QOL scales

Table 4—Descriptive statistics and group comparisons of demographic and neurobehavioral measures by sleep category: noninjured control group.

Measures	Noninjured Controls				*P*	d[c]	Summary (d ≥ .40)
	Poor Sleep (n = 37)		Good Sleep (n = 55)				
	M	SD	M	SD			
Demographics							
Age (in years)	42.6	10.1	40.7	9.9	.376	.19	–
Education (in years)	16.0	2.3	16.9	2.2	.067	.39	–
# Combat Deploy	2.9	3.1	1.6	1.8	.015	.55	Poor > Good
# Lifetime Blasts	15.4	47.7	13.7	46.4	.866	.04	–
Time Since Injury	–	–	–	–	–	–	–
Neurobehavioral							
PCLC Total	30.1	11.6	18.3	2.1	< .001	1.98	Poor > Good
PCLC Total-Mod[b]	16.6	7.5	10.5	1.1	< .001	1.64	Poor > Good
NSI Total	19.6	14.1	4.1	4.9	< .001	1.79	Poor > Good
TBI-QOL Anger	49.8	9.7	41.4	5.7	< .001	1.15	Poor > Good
TBI-QOL Anxiety	52.7	9.5	42.6	6.7	< .001	1.29	Poor > Good
TBI-QOL Depression	47.0	8.7	41.1	4.5	< .001	.94	Poor > Good
TBI-QOL EBDYS	43.6	9.3	37.5	5.2	< .001	.90	Poor > Good
TBI-QOL Grief	38.2	6.1	33.8	2.5	< .001	1.14	Poor > Good
TBI-QOL PAWB[a]	55.7	8.1	61.4	7.3	.001	.75	Poor < Good
TBI-QOL Fatigue	53.5	7.9	43.5	6.6	< .001	1.41	Poor > Good
TBI-QOL Headache	47.5	7.6	42.6	5.6	.001	.77	Poor > Good
TBI-QOL Pain	52.2	8.9	44.1	5.9	< .001	1.15	Poor > Good
TBI-QOL Cogn-EF[a]	42.0	8.2	50.7	6.6	< .001	1.21	Poor < Good
TBI-QOL Cogn-Gen[a]	41.7	8.9	50.9	6.7	< .001	1.21	Poor < Good
TBI-QOL Social-Int[a]	46.6	7.4	50.0	8.9	.063	.40	Poor < Good
TBI-QOL Self-Eval[a]	56.1	8.1	62.0	5.0	< .001	.94	Poor < Good

[a]For the majority of measures, high scores reflect worse functioning, with the exception of the measures indicated. For these measures, low scores reflect worse functioning. [b]Modified PCL-C total score summing items 1 through 8, 16, and 17. [c]Cohen's effect size (d): Small (0.2), Medium (0.5), Large (0.8). Sex comparisons: Female Poor Sleep=27.0%, Female Good Sleep=36.4% (*P* = .349). Cogn-EF = Cognitive Complaints-Executive Functioning, Cogn-Gen = Cognitive Complaints-General Concerns, EBDYS = Emotional and Behavioral Dyscontrol, M = mean, NSI = Neurobehavioral Symptom Inventory, PAWB = Positive Affect and Well Being, PCLC = posttraumatic stress disorder (PTSD) Checklist-Civilian version, SD = standard deviation, Self-Eval = Self Evaluation, Social-Int = Social Interaction, TBI-QOL = Traumatic Brain Injury Quality of Life.

compared to the Good Sleep subgroup for many comparisons (**Table 6**). For example, 66.9% of the PTSD-Present/Poor Sleep subgroup had 4 or more abnormal TBI-QOL scores compared to 25.0% of the PTSD-Present/Good Sleep subgroup (H = .87, large effect size). Select pairwise comparisons designed to examine the influence of PTSD within the same Sleep subgroups (ie, Good Sleep/PTSD Present vs Absent; Poor Sleep/PTSD Present vs Absent) revealed that the PTSD-Present subgroup had a higher number of abnormal TBI-QOL scales compared to the PTSD-Absent subgroup for many comparisons. For example, 52.9% of the PTSD-Present/Poor Sleep subgroup had 5 or more abnormal TBI-QOL scores compared to 9.4% of the PTSD-Absent/Poor Sleep subgroup (H = 1.04, very large effect size). Singularly, PTSD and Poor Sleep had a strong influence on neurobehavioral functioning, but when combined, this influence was very strong.

A cumulative effect of the influence of PTSD and Poor Sleep on neurobehavioral functioning can be seen in **Figure 2**. Overall neurobehavioral functioning was the highest in those participants without PTSD and who had Good Sleep (represented by the orange line). When participants without PTSD had Poor Sleep, neurobehavioral functioning declined (yellow line). Overall neurobehavioral functioning became progressively

Table 5—Cumulative frequency of the number of abnormal (1 SD) TBI-QOL scales by sleep subgroup in each experimental group.

Number of Abnormal TBI-QOL Scales[b]	Uncomplicated MTBI				CTBI			
	Poor Sleep %	Good Sleep %	H[a]	Summary (H ≥ .40)	Poor Sleep %	Good Sleep %	H	Summary (H ≥ .40)
10 or more	6.9	2.7	.22	–	12.2	0	.71	Poor > Good
9 or more	10.8	2.7	.34	–	16.3	0	.84	Poor > Good
8 or more	16.9	2.7	.53	Poor > Good	28.6	2.6	.81	Poor > Good
7 or more	21.5	5.4	.50	Poor > Good	28.6	2.6	.81	Poor > Good
6 or more	30.8	8.1	.61	Poor > Good	32.7	2.6	.90	Poor > Good
5 or more	39.2	8.1	.78	Poor > Good	46.9	5.1	1.06	Poor > Good
4 or more	51.5	10.8	.94	Poor > Good	57.1	7.7	1.16	Poor > Good
3 or more	66.2	13.5	1.14	Poor > Good	67.3	15.4	1.12	Poor > Good
2 or more	80.0	35.1	.95	Poor > Good	83.7	46.2	.81	Poor > Good
1 or more	87.7	51.4	.82	Poor > Good	89.8	59.0	.75	Poor > Good
None	100	100	–	–	100	100	–	–
Number of Abnormal TBI-QOL Scales[b]	**Injured Controls (IC)**				**Non-Injured Controls (NIC)**			
	Poor Sleep %	Good Sleep %	H	Summary (H ≥ .40)	Poor Sleep %	Good Sleep %	H	Summary (H ≥ .40)
10 or more	3.8	2.2	.12	–	3.1	–	–	–
9 or more	6.4	2.2	.23	–	3.1	–	–	–
8 or more	9.0	2.2	.33	–	3.1	–	–	–
7 or more	15.4	2.2	.53	Poor > Good	3.1	–	–	–
6 or more	26.9	4.4	.67	Poor > Good	9.4	0	.63	Poor > Good
5 or more	32.1	4.4	.78	Poor > Good	9.4	0	.63	Poor > Good
4 or more	43.6	4.4	1.01	Poor > Good	21.9	1.9	.69	Poor > Good
3 or more	56.4	4.4	1.27	Poor > Good	34.4	1.9	.97	Poor > Good
2 or more	66.7	22.2	.93	Poor > Good	46.9	5.7	1.04	Poor > Good
1 or more	85.9	48.9	.82	Poor > Good	62.5	18.9	.92	Poor > Good
None	100	100	–	–	100	100	–	–

n = 509 (Uncomplicated Mild TBI = 183 [145 Poor Sleep, 38 Good Sleep], CTBI = 96 [56 Poor Sleep, 40 Good Sleep], Injured Controls = 138 [89 Poor Sleep, 49 Good Sleep], Noninjured Controls = 92 [37 Poor Sleep, 55 Good Sleep]). [a]Cohen's effect size (H): Small (0.2), Medium (0.5), Large (0.8). [b]Maximum of 13 scales. SD = standard deviation, TBI-QOL = Traumatic Brain Injury Quality of Life.

worse in participants with PTSD and Good Sleep (green line), and was the worst in those participants with PTSD and Poor Sleep (brown line).

DISCUSSION

This study aimed to examine the association between sleep disturbances and neurobehavioral functioning following TBI, as well as in injured and noninjured participants. Sleep disturbances in this study captured by the PROMIS scale included difficulties getting to sleep or staying asleep, as well as adequacy of and satisfaction with sleep. In line with prior research, prevalence of any reported sleep disturbances was high across all groups of service members and veterans and particularly for those with a history of MTBI (82.6%). This finding supports prior literature that has shown that people who have sustained an MTBI self-report more sleep problems than those with more severe TBIs.[32,33] While it is noted that self-reported sleep disturbances do not always correspond with objective measures of sleep, especially for those with MTBI,[34,35] the cause of these perceived sleep disturbances is important. However, the reason for this pattern remains unclear. Some have postulated that this phenomena may be due to 1) people who sustain an MTBI remain more self-aware and therefore have more awareness of their symptoms than those who sustain more severe TBIs[36,37] and/or 2) it may be the area of the lesion rather than injury severity itself that is the root cause of their perceived sleep disturbances.[36] However, only advances in neuroimaging will aid in disentangling this relationship more clearly in the future.[4]

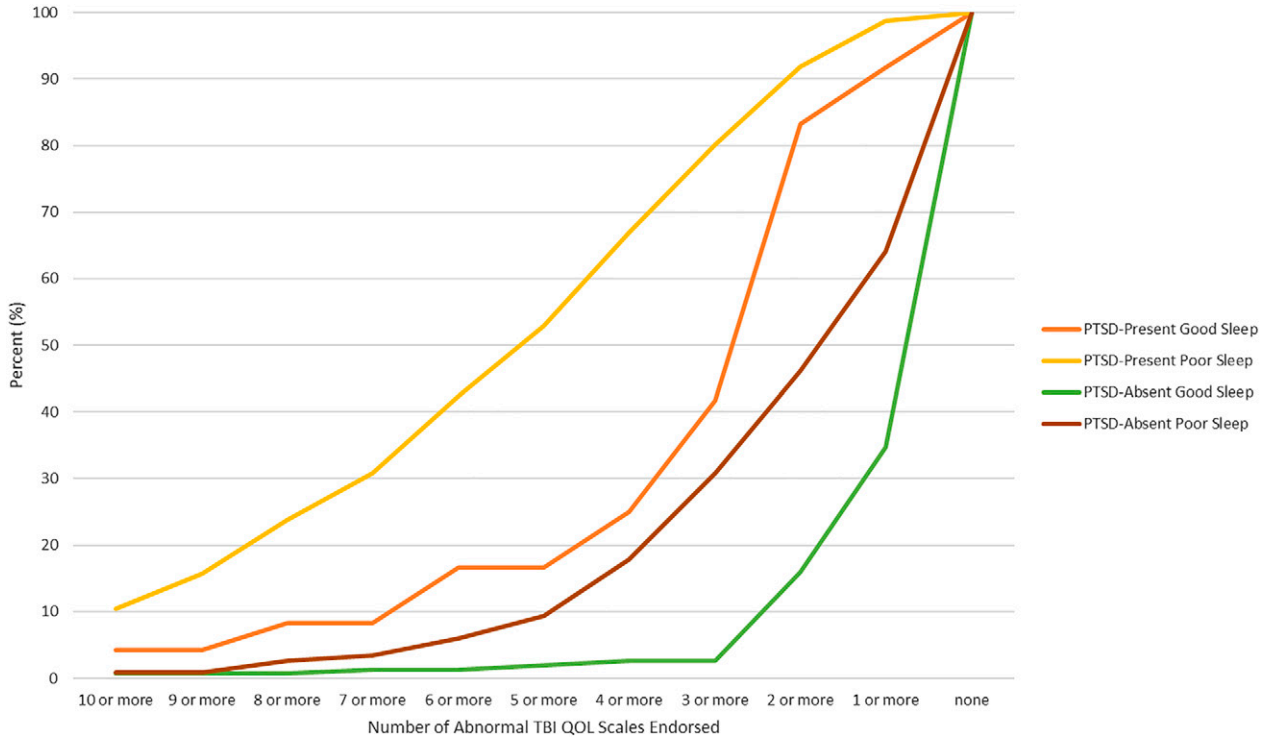
We found that in each of the 3 injury groups (MTBI, CTBI, IC) and the NIC group, poor sleep was associated with significantly worse neurobehavioral scores across the TBI-QOL scales when compared to the Good Sleep subgroup. The only exception was on the TBI-QOL Social Interaction scale, which was significantly different between the sleep categories in the CTBI group only. It is possible that participation in social roles and activities is especially impaired in participants with CTBI, and this may be

Table 6—Cumulative frequency of the number of abnormal (1 SD) TBI-QOL scales by PTSD × sleep subgroups in total sample.

Number of Abnormal TBI-QOL Scales[b]	1. PTSD-Present Good Sleep	2. PTSD-Present Poor Sleep	3. PTSD-Absent Good Sleep	4. PTSD-Absent Poor Sleep	Select Pairwise Comparisons							
					Influence of SLEEP within Same PTSD Categories				Influence of PTSD within Same SLEEP Categories			
					1 v 2 PTSD Present: Good v Poor Sleep		3 v 4 PTSD Absent: Good v Poor Sleep		1 v 3 Good Sleep: PTSD Pres v Abs		2 v 4 Poor Sleep: PTSD Pres v Abs	
	%	%	%	%	H[a]	Summary (H ≥ .40)	H	Summary (H ≥ .40)	H	Summary (H ≥ .40)	H	Summary (H ≥ .40)
10 or more	4.2	10.5	0.7	0.9	.26	–	–	–	—	–	.46	Pres > Abs
9 or more	4.2	15.7	0.7	0.9	.41	Poor > Good	–	–	—	–	.61	Pres > Abs
8 or more	8.3	23.8	0.7	2.6	.43	Poor > Good	–	–	—	–	.71	Pres > Abs
7 or more	8.3	30.8	1.3	3.4	.59	Poor > Good	–	–	—	–	.81	Pres > Abs
6 or more	16.7	42.4	1.3	6.0	.58	Poor > Good	–	–	.59	Pres > Abs	.93	Pres > Abs
5 or more	16.7	52.9	2.0	9.4	.79	Poor > Good	–	–	.55	Pres > Abs	1.00	Pres > Abs
4 or more	25.0	66.9	2.7	17.9	.87	Poor > Good	.56	Poor > Good	.73	Pres > Abs	1.04	Pres > Abs
3 or more	41.7	80.2	2.7	30.8	.81	Poor > Good	.87	Poor > Good	1.08	Pres > Abs	1.03	Pres > Abs
2 or more	83.3	91.9	16.0	46.2	.26	–	.67	Poor > Good	1.48	Pres > Abs	1.08	Pres > Abs
1 or more	91.7	98.8	34.7	64.1	.39	–	.60	Poor > Good	1.29	Pres > Abs	1.09	Pres > Abs
none	100	100	100	100	–	–	–	–	–	–	–	–

n = 509 (PTSD-Present/Good Sleep, n = 27 [29.6% MTBI, 48.1% CTBI, 22.2% IC, 0% NIC]; PTSD-Present/Poor Sleep, n = 201 [50.7% MTBI, 16.9% CTBI, 24.9% IC, 7.5% NIC]; PTSD-Absent/Good Sleep, n = 155 [19.4% MTBI, 17.4% CTBI, 27.7% IC, 35.5% NIC]; PTSD-Absent/Poor Sleep, n = 126 [34.1% MTBI, 17.5% CTBI, 31.0% IC, 17.5% NIC]). [a]Cohen's effect size (H): Small (0.2), Medium (0.5), Large (0.8). [b]Maximum of 13 scales. Abs = absent, IC = injured controls, PTSD = posttraumatic stress disorder, Pres = present, SD = standard deviation, TBI-QOL = Traumatic Brain Injury Quality of Life (13 scales maximum).

Figure 2—Cumulative frequency of the number of abnormal TBI-QOL scales by PTSD × sleep groups in total sample.



PTSD = posttraumatic stress disorder, TBI-QOL = Traumatic Brain Injury Quality of Life.

due to the brain injury itself, with problems of attention, executive function, and/or behavior that result in declines in communication skills following a CTBI.[38] Indeed, research has frequently reported increased difficulties in return to productivity and increased social difficulties following TBI in both military and nonmilitary populations.[39–41] Alternatively, researchers have suggested that social cognition, which includes being able to perceive social cues, understand or empathize with other's experiences, and understand other people's intentions, may be impaired after injury, even when cognitive function remains intact.[42] Unfortunately, this study is unable to determine the underlying cause of this difference; however, it seems that this may be an important factor to consider for service members and veterans who have a history of TBI.

Across each of the 3 injury groups and the NIC controls, participants who identified as having poor sleep were substantially more likely to have a higher number of abnormal TBI-QOL scales than those in the Good Sleep subgroup. For example, across each injury group, the proportion of participants in the Poor Sleep subgroup who had 4 or more abnormal TBI-QOL scales ranged from 21.9% (NIC) to 51.5% (MTBI) in comparison to just 1.9% (NICs) to 10.8% (MTBIs) of those in the Good Sleep subgroup. Clinically, the evaluation of sleep disturbances may be a useful tool to identify service members and veterans at risk of poor neurobehavioral functioning for targeted treatment and intervention. It is well recognized that sleep disturbances are highly prevalent in military populations,[43–45] especially following TBI.[9,46] However, sleep is malleable and, as such, improving sleep may indeed improve symptom reporting, even in noninjured personnel. Interventions that have successfully improved sleep have reported concurrent reductions in PTSD and depression symptoms,[47] as well as increased cognitive functioning.[48,49] However, efficacy of interventions to improve sleep in military personnel, especially with a history of TBI have produced inconsistent results.[43] Thus, finding ways to more specifically target sleep interventions is necessary. One way may be to target interventions to those personnel with other co-occurring conditions such as PTSD.

Our exploratory analysis indicated that ∼52% of service members and veterans who had PTSD symptoms and concurrent sleep disturbances had 5 or more abnormal TBI-QOL scales. This is compared to ∼16% in the PTSD-Present Good Sleep group, 9% in the PTSD-Absent-Poor Sleep group, and just 2% of the PTSD-Absent-Good Sleep group. Prior research has consistently shown a strong association between PTSD and sleep disturbances in military and veteran populations.[43] Furthermore, a recent study from our research team indicated that when experienced concurrently, sleep disturbances, such as excessive daytime sleepiness and PTSD, result in significant disruption to gene regulation.[50] Taken together with research indicating the profound effects of PTSD on neurobehavioral functioning,[1] it is evident that targeted interventions to improve sleep in service members and veterans with concurrent PTSD is vital.

This paper has a number of strengths, including a rigorous protocol for characterizing TBI severity in a relatively large sample of service members and veterans, with exclusions made

for symptom exaggeration. However, there are limitations to consider. First, all measures were self-reported. Research has shown that subjective reports of sleep problems do not always correspond with objective measures of sleep problems.[51] As such, further investigation using objective measures of sleep, such as actigraphy or polysomnography, is needed. However, it is important to note that the sleep disturbances reported in this study were deemed significant to these individuals and thus remain an important consideration in future investigations. Another limitation of the current analysis is that in the CTBI group, the Poor Sleep subgroup reported significantly more lifetime blast exposures (mean = 28.2, standard deviation = 55.6) compared to the Good Sleep subgroup (mean = 9.0, standard deviation = 16.7). We were unable to account for these differences between the groups, and as such the effect of lifetime blast exposures may be accounting for some of the variance in neurobehavioral symptom reporting in the CTBI group. However, this seems unlikely given the high consistency of the findings. Furthermore, each of the 3 injury groups and the NIC reported variable, but quite high, lifetime blast exposures. Prior studies into the effects of lifetime blast exposure on sleep have been mixed,[20,52] with some finding no effect of lifetime blast exposure on sleep.[53] Furthermore, exposure to a blast or multiple blasts across time does not necessarily result in a TBI. Lifetime exposure to blast is a self-reported item, which asks participants to determine the number of blasts they have been exposed to across their military career. This information is free from context such as proximity to the blast site and use of protective equipment and machinery not accounted for. Injuries from blast may include primary (due to exposure to the blast wave), secondary (ie, caused by shrapnel from the blast), and tertiary injuries (ie, exposure to toxic fumes created from a blast).[54] Thus, studies are needed to more fully explore the association between blast exposure and neurobehavioral outcomes; however, the measurement of these events, especially across a military career, is beyond current wearable technology bounds. Finally, the participants in this study were recruited from advertising in the community, as such, there may be some selection bias of those who chose to take part in this study vs those who did not. However, the inclusion of the 2 control groups paints a compelling picture that both sleep and PTSD, especially when experienced concurrently, are important for neurobehavioral functioning.

CONCLUSIONS

This study demonstrates that self-reported sleep disturbances are very common following TBI of all severities and following injury without TBI and had a strong influence on neurobehavioral functioning. Singularly, PTSD and poor sleep had a strong influence on neurobehavioral outcome. However, when PTSD and poor sleep occur concurrently, this influence became very strong. Poor sleep may be a useful "risk factor" that can be used clinically to identify individuals in need of early intervention to improve sleep quality. Improving sleep quality may improve overall neurobehavioral outcome in service members and veterans with and without a history of TBI.

ABBREVIATIONS

CTBI, combined traumatic brain injury; complicated mild, moderate, severe, and penetrating traumatic brain injury
IC, injured controls
MTBI, mild traumatic brain injury
NIC, noninjured controls
NSI, Neurobehavioral Symptom Inventory
PCLC, Posttraumatic Stress Disorder Checklist-Civilian version
PROMIS, Patient-Reported Outcomes Measurement Information System
PTSD, Posttraumatic Stress Disorder
TBI, traumatic brain injury
TBI-QOL, Traumatic Brain Injury Quality of Life

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Address correspondence to: Cassandra L. Pattinson, PhD, The Institute for Social Science Research, The University of Queensland, 80 Meiers Rd, Building 1018, Room 305; Tel: +61 7 334 6707; Email: c.pattinson@uq.edu.au

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