

Sleep problems contribute to post-concussive symptoms in service members with a history of mild traumatic brain injury without posttraumatic stress disorder or major depressive disorder

Lisa H. Lu^{a,b,*}, Matthew W. Reid^{a,b}, Douglas B. Cooper^{b,c} and Jan E. Kennedy^{a,b}

^a*Defense and Veterans Brain Injury Center, Brooke Army Medical Center, TX, USA*

^b*General Dynamics Information Technology, San Antonio, TX, USA*

^c*Defense and Veterans Brain Injury Center, South Texas Veterans Health Care System, San Antonio, TX, USA*

Abstract.

BACKGROUND: Many with a history of mild traumatic brain injury (TBI) experience sleep problems, which are also common symptoms of stress-related and mood disorders.

OBJECTIVE: To determine if sleep problems contributed unique variance to post-concussive symptoms above and beyond symptoms of posttraumatic stress disorder/major depressive disorder (PTSD/MDD) after mild TBI.

METHODS: 313 active duty service members with a history of mild TBI completed sleep, PTSD, and mood symptom questionnaires, which were used to determine contributions to the Neurobehavioral Symptom Inventory.

RESULTS: 59% of the variance in post-concussive symptoms were due to PTSD symptom severity while depressive symptoms and sleep problems contributed an additional 1% each. This pattern differed between those with and without clinical diagnosis of PTSD/MDD. For those with PTSD/MDD, PTSD and depression symptoms but not sleep contributed to post-concussive symptoms. For those without PTSD/MDD, PTSD symptoms and sleep contributed specifically to somatosensory post-concussive symptoms. Daytime dysfunction and sleep disturbances were associated with post-concussive symptoms after PTSD and depression symptoms were controlled.

CONCLUSIONS: PTSD symptom severity explained the most variance for post-concussive symptoms among service members with a history of mild TBI, while depression symptoms, daytime dysfunction, and sleep disturbances independently contributed small amounts of variance.

Keywords: Concussion, sports, combat, blast, insomnia, sleep apnea, psychiatry, primary care, stress, dysthymia

1. Background

A meta-analysis of patients with a history of TBI revealed 50% experience some form of sleep problem, which was higher than the 41% in the general community (Mathias & Alvaro, 2012). Among military service members, estimated prevalence of sleep

*Address for correspondence: Lisa H. Lu, PhD, Defense and Veterans Brain Injury Center (DVBIC), Contractor, General Dynamic Health Solutions, Neurology Service (DVBIC), Brooke Army Medical Center, 3551 Roger Brooke Drive, JBSA Ft. Sam Houston, TX 78234-4504, USA. Tel.: +1 210 916 6029; E-mail: lisa.h.lu.ctr@mail.mil.

problems is between 45–84% (Hoge et al., 2008; Lew et al., 2007). Sleep problems include problems falling or staying asleep, frequent nighttime awakenings, early morning awakenings, breathing problems interrupting sleep, pain disturbing sleep, sleep-wake cycle problems, or other self-reported problems of sleep. Such problems can contribute to daytime sleepiness, fatigue, and have been reported to predict persistence of post-concussive symptoms (Sullivan, Berndt, Edmed, Smith, & Allan, 2016). Sleep deprivation studies have shown impaired attention, working memory and divergent thinking skills, with sleep fragmentation showing similar detrimental effects as sleep deprivation (Durmer & Dinges, 2005). Among those with moderate to severe TBI, evidence suggests that sleep disturbance during the acute stage of recovery predicts poorer cognitive recovery (Holcomb et al., 2016). This has been extended to the mild TBI population with the idea that improved sleep may facilitate recovery and/or mitigate post-concussive symptoms. Polysomnography studies of those with mild TBI have mixed findings, with some showing no difference between patients with a history of mild TBI and controls (Gosselin et al., 2009) while others show increased nocturnal wakefulness (Mollayeva et al., 2017), less total sleep time (Schreiber et al., 2008), less time in non-rapid eye movement stage (Mollayeva et al., 2017) and in rapid eye movement sleep (Mollayeva et al., 2017; Schreiber et al., 2008). One study showed that patients with mild TBI had much greater variability on objective sleep measures, such that lower sleep efficiency in the mild TBI group was not significant after statistical correction to account for different variances between groups (Williams, Lasic, & Ogilvie, 2008). This greater variance amongst those with a history of mild TBI likely contributes to inconsistent findings across studies.

Complicating the relationship between sleep and mild TBI in the military is the high rate of mental health co-morbidities in this population. Sleep problems are common symptoms of stress-related and mood disorders; in fact sleep disturbance is part of the symptom criteria for both PTSD and MDD, but studies on mild TBI and sleep often do not control for mental health co-morbidities (Gosselin et al., 2009; Williams et al., 2008). Among Operation Enduring Freedom (OEF)/Operation Iraqi Freedom (OIF)/Operation New Dawn (OND) veterans, those with PTSD reported worse sleep than trauma-exposed controls (Lind et al., 2017), and controlling for PTSD symptoms removed the reported sleep difference between PTSD only and PTSD + TBI groups,

suggesting that greater PTSD symptoms drove the higher scores in the PTSD + TBI comorbid group (DeGutis et al., 2018). A longitudinal study of change in sleep over time among OEF/OIF veterans with PTSD showed that nightmares increased over time although overall sleep complaints decreased (King, Donnelly, Warner, Wade, & Pigeon, 2017). This was consistent with a meta-analysis of polysomnography findings showing more rapid eye movement abnormalities among older patients with PTSD, although younger patients with PTSD have less total sleep time than age-matched controls (Kobayashi, Boarts, & Delahanty, 2007). The same meta-analysis study supported that patients with PTSD have more stage 1 sleep, less slow wave sleep, and greater rapid-eye-movement density, consistent with hyperarousal during sleep (Kobayashi et al., 2007).

Among active duty and veteran populations with a history of mild TBI, estimates of PTSD range from 33% to 39% (Carlson et al., 2011), and estimates of mood disorder range from 21% to 57% (Scholten et al., 2016). PTSD and major depressive disorder have a comorbidity rate of 48% (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). PTSD with a TBI history was associated with worse insomnia severity over an 18-month interval than PTSD alone (King et al., 2017). For patients with mental health co-morbidities, the question arises as to whether sleep problems should be addressed as part of a comprehensive treatment for mental health problems or do they warrant clinical attention independent of accompanying mental health issues? What about for patients with no mental health co-morbidities? One study of 109 OEF/OIF veterans suggested that poor sleep quality contributed to cognitive deficits beyond those attributable to PTSD and mild TBI history (Martindale, Morissette, Rowland, & Dolan, 2017). This would suggest that addressing sleep issues independent of mental health issues might be beneficial.

In the present study, we examined whether sleep quality contributed unique variance to post-concussive symptoms above and beyond symptoms of PTSD and depression, and whether the relative contribution of sleep differs for patients with comorbid PTSD/depression versus those without these co-morbidities. Such data might help with conceptualization of sleep problems within a context of mental health comorbidities and guide treatment priorities for patients with complex needs. We hypothesized that sleep problems are a manifestation of mood and PTSD issues, and that sleep quality would not contribute unique variance after symptoms of PTSD

and depression are controlled. If sleep were to make unique contributions, we wanted to follow up and explore which components of sleep quality mattered, and to which types of post-concussive symptoms they contribute.

2. Methods

2.1. Participants

Data were analyzed from a repository database of service members who endorsed a history of TBI during a primary care visit screen in a military treatment facility from November 2014 through May 2017 and completed a battery of questionnaires. The presence of TBI was confirmed for all cases, based on electronic medical record review and patient self-report elicited from a study-specific semi-structured interview with a trained research nurse. The presence of PTSD or MDD was coded as positive if there was documentation of a current (within 30 days of study participation) diagnosis in the electronic medical record system used in military treatment facilities (AHLTA). All research procedures were performed in compliance with Department of Defense (DoD) guidelines and approved by the local Institutional Review Board. Written informed consent was obtained from all participants. Of 465 total cases, 313 were determined to have had a history of mild TBI via objective criteria and complete scores on outcome and predictor measures and served as the mild TBI sample for this study. Mild TBI was defined using the Department of Veterans Affairs/Department of Defense (VA/DoD) criteria: Loss of consciousness no greater than 30 minutes and/or posttraumatic amnesia no greater than 1 day and/or alteration of consciousness no greater than 24 hours (Department of Veterans Affairs and Department of Defense, 2016). Thirty-four cases were omitted from the sample due to questionable validity of symptom report, based on a cutoff of 22 on the Neurobehavioral Symptom Inventory Validity-10 measure (Vanderploeg et al., 2014), yielding 279 cases as the final sample for analyses.

2.2. Measures

The primary outcome measure was the Neurobehavioral Symptom Inventory (NSI), which is a 22-item self-report symptom measure endorsed by the DoD and Veterans Administration to track

neurocognitive complaints after TBI. Internal consistency is high (0.95) (King et al., 2012). Two independent large-scale factor analytic studies of the NSI have converged to support a four-factor model of symptom clusters: cognitive, somatosensory, vestibular, and affective (Pogoda et al., 2012; Vanderploeg et al., 2015). Because our predictor variables were affective measures, inclusion of the NSI affective items (fatigue; sleep problems; anxious; depressed/sad; irritable; low frustration) in the outcome variable would lead to affective predictors accounting for more variance in the outcome due to symptom overlap. Thus an adjusted NSI score (Adj NSI) was calculated based on total score for items other than those on the affective scale. This Adj NSI was the sum of the remaining 16 items, which yielded a maximum score of 64 that reflected cognitive, somatosensory, and vestibular complaints. The affective scale of the NSI also included an item on sleep problems. Thus, removal of this item as part of the affective scale also eliminated the overlap between the Adj NSI and the sleep predictor measure. The NSI cluster scores from the somatosensory (7 items), cognitive (4 items), and vestibular (3 items) factors were also evaluated to discern more granular relationships between our predictor variables and the Adj NSI score (2 items did not contribute to any unique factor) (Pogoda et al., 2012; Vanderploeg et al., 2015). Because post-concussive symptoms are reliant on self-report, validity cutoffs have been proposed using responses to 10 items on the NSI that are infrequently endorsed by service members and veterans with a history of mild TBI (Vanderploeg et al., 2014). We used the cutoff score recommended by the developers of the NSI Validity-10 (>22) to exclude cases where there was a potential for symptom exaggeration (Vanderploeg et al., 2014), in order to achieve a sample that was representative of the more typical active duty population and less likely to be impacted by secondary gain or other factors that influence symptom over-reporting.

Posttraumatic stress symptoms were measured using the PTSD Checklist – Civilian version (PCL-C) (Weathers et al., 1993), a 17-item self-report measure of symptom severity rated on a 5-point Likert-like scale that corresponds to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria for PTSD. Internal consistency for the military version of this scale is high (0.97), as is test-retest reliability over 2–3 days (0.96) (Norris & Hamblen, 2003). The PCL-C and PCL-M consist of the same questions, with the civilian version ask-

ing about “stressful life experiences” and the military version asking about “stressful military experiences.” We chose the civilian version because we did not want to constrain sources of stress to military experiences. This scale has good concurrent validity as evidenced by high correlation with the Mississippi Scale for Combat Related PTSD (0.93) and the Impact of Events Scale (0.90) (Norris & Hamblen, 2003). An adjusted PCL-C score (Adj PCL-C) was used that excluded the sleep and concentration items in order to remove the overlap with the primary sleep measure and the cognitive factor of the NSI. There is also an overlap between the PCL-C item on disturbing dreams and sleep disturbances measured by the primary sleep measure. Because disturbing dreams is a significant presentation of PTSD, this item was not removed in order to capture this important symptom in the Adj PCL-C score.

Depressive symptoms were measured using the Center for Epidemiological Studies – Depression scale (CES-D), a 20-item self-report measure of depressive symptom severity rated on a 4-point Likert-like scale. Internal consistency is high (0.84–0.90) and test-retest reliability between 2–8 weeks ranges from 0.51 to 0.59, with an average of 0.57 (Radloff, 1977). The CES-D has evidence of construct validity via high correlations with clinician ratings of depression severity (0.56) and other scales designed to measure depressive symptoms (0.51–0.61) but low correlations with measures such as disability or aggression (0.19–0.28) (Radloff, 1977). An adjusted CES-D score (Adj CES-D) was used that excluded the sleep and concentration items to remove the overlap with the sleep measure and the cognitive factor of the NSI.

The primary sleep measure was the Pittsburgh Sleep Quality Index (PSQI), a self-report of sleep habits and problems scored using a 4-point Likert-like scale to yield seven component scores: Subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, medication use, and daytime dysfunction (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Lower scores reflect more desirable sleep characteristics. The correlation between the global and component scores ranges from 0.53 to 0.83. The global score has good internal consistency (0.80) and evidence of convergent validity with related constructs (0.65–0.77) and discriminant validity with unrelated constructs (0.03–0.45) (Carpenter & Andrykowski, 1998). To address the overlap between the sleep disturbance component of the PSQI (Component 5, which queried

eight things that might disturb sleep, such as bad dreams, using the bathroom, pain etc.) and the PCL-C item on disturbing dreams, we excluded bad dreams from the PSQI Component 5 score. This Adj Component 5 score was combined with other component scores to derive the Adj PSQI Global score used in this study.

2.3. Statistical analyses

Multiple regression to determine the effect of sleep while covarying for depression and stress-related symptoms would not be appropriate due to the multicollinearity between predictor variables. Furthermore, such an analysis would not address if sleep contributed unique variance *after* depression and stress-related symptoms have been controlled. Hierarchical regression is an approach that determines if a predictor contributes variance *after* variance due to related predictor variables has been removed. Thus we used hierarchical regression to predict the Adj NSI score from the Adj PCL-C and Adj CES-D scores using stepwise entry within the first block of predictors and the Adj PSQI Global score entered as the predictor in the second block. This method controlled for PTSD and depressive symptom severity before variance from sleep problems was considered, which allowed us to address the question of whether sleep problems contributed unique variance to post concussive symptoms above and beyond effects of stress and mood. To explore whether comorbid diagnosis of PTSD/MDD affected sleep differentially in our sample, we repeated the above analysis with our sample divided into those with AHLTA documentation of PTSD or MDD versus those without. Two sets of analyses were conducted to follow up on significant effects of sleep problems: First, to examine which component(s) of sleep problems contributed unique variance, the Adj PSQI Global score entered in the second block of predictors was replaced by the seven PSQI component scores using stepwise entry. Second, to examine which specific post-concussive symptoms were influenced by sleep problems, the Adj NSI score was replaced by NSI somatosensory, cognitive, and vestibular cluster scores. For all analyses, significance was determined using a *p*-value of 0.05.

3. Results

Table 1 shows the demographic characteristics of this sample of active duty service members. Of note,

Table 1
Demographic characteristics of our sample of active
duty service members with a history of mild TBI ($N=279$ unless otherwise indicated)

	Mean	SD
Age	36.5	7.5
Years in service	14.7	6.6
Number of deployments ($n=277$)	2.3	1.8
Months since injury	61.5	51.4
	Count	Percentage
Gender (M:F)	240:39	86:14
Rank		
Junior enlisted (E1-E4)	24	9
Senior enlisted (E5-E9)	191	68
Officers (CW1-O9)	64	23
Branch of service		
Army ^a	258	92
Air Force	13	5
Navy ^b	5	2
Marine	3	1
Marital status		
Single	18	6
Partnered	201	72
Post-partnership	60	22
Race ($n=278$) ^c		
Caucasian	217	78
African-American	56	20
Indian American	13	5
Asian	10	4
Native Hawaiian/Pacific Islander	1	0
Ethnicity ($n=276$)		
Hispanic/Latino	71	26
Non-Hispanic/Latino	205	74
Education		
GED or 12th grade without diploma	7	2
High school diploma	52	19
Post high school/military training courses	54	19
Associates degree	63	23
Bachelor's degree	66	24
Post-graduate degree	37	13

^aArmy includes Reserves and Guards. ^bNavy includes Reserves. ^cIt was possible to endorse more than one category, thus summed percentage is greater than 100.

the time since the TBI ranged from 0 to 340 months, with a median of 52 months since injury (interquartile range = 80 months). Thus, this represented a sample of service members with a remote history of mild TBI and chronic symptoms. In this sample ($N=279$), 133 individuals (47%) had comorbid diagnoses of PTSD ($n=112$; 40%), MDD ($n=78$; 30%), or both ($n=57$; 20%) documented in AHLTA within 30 days prior to the evaluation where the questionnaires for this study were completed. The remaining 53% ($n=146$) did not have AHLTA documentation of 'current' PTSD or MDD (i.e., within 30 days before evaluation).

Table 2 reports the unadjusted descriptive statistics of measures for comparison to other samples in the literature. The NSI mean of 33 in our sample falls in the 10–24th percentile range amongst

deployed service members with a history of mild TBI and in the 2–4th percentile range compared to deployed service members without mild TBI (Soble et al., 2014). The PCL-C mean of 44 is above cut-offs used to screen for PTSD in primary care settings (Bliese et al., 2008) and hovers around the cutoffs used in specialized clinics (Orff, Ayalon, & Drummond, 2009), which is consistent with 40% of our sample having a current PTSD diagnosis. The CES-D mean of 20 is above the cutoff score of 16 used to screen for depression in civilian populations (Radloff, 1977) and consistent with 30% of our sample having a current MDD diagnosis. The PSQI Global score of 12 is above the cutoff of 5 in distinguishing poor sleepers (Buysse et al., 1989). Despite identification from primary care visit screens as opposed to from

Table 2
Means, standard deviations, and correlations amongst unadjusted measure scores (N = 279)

	NSI	PCL-C	CES-D	PSQI Global
Mean (SD)	33 (16)	44 (17)	20 (14)	12 (5)
Pearson's correlation coefficients				
PCL-C	0.86**	—	—	—
CES-D	0.78**	0.81**	—	—
PSQI Global	0.60**	0.58**	0.54**	—

**p < 0.01.

Table 3
Mean (and standard deviation) on adjusted outcome and predictor measures

	Entire sample (N = 279)	PTSD/MDD (n = 133)	No PTSD/MDD (n = 146)
Adj NSI	20 (11)	25 (10)	16 (10)
Adj PCL-C	38 (16)	46 (14)	30 (13)
Adj CES-D	16 (13)	22 (12)	10 (10)
Adj PSQI Global	12 (5)	14 (4)	10 (4)
1. Subjective sleep quality	1.85 (0.88)	2.13 (0.77)	1.60 (0.90)
2. Sleep latency	1.90 (1.10)	2.06 (1.06)	1.76 (1.12)
3. Sleep duration	2.12 (0.89)	2.34 (0.78)	1.92 (0.94)
4. Habitual sleep efficiency	1.29 (1.28)	1.53 (1.29)	1.08 (1.24)
5. Adj Sleep disturbances	1.61 (0.59)	1.72 (0.59)	1.51 (0.58)
6. Use of sleeping medication	1.48 (1.40)	1.95 (1.34)	1.04 (1.32)
7. Daytime dysfunction	1.47 (0.92)	1.80 (0.84)	1.16 (0.89)

Adj NSI = adjusted Neurobehavioral Symptom Inventory score. Adj PCL-C = adjusted PTSD Checklist, Civilian version score. Adj CES-D = adjusted Center for Epidemiological Studies, Depression score. Adj PSQI = adjusted Pittsburgh Sleep Quality Index.

a specialized clinic, our sample reported a high level of symptom severity across post-concussive, PTSD, mood, and sleep domains. Table 2 shows that scores reflecting symptom severity across these domains are highly correlated with each other, which makes relevant our question of whether sleep problems contribute unique variance to post-concussive symptoms above and beyond effects of PTSD and mood.

Table 3 reports the means and standard deviations of the Adj NSI, Adj PCL-C, Adj CES-D, Adj PSQI Global and component scores for the entire sample and for subsamples categorized by PTSD/MDD presence. Table 4 summarizes the results of the hierarchical regression to predict post-concussive symptoms (Adj NSI) from PTSD (Adj PCL-C) and depression (Adj CES-D) symptoms using stepwise entry in block 1 and sleep problems (Adj PSQI Global) in block 2. For the entire sample, three models reflecting stepwise selection of each predictor variable were significant, with the Adj PCL-C in model 1, Adj PCL-C and Adj CES-D in model 2, and all three predictors in model 3 (Entire sample). Across all three models, PTSD symptom severity was the most significant contributor to post-concussive symptoms. When Adj PCL-C was the only predictor (Entire sample model 1), the Adj NSI increased by 0.77 standard deviation for every standard deviation change in Adj

PCL-C. Depressive symptom severity (Adj CES-D) also explained a small, albeit significant amount of variance in post-concussive symptoms (Entire sample model 2; 1% change in unadjusted R²). After both PTSD and mood symptoms were accounted for (Entire sample model 3), sleep problems (Adj PSQI Global) contributed an additional 1% variance to post-concussive symptoms, which was statistically significant.

Dividing the sample by PTSD/MDD status showed that the contribution of sleep problems to post-concussive symptoms were driven by those without PTSD or MDD. In the subsample of service members without documentation of current PTSD or MDD in their medical record (No PTSD/MDD model 2), sleep problems contributed 2% to post-concussive symptoms in addition to the variance from PTSD symptom severity (depressive symptoms did not contribute unique variance). For service members with either PTSD and/or MDD diagnosis, their PTSD and depressive symptom severity contributed to their post-concussive symptoms (PTSD/MDD models 1 and 2), but sleep problems did not add additional explanatory power (PTSD/MDD model 3).

To explore the specific sleep problems in the subsample of service members without PTSD or MDD, we replaced block two of the hierarchical regres-

Table 4
Hierarchical regressions to predict post-concussive symptoms (Adj NSI) from PTSD (Adj PCL-C), depression (Adj CES-D), and sleep problems (Adj PSQI Global)

Variable	Entire sample ($N = 279$)			PTSD/MDD ($n = 133$)			No PTSD/MDD ($n = 146$)	
	Model 1 β	Model 2 β	Model 3 β	Model 1 β	Model 2 β	Model 3 β	Model 1 β	Model 2 β
Adj PCL-C	0.77	0.64	0.59	0.64	0.48	0.45	0.77	0.69
Adj CES-D		0.16	0.14		0.23	0.22		
Adj PSQI Global			0.13			0.08		0.16
Adjusted R^2	0.59	0.60	0.61	0.41	0.43	0.43	0.59	0.60
F	399.97**	208.84**	145.72**	91.52**	50.18**	34.04**	205.84**	110.93**
ΔR^2	0.591	0.011	0.012	0.41	0.02	<0.01	0.59	0.02
ΔF	399.98**	7.84**	8.36**	91.52**	5.62*	1.42	205.84**	7.18**

** $p < 0.01$; * $p < 0.05$.

Table 5
Hierarchical regression to explore the type of sleep problems that contributed to post-concussive symptoms (Adj NSI) in service members without PTSD or MDD ($n = 146$)

Variable	Model 1 β	Model 2 β	Model 3 β
Adj PCL-C	0.77	0.65	0.60
Adj CES-D			
PSQI component 7 ^a		0.21	0.18
Adj PSQI component 5 ^b			0.16
Adjusted R^2	0.59	0.61	0.63
F	205.84**	116.18**	83.76**
ΔR^2	0.59	0.03	0.02
ΔF	205.84**	11.50**	7.83**

** $p < 0.01$; * $p < 0.05$. ^aDaytime dysfunction. ^bSleep disturbances, adjusted by excluding disturbances due to dreams.

sion with the seven PSQI component scores using stepwise entry (Table 5). Two PSQI components, daytime dysfunction (component 7) and sleep disturbances (component 5), contributed an additional 4% to post-concussive symptoms above and beyond stress-related issues (models 2 and 3; depressive symptoms did not contribute unique variance). Daytime dysfunction includes difficulty staying awake during activities and having enough enthusiasm to complete tasks. Sleep disturbances include nighttime disturbances that interrupt sleep, such as pain, using the bathroom, breathing difficulties, etc. In contrast, components such as subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, and use of sleeping medication did not explain post-concussive symptoms after stress and mood issues were controlled.

To explore which post-concussive symptoms were vulnerable to the influence of sleep in those without PTSD or MDD, we repeated hierarchical regressions to predict the NSI somatosensory, cognitive, and vestibular cluster scores as the dependent variable (Table 6). Sleep problems only contributed significantly to somatosensory symptoms (Somatosensory model 2), accounting for 4% of the variance in somatosensory symptoms above and beyond con-

tributions from PTSD symptom severity in those without PTSD or MDD (depressive symptoms did not contribute unique variance). Somatosensory symptoms included headaches, nausea, vision problems (blurring, trouble seeing), sensitivity to light, sensitivity to noise, numbness or tingling on parts of the body, and change in taste and/or smell. Sleep problems did not contribute to cognitive symptoms such as poor concentration, forgetfulness, difficulty making decisions, or slowed thinking, after accounting for PTSD and depressive symptom severity (Cognitive model 3). Sleep problems did not contribute to vestibular symptoms such as feeling dizzy, loss of balance, or poor coordination (Vestibular model 2).

4. Discussion

In this sample of active duty service members with a remote history of mild TBI, PTSD symptom severity contributed more unique variance than depressive or sleep problems to post-concussive symptoms. This is consistent with earlier findings that anxiety predicts sleep problems after TBI (Rao et al., 2008) and that PTSD symptoms are strongly associated with post-concussive symptoms (Brenner et al., 2010;

Table 6

Hierarchical regressions to predict NSI cluster scores from PTSD (Adj PCL-C), depression (Adj CES-D), and sleep problems (Adj PSQI Global) in service members without PTSD or MDD ($n = 146$)

Variable	Somatosensory		Cognitive			Vestibular	
	Model 1 β	Model 2 β	Model 1 β	Model 2 β	Model 3 β	Model 1 β	Model 2 β
Adj PCL-C	0.66	0.55	0.68	0.52	0.52	0.43	0.37
Adj CES-D				0.25	0.25		
Adj PSQI Global		0.22			-0.00		0.12
Adjusted R^2	0.43	0.46	0.46	0.50	0.50	0.18	0.19
F	111.00**	63.50**	127.26**	72.99**	48.32**	33.48**	17.89**
ΔR^2	0.43	0.04	0.47	0.04	0.00	0.19	0.01
ΔF	111.00**	9.47**	127.26**	10.41**	0.00	33.48**	2.05

** $p < 0.01$.

Schneiderman, Braver, & Kang, 2008), though others have found that depressive symptoms or psychological distress are significant contributors as well (Lange et al., 2014; Stein et al., 2016). It was not possible to disentangle the overlap between PTSD and depressive symptoms in the present study. In this sample, 47% of service members with a remote history of mild TBI have medical record documentation of either PTSD or MDD, with 20% having both diagnoses. Among those with PTSD and/or MDD, sleep problems did not contribute unique variance to post-concussive symptoms. However, we note that our sample of service members with PTSD or MDD reported significant sleep problems. Table 3 shows mean adjusted PSQI Global score of 14 in those with PTSD/MDD, which is significantly higher than a cut-off of 5 that indicates poor sleep (Buysse et al., 1989). These service members' sleep problems should be conceptualized as part of their PTSD/MDD presentation, and should be incorporated into the overall treatment plan for PTSD or MDD.

For service members with a history of mild TBI and no medical record of PTSD or MDD, sleep problems independently contributed to post-concussive symptoms. This is consistent with Sullivan and colleagues' finding that tiredness, alertness, and sleepiness during waking hours contributed to NSI score amongst a community sample with self-reported history of mild TBI (Sullivan et al., 2016). Interestingly, across both Sullivan et al.'s and our study, among the different types of sleep-related problems examined, daytime dysfunction (e.g., trouble staying awake during the day) contributed statistical variance to NSI score more than other types of sleep problems, suggesting a relationship between post-concussive symptoms and daytime dysfunction that is above and beyond the influence of stress, mood, or other sleep issues.

Post hoc analyses of the type of post-concussive symptoms associated with sleep revealed that somatosensory symptoms but not cognitive or

vestibular symptoms were predicted by sleep problems in service members with a history of mild TBI without PTSD or MDD. Somatosensory symptoms included headaches, light and noise sensitivity, and vision problems. One potential explanation comes from the restorative theory of sleep which posits that the body engages in repair functions during sleep (Adam & Oswald, 1983). This association could reflect suboptimal sensory functioning in individuals with a disrupted restorative process after mild TBI. Alternatively, headaches and sensory sensitivities could also disrupt sleep. Unexpectedly, sleep problems did not contribute to cognitive symptoms such as slowed thinking, concentration difficulty, or forgetfulness. This is in contrast with literature showing that sleep deprivation is associated with cognitive impairment (Durmer & Dinges, 2005). Our patients self-reported sleep problems; we have no objective data on actual sleep habitually achieved. Thus we do not know the degree of sleep deprivation in our sample. Reviews of the sleep literature have consistently shown discrepancies in sleep disturbance when measured by self-report compared to objective tests, where subjective reports of sleep disturbances often are not substantiated by objective polysomnography findings (Mathias & Alvaro, 2012; Orff et al., 2009).

4.1. Clinical implications

For service members with a history of mild TBI but no PTSD or MDD, our data suggests that addressing sleep problems, especially those that contribute to daytime dysfunction and nighttime disturbances such as pain and breathing difficulty may improve somatosensory complaints. Although the 4% variance in post-concussive symptoms associated with sleep problems was statistically significant, it remained undetermined if sleep improvements would affect a clinically meaningful change to patients. PTSD symptom severity was the most significant fac-

tor and explained 59% of variance in post-concussive symptoms in this subsample. The mean Adj PCL-C score of 30 suggests that many in this sample were experiencing subclinical levels of stress-related issues. These patients are most likely to seek treatment from medical providers, in contrast to patients with a co-morbid mental health diagnosis who may be followed by a behavioral health provider. Within a context of myriad health issues tracked by medical providers, for these service members without co-morbid mental health diagnoses who have difficulty with headaches, vision, or sensitivity to light/noise, referrals to improve subclinical stress-related issues via stress management or relaxation and to improve sleep with sleep hygiene or treatment of factors that disrupt sleep (e.g., pain, apnea) may help alleviate these symptoms. These options should be considered and prioritized by medical providers treating these service members. In contrast, for service members with comorbid PTSD and/or MDD, our data suggests that sleep problems should be conceptualized as part of these patients' behavioral health issue. These patients may still need to be referred for sleep evaluations and treatment of medical issues that contribute to sleep problems, but their sleep should be monitored within a context of overall mental health.

4.2. Limitations and strengths

Conclusions are limited by some methodological shortcomings. First, our sample had an unequal gender distribution that reflected the composition of the military, and accordingly our conclusions, while appropriate for military populations, may not generalize to female or civilian populations. Second, our primary sleep measure was a self-report of sleep habits and complaints, which may differ from objective measures of sleep and was vulnerable to response bias. We excluded from our sample participants who may have engaged in symptom exaggeration, but perception of sleep is known to differ from actual sleep architecture and from formal diagnoses of sleep disorders (Mathias & Alvaro, 2012; Orff et al., 2009). Objective measures of sleep habitually achieved will inform the degree of chronic sleep deprivation and may yield different findings. Our conclusions pertained to perceived sleep quality without information on actual sleep architecture or sleep disorder diagnosis. Third, because PTSD and MDD diagnoses were obtained from medical records, we could not verify that all clinicians based their diagnosis on DSM criteria. However, concurrent documentation of these

disorders in an electronic medical record was deemed to engender more confidence than self-report alone given that patients are often unaware of the conceptualization for their treatment. A strength of this study was that our conclusions apply to a general population of service members because our sample was recruited from primary care clinics rather than from specialty TBI clinics.

Acknowledgments

We would like to acknowledge the hard work of our research team, John Bruno, Maria Lara, Jennifer Tsagaratos, Cynthia Muncy, Jody Warren and Felix Leal, and the many service members who have participated in this study, without whom this research would not have been possible.

The views expressed herein are those of the authors and do not reflect the official policy or position of Brooke Army Medical Center, The US Army Medical Department, the US Army Office of the Surgeon General, The Department of the Air Force, the Department of the Army, the Department of Defense, or the U.S. Government.

Conflict of interest

No authors have conflicts of interest to declare.

Funding

Funding for all authors were received from the Defense and Veterans Brain Injury Center (W91 YZT-13-C-0015 25Mar2019).

References

- Adam, K., & Oswald, I. (1983). Protein synthesis, bodily renewal and the sleep-wake cycle. *Clin Sci (Lond)*, 65(6), 561-567.
- Bliese, P. D., Wright, K. M., Adler, A. B., Cabrera, O., Castro, C. A., & Hoge, C. W. (2008). Validating the primary care posttraumatic stress disorder screen and the posttraumatic stress disorder checklist with soldiers returning from combat. *J Consult Clin Psychol*, 76(2), 272-281. doi:10.1037/0022-006X.76.2.272
- Brenner, L. A., Ivins, B. J., Schwab, K., Warden, D., Nelson, L. A., Jaffee, M., & Terrio, H. (2010). Traumatic brain injury, post-traumatic stress disorder, and postconcussive symptom reporting among troops returning from Iraq. *J Head Trauma Rehabil*, 25(5), 307-312. doi:10.1097/HTR.0b013e3181cada03

- Buyse, D. J., Reynolds, C. F., 3rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Res*, 28(2), 193-213.
- Carlson, K. F., Kehle, S. M., Meis, L. A., Greer, N., Macdonald, R., Rutks, L.,... Wilt, T. J. (2011). Prevalence, assessment, and treatment of mild traumatic brain injury and posttraumatic stress disorder: A systematic review of the evidence. *J Head Trauma Rehabil*, 26(2), 103-115. doi:10.1097/HTR.0b013e3181e50ef1
- Carpenter, J. S., & Andrykowski, M. A. (1998). Psychometric evaluation of the Pittsburgh Sleep Quality Index. *J Psychosom Res*, 45(1), 5-13.
- DeGutis, J., Chiu, C., Thai, M., Esterman, M., Milberg, W., & McGlinchey, R. (2018). Trauma Sequelae are Uniquely Associated with Components of Self-Reported Sleep Dysfunction in OEF/OIF/OND Veterans. *Behav Sleep Med*, 16(1), 38-63. doi:10.1080/15402002.2016.1173550
- Department of Veterans Affairs and Department of Defense (2016). VA/DoD Clinical Practice Guideline for the Management of Concussion-Mild Traumatic Brain Injury. 23 May 2019, URL: <https://www.healthquality.va.gov/guidelines/Rehab/mtbi/mTBICPGFullICPG50821816.pdf>
- Durmer, J. S., & Dinges, D. F. (2005). Neurocognitive consequences of sleep deprivation. *Semin Neurol*, 25(1), 117-129. doi:10.1055/s-2005-867080
- Gosselin, N., Lassonde, M., Petit, D., Leclerc, S., Mongrain, V., Collie, A., & Montplaisir, J. (2009). Sleep following sport-related concussions. *Sleep Med*, 10(1), 35-46. doi:10.1016/j.sleep.2007.11.023
- Hoge, C. W., McGurk, D., Thomas, J. L., Cox, A. L., Engel, C. C., & Castro, C. A. (2008). Mild traumatic brain injury in U.S. Soldiers returning from Iraq. *N Engl J Med*, 358(5), 453-463. doi:10.1056/NEJMoa072972
- Holcomb, E. M., Towns, S., Kamper, J. E., Barnett, S. D., Sherer, M., Evans, C., & Nakase-Richardson, R. (2016). The Relationship Between Sleep-Wake Cycle Disturbance and Trajectory of Cognitive Recovery During Acute Traumatic Brain Injury. *J Head Trauma Rehabil*, 31(2), 108-116. doi:10.1097/HTR.0000000000000206
- Kessler, R. C., Sonnega, A., Bromet, E., Hughes, M., & Nelson, C. B. (1995). Posttraumatic stress disorder in the National Comorbidity Survey. *Arch Gen Psychiatry*, 52(12), 1048-1060.
- King, P. R., Donnelly, K. T., Donnelly, J. P., Dunnam, M., Warner, G., Kittleson, C. J.,... Meier, S. T. (2012). Psychometric study of the Neurobehavioral Symptom Inventory. *J Rehabil Res Dev*, 49(6), 879-888.
- King, P. R., Donnelly, K. T., Warner, G., Wade, M., & Pigeon, W. R. (2017). The natural history of sleep disturbance among OEF/OIF veterans with TBI and PTSD and the role of proxy variables in its measurement. *J Psychosom Res*, 96, 60-66. doi:10.1016/j.jpsychores.2017.03.012
- Kobayashi, I., Boarts, J. M., & Delahanty, D. L. (2007). Polysomnographically measured sleep abnormalities in PTSD: A meta-analytic review. *Psychophysiology*, 44(4), 660-669. doi:10.1111/j.1469-8986.2007.537.x
- Lange, R. T., Brickell, T. A., Kennedy, J. E., Bailie, J. M., Sills, C., Asmussen, S.,... French, L. M. (2014). Factors influencing postconcussion and posttraumatic stress symptom reporting following military-related concurrent polytrauma and traumatic brain injury. *Arch Clin Neuropsychol*, 29(4), 329-347. doi:10.1093/arclin/acu013
- Lew, H. L., Poole, J. H., Vanderploeg, R. D., Goodrich, G. L., Dekelboum, S., Guillory, S. B.,... Cifu, D. X. (2007). Program development and defining characteristics of returning military in a VA Polytrauma Network Site. *J Rehabil Res Dev*, 44(7), 1027-1034.
- Lind, M. J., Brown, E., Farrell-Carnahan, L., Brown, R. C., Hawn, S., Berenz, E.,... Amstadter, A. B. (2017). Sleep Disturbances in OEF/OIF/OND Veterans: Associations with PTSD, Personality, and Coping. *J Clin Sleep Med*, 13(2), 291-299. doi:10.5664/jcsm.6466
- Martindale, S. L., Morissette, S. B., Rowland, J. A., & Dolan, S. L. (2017). Sleep quality affects cognitive functioning in returning combat veterans beyond combat exposure, PTSD, and mild TBI history. *Neuropsychology*, 31(1), 93-104. doi:10.1037/neu0000312
- Mathias, J. L., & Alvaro, P. K. (2012). Prevalence of sleep disturbances, disorders, and problems following traumatic brain injury: A meta-analysis. *Sleep Med*, 13(7), 898-905. doi:10.1016/j.sleep.2012.04.006
- Mollayeva, T., Colantonio, A., Cassidy, J. D., Vernich, L., Moineddin, R., & Shapiro, C. M. (2017). Sleep stage distribution in persons with mild traumatic brain injury: A polysomnographic study according to American Academy of Sleep Medicine standards. *Sleep Med*, 34, 179-192. doi:10.1016/j.sleep.2017.02.021
- Norris, F. H., & Hamblen, J. L. (2003). Standardized self-report measures of civilian trauma and PTSD. In J. Wilson & T. Keane (Eds.), *Assessing Psychological Trauma and PTSD: A Practitioner's Handbook* (Second ed., pp. 63-102). New York: Guilford.
- Orff, H. J., Ayalon, L., & Drummond, S. P. (2009). Traumatic brain injury and sleep disturbance: A review of current research. *J Head Trauma Rehabil*, 24(3), 155-165. doi:10.1097/HTR.0b013e3181a0b281
- Pogoda, T. K., Hendricks, A. M., Iverson, K. M., Stolzmann, K. L., Krengel, M. H., Baker, E.,... Lew, H. L. (2012). Multi-sensory impairment reported by veterans with and without mild traumatic brain injury history. *J Rehabil Res Dev*, 49(7), 971-984.
- Radloff, L. S. (1977). The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Applied Psychological Measurement*, 1(3), 385-401.
- Rao, V., Spiro, J., Vaishnavi, S., Rastogi, P., Mielke, M., Noll, K.,... Makley, M. (2008). Prevalence and types of sleep disturbances acutely after traumatic brain injury. *Brain Inj*, 22(5), 381-386. doi:10.1080/02699050801935260
- Schneiderman, A. I., Braver, E. R., & Kang, H. K. (2008). Understanding sequelae of injury mechanisms and mild traumatic brain injury incurred during the conflicts in Iraq and Afghanistan: Persistent postconcussive symptoms and post-traumatic stress disorder. *Am J Epidemiol*, 167(12), 1446-1452. doi:10.1093/aje/kwn068
- Scholten, A. C., Haagsma, J. A., Cnossen, M. C., Olf, M., van Beeck, E. F., & Polinder, S. (2016). Prevalence of and Risk Factors for Anxiety and Depressive Disorders after Traumatic Brain Injury: A Systematic Review. *J Neurotrauma*, 33(22), 1969-1994. doi:10.1089/neu.2015.4252
- Schreiber, S., Barkai, G., Gur-Hartman, T., Peles, E., Tov, N., Dolberg, O. T., & Pick, C. G. (2008). Long-lasting sleep patterns of adult patients with minor traumatic brain injury (mTBI) and non-mTBI subjects. *Sleep Med*, 9(5), 481-487. doi:10.1016/j.sleep.2007.04.014

- Soble, J. R., Silva, M. A., Vanderploeg, R. D., Curtiss, G., Belanger, H. G., Donnell, A. J., & Scott, S. G. (2014). Normative Data for the Neurobehavioral Symptom Inventory (NSI) and post-concussion symptom profiles among TBI, PTSD, and nonclinical samples. *Clin Neuropsychol*, 28(4), 614-632. doi:10.1080/13854046.2014.894576
- Stein, M. B., Ursano, R. J., Campbell-Sills, L., Colpe, L. J., Fullerton, C. S., Heeringa, S. G., . . . Kessler, R. C. (2016). Prognostic Indicators of Persistent Post-Concussive Symptoms after Deployment-Related Mild Traumatic Brain Injury: A Prospective Longitudinal Study in U.S. Army Soldiers. *J Neurotrauma*, 33(23), 2125-2132. doi:10.1089/neu.2015.4320
- Sullivan, K. A., Berndt, S. L., Edmed, S. L., Smith, S. S., & Allan, A. C. (2016). Poor sleep predicts subacute postconcussion symptoms following mild traumatic brain injury. *Appl Neuropsychol Adult*, 23(6), 426-435. doi:10.1080/23279095.2016.1172229
- Vanderploeg, R. D., Cooper, D. B., Belanger, H. G., Donnell, A. J., Kennedy, J. E., Hopewell, C. A., & Scott, S. G. (2014). Screening for postdeployment conditions: Development and cross-validation of an embedded validity scale in the neurobehavioral symptom inventory. *J Head Trauma Rehabil*, 29(1), 1-10. doi:10.1097/HTR.0b013e318281966e
- Vanderploeg, R. D., Silva, M. A., Soble, J. R., Curtiss, G., Belanger, H. G., Donnell, A. J., & Scott, S. G. (2015). The structure of postconcussion symptoms on the Neurobehavioral Symptom Inventory: A comparison of alternative models. *J Head Trauma Rehabil*, 30(1), 1-11. doi:10.1097/HTR.000000000000009
- Weathers, F., Litz, B., Herman, D., Huska, J., & Keane, T. (1993). The PTSD Checklist (PCL): *Reliability, Validity, and Diagnostic Utility*. Paper presented at the Annual Convention of the International Society for Traumatic Stress Studies, San Antonio, TX.
- Williams, B. R., Lazic, S. E., & Ogilvie, R. D. (2008). Polysomnographic and quantitative EEG analysis of subjects with long-term insomnia complaints associated with mild traumatic brain injury. *Clin Neurophysiol*, 119(2), 429-438. doi:10.1016/j.clinph.2007.11.003