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The bi-directional relationship between post-traumatic stress disorder and obstructive sleep apnea and/or insomnia in a large U.S. military cohort

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ABSTRACT

Objectives: Determine if a bi-directional relationship exists between the development of sleep disorders (obstructive sleep apnea [OSA] and/or insomnia) and existing post-traumatic stress disorder (PTSD), and vice versa; and examine military-related factors associated with these potential relationships.
Design: Longitudinal analyses of a prospective representative U.S. military cohort.
Participants: Millennium Cohort Study responders in 2011-2013 (Time 1 [T1]) and 2014-2016 (Time 2 [T2]) without insomnia or OSA at T1 (N = 65,915) or without PTSD at T1 (N = 71,256).
Measurements: Provider-diagnosed OSA, self-reported items for insomnia, provider-diagnosed PTSD, and current PTSD symptoms were assessed at T1 and T2. Adjusted multivariable models identified military-related factors associated with new-onset PTSD in those with OSA and/or insomnia, and vice versa.
Results: Self-reported history of provider-diagnosed PTSD without current symptoms at T1 was associated with new-onset OSA only and comorbid OSA/insomnia at T2, while current PTSD symptoms and/or diagnosis was associated with new-onset insomnia only. OSA/insomnia at T1 was consistently associated with newly reported PTSD symptoms or diagnosis except that insomnia only was not associated with newly reported provider-diagnosed PTSD. Military-related risk factors significantly associated with the bi-directional relationship for new-onset PTSD or OSA/insomnia included prior deployment with higher combat exposure and recent separation from the military; being an officer was protective for both outcomes.
Conclusions: In this large military cohort, findings suggest that PTSD and OSA and/or insomnia are bi-directionally predictive for their development, which was sometimes revealed by health care utilization. Relevant military-related risk factors should be considered in efforts to prevent or treat PTSD and/or sleep disorders.

Introduction

Post-traumatic stress disorder (PTSD) is among the most serious conditions affecting service members and veterans, with high rates over the past 2 decades since the increase in U.S. military combat operations overseas.[1-3] Those with PTSD may suffer many comorbid problems after the initial trauma that worsen their physical and mental health for years afterward.[2,4] Common symptoms of PTSD include mental replay of the traumatic events, heightened stress response, and altered brain activity.[5-8] These symptoms can manifest at night, disrupt bedtime routines, and negatively impact sleep, leading to a variety of sleep disorders.[9,10] With the demanding and stressful conditions required of military service (eg, continuous operations day and night, frequent travel, intensive training, long-duration work shifts, and uncomfortable sleeping conditions), regularly achieving healthy sleep while actively serving, especially during or after deployment, is challenging.[9,11] Thus, the conditions inherent to military service may contribute to high rates of sleep disorders in military populations.[9,11-13]

Beyond the essential role sleep plays in alertness and performance, sleep also impacts short- and long-term health outcomes, with insufficient or poor-quality sleep raising the risk for physical and mental

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health disorders, including PTSD.[5,7,8,11,14] Sleep disorders additionally may emerge as a consequence of PTSD; thus, there is a bi-directional relationship that, unless treated early, may cause a positive feedback loop, perpetuating a cycle of ever-worsening comorbid PTSD and sleep disorders.[5-8] Several studies have examined risk factors for PTSD and sleep disorders in military members and found associations with deployment and combat exposure.[1,4,9,15-19] However, the longitudinal relationships between PTSD and sleep disorders, and the military-related factors that predict their development, are not well established. Determining which military-related factors predict new-onset cases could help in targeting future screening and treatment efforts for PTSD and sleep disorders in military populations.

OSA and insomnia are 2 of the most prevalent and costly sleep disorders, are often comorbid, and have been associated with PTSD in military populations.[9,12-16,18-21] We utilized data from the largest tri-service longitudinal survey of U.S. military members and veterans at 2 time points to address 2 main aims: (1) determine if a bi-directional relationship exists between sleep disorders and PTSD, such that PTSD is associated with the onset of OSA and/or insomnia, and vice versa, and (2) examine military-related factors associated with this potential relationship.

Participants and methods

Study population

Participants were from the Millennium Cohort Study, the largest, longitudinal military study tracking over 200,000 U.S. service members and veterans since 2001.[22] Participants were recruited in 4 separate panels between 2001 and 2013, with paper or web-based follow-up surveys occurring every 3-5 years since baseline. The current study uses data from the 2011-2013 (Time 1 [T1]) and 2014-2016 (Time 2 [T2]) Millennium Cohort survey waves to examine the reciprocal, longitudinal relationship between PTSD and OSA and/or insomnia, referred to throughout the rest of the paper as "OSA/insomnia." This study was approved by the Naval Health Research Center Institutional Review Board and all participants provided informed consent.

Supplemental data describing the prevalence of OSA and PTSD among the full cohort of participants who responded to the T1 (N = 138,949) *or* T2 (N = 112,655) surveys are presented in Supplemental Table 1, with specific sample sizes of participants by service status (active duty, Reserve/Guard, or veteran). Sample sizes for insomnia at T1 and T2 in this population have been previously reported.[23]

The base sample for these analyses was drawn from participants who completed both T1 *and* T2 surveys (N = 98,359). Participants were excluded if they were missing on PTSD at T1 (n = 2029), OSA at T1 (n = 530), insomnia at T1 (n = 2092), PTSD at T2 (n = 8987), OSA at T2 (n = 459), or insomnia at T2 (n = 1830), resulting in an eligible sample of 82,432 participants. Exclusion criteria for the bi-directional relationships examined in these analyses are reported below.

Analytic Sample

PTSD at T1 Predicting New-Onset OSA/Insomnia at T2

Of the eligible sample, 8.4% (n = 6938) of participants had existing OSA at T1 and an additional 11.6% (n = 9579) had existing insomnia at T1 (ie, Insomnia Severity Index [ISI] score ≥15) and were excluded from the population. This resulted in an analytic sample size of 65,915.

OSA/insomnia at T1 predicting new-onset PTSD at T2

Of the eligible sample, 13.6% (n = 11,176) of participants screened positive for PTSD and/or reported being diagnosed with PTSD at T1 and were excluded from the population. This resulted in an analytic sample size of 71,256.

Study measures

OSA and/or insomnia

OSA was assessed via a self-reported item asking participants if a doctor had told them they *ever* had sleep apnea at T1, or in the previous 3 years at T2. Insomnia was assessed as a positive screen using the 7-item ISI, which measures the severity of insomnia symptoms in the last 2 weeks.[24] Items were summed for a total ISI score (range: 0-28) and dichotomized using a cut point of 15, where ≥15 represented a positive screen for insomnia. The cut point of 15 has been established[24] for classifying those with probable cases of "moderate" or "severe" insomnia (vs. no insomnia or only "sub-threshold" insomnia), and was utilized in our previous study on insomnia in the same cohort[23] and in another recent active duty sample.[25] If participants were missing 1 item on the ISI, this missing item was replaced with an item that was calculated via multiple imputation and summed with the other 6 items to obtain the overall ISI score. Participants missing more than 1 ISI item had their score set to missing and were not included in these analyses.

OSA and insomnia were combined into a single 4-level item at each time point, classified as having neither OSA nor insomnia, OSA only, insomnia only, or both OSA and insomnia. New-onset OSA/insomnia at T2 was assessed among those who did not have OSA or insomnia at T1.

PTSD

A positive screen for current PTSD symptoms was assessed using the 17 item PTSD Checklist-Civilian Version (PCL-C), classified using Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition specific criteria (ie, endorsing moderate or greater on ≥1 intrusion items, ≥2 hyperarousal symptoms, and ≥3 avoidance symptoms).[26,27] Participants also self-reported if they had *ever* been diagnosed with PTSD by a doctor at T1, or in the past 3 years at T2. Participants were categorized using 4 levels: (1) no current PTSD symptoms or self-reported diagnosis, (2) current PTSD symptoms only (positive screen on the PCL-C), (3) self-reported PTSD diagnosis only, or (4) current PTSD symptoms *and* self-reported diagnosis. New-onset PTSD at T2 was assessed among those who did not have PTSD symptoms or a self-reported diagnosis at T1.

Other exposures of interest

Military factors

Combat deployment was assessed based on Defense Manpower Data Center (DMDC) records of deployments in support of the operations in Iraq and Afghanistan prior to T2 and survey responses to 13 items at T1 and T2 assessing combat-related experiences during deployment (eg, being attacked or ambushed, being wounded or injured), categorized as having never deployed, deployed with no combat (0 combat exposures), deployed with low combat (≤3 combat exposures), or deployed with medium-to-high combat (≥4 combat exposures).[28] The number of deployments between T1 and T2 were categorized as 0, 1, or ≥2 deployments. The average length of deployment between T1 and T2 was compared with the participant's service branch's average length of deployment (in months: Army=9, Navy=6, Marine Corps=8, and Air Force=4)[29] and categorized as at or above branch average (yes or no).

Military characteristics at T1 (service component, service branch, pay grade, military occupation, and time in service) and separation status prior to T2 were obtained from DMDC records.

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Demographic and behavioral characteristics at T1

Participants' age, sex, and race/ethnicity were obtained from DMDC records. Marital status, education level, and all behavioral characteristics were self-reported.

The mental and physical component summary scores from the Short Form 36 Health Survey for Veterans (SF-36V)[30,31] were used as global measures of mental and physical health. Experiences of 5 life stressors in the past 3 years (sexual assault, sexual harassment, physical assault, divorce or separation, major financial problems) were measured using the Social Readjustment Rating Scale,[32] based on the documented relationship between stress and mental health and stress and sleep challenges.[33] Since substance use is associated with sleep issues and mental health,[34] heavy weekly drinking and smoking status were assessed. Men who reported consuming >14 drinks/week and women who reported consuming >7 drinks/week were considered heavy weekly drinkers[35]; and tobacco use was categorized as current, former, or never smoker. Finally, self-reported physician-diagnosed traumatic brain injury (TBI) in the past 3 years (not including injuries that had resulted in a concussion only) was examined at T2 based on prior reports of TBI being associated with mental health and sleep.[36]

Statistical analyses

Prevalence estimates for T1 and new-onset PTSD and OSA/insomnia and descriptive frequencies of military and demographic characteristics for each analytic sample were reported. Multiple imputation was used among the largest base sample of those responding at T1 and T2 (N = 98,359) to generate 10 datasets with missing covariates imputed. This population was subset to the eligible population (n = 82,432) based on missing outcome variables (OSA, PTSD, insomnia), and then further subset to the analytic new-onset populations at T2 for OSA/insomnia (n = 65,915) and PTSD symptoms/diagnosis (n = 71,256). As it is not recommended to use multiple imputation for outcomes,[37] we did not impute OSA, insomnia (among those missing 2 or more items), or PTSD at the scale level and instead used complete case deletion to address missingness among outcome variables. Among the base population (N = 98,359), the percent missing among covariates prior to multiple imputation ranged between 0 and 7.76%. All statistical models were calculated among each imputed dataset and the reported results were pooled across the 10 imputed datasets.[38] Factors associated with attrition in this sample (eg, age, education, sex)[39] were included in the multiple imputation model to reduce bias due to missing data.[40] Logistic regression models examined whether PTSD at T1, military experiences (combat deployment before T2, separation status at T2, number and length of deployments between T1 and T2), and military characteristics (service branch, pay grade, service component, occupation) predicted new-onset OSA/insomnia at T2. Models were adjusted for all demographic and behavioral characteristics and controlled for time in service and follow-up time. Similarly, additional adjusted logistic regression models examined whether OSA/insomnia at T1, military experiences, and military characteristics predicted new-onset PTSD at T2. All analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC).

Sensitivity analyses

To determine the reliability of self-reported OSA, inpatient and outpatient records from the Military Health System Data Repository (MDR) identified potential diagnosed cases of OSA among active duty personnel at T1 who appeared in MDR records at any time between 2000 and 2016 (n = 46,394). Case definitions of OSA within MDR records were classified based on Armed Forces Health Surveillance Branch guidelines.[41] The prevalence of OSA and proportion of observed agreement between self-reported and MDR records were examined. To further determine the level of agreement between both methods, Cohen's kappa coefficient (affected by prevalence) and positive and negative agreement (less affected by prevalence) were calculated at each time point.[42]

Results

Descriptive statistics: OSA/insomnia and PTSD

Among participants who did not have OSA/insomnia at T1 (N = 65,915), 2.2% had current PTSD symptoms, 3.1% had a self-reported provider PTSD diagnosis, and 1.1% had current symptoms and a diagnosis. At T2, 5.1% reported new OSA only, 4.1% reported new insomnia only, and 0.9% reported both new OSA and new insomnia (Table 1). Among those who did not have current PTSD symptoms or diagnosis at T1 (N = 71,256), 5.3% reported OSA only, 6.7% screened positive for insomnia only, and 1.3% had comorbid OSA and insomnia. At T2, 3.9% developed PTSD symptoms, 2.9% newly reported provider-diagnosed PTSD, and 2.1% newly reported symptoms and a diagnosis (Table 1).

Descriptive statistics: Military characteristics and demographics

The sample for these 2 populations were similar in terms of military experiences and characteristics, as well as demographics

Table 1
Descriptive frequencies for PTSD and OSA and/or insomnia symptoms among Millennium Cohort Study participants for each analytic population

	Analytic sample: PTSD at T1 predicting OSA/insomnia at T2, N = 65,915		Analytic sample: OSA/insomnia at T1 predicting PTSD at T2, N = 71,256	
Prevalence of PTSD and OSA/insomnia	PTSD at T1	New onset OSA/insomnia at T2	OSA/insomnia at T1	New onset PTSD at T2
	n (%)	n (%)	n (%)	n (%)
PTSD				
No symptoms or self-reported diagnosis	61,699 (93.6)			64,987 (91.2)
Current symptoms (PCL) only	1419 (2.2)			2740 (3.9)
Diagnosis (self-reported) only	2056 (3.1)			2052 (2.9)
Current symptoms and diagnosis	741 (1.1)			1477 (2.1)
OSA and/or insomnia				
No OSA or insomnia		59,254 (89.9)	61,699 (86.6)	
OSA only		3382 (5.1)	3808 (5.3)	
Insomnia only		2686 (4.1)	4803 (6.7)	
OSA and insomnia		593 (0.9)	946 (1.3)	

OSA, obstructive sleep apnea; PCL, PTSD Checklist-Civilian Version; PTSD, post-traumatic stress disorder; T1, Time 1 (2011-2013); T2, Time 2 (2014-2016).

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Table 2
Descriptive frequencies for military experiences and characteristics and demographics among Millennium Cohort Study participants for each analytic population

	Analytic sample: PTSD at T1 predicting OSA/insomnia at T2, N = 65,915	Analytic sample: OSA/insomnia at T1 predicting PTSD at T2, N = 71,256
Military experiences and characteristics	%	%
Combat deployment before T1		
Never deployed	41.6	43.2
Deployed, no combat	33.1	32.6
Deployed, low combat	12.0	11.8
Deployed, medium-to-high combat	13.2	12.4
Separation status		
On active service at T2	48.1	46.5
Separated before T1	38.8	40.2
Separated between T1 and T2	13.1	13.4
No. of deployments, T1-T2		
0	80.6	81.2
1	13.0	12.6
2 or more	6.4	6.2
Deployed equal to or longer than branch average from T1 to T2[a]		
No	94.1	94.2
Yes	5.9	5.8
Service component		
Reserve/Guard	45.6	44.7
Active duty	54.4	55.3
Service branch		
Army	41.8	41.4
Navy/Coast Guard	18.6	19.1
Marine Corps	7.3	7.0
Air Force	32.3	32.4
Pay grade		
Enlisted	69.0	69.4
Officer	31.0	30.6
Occupation		
Combat specialist	18.3	17.9
Functional support/admin	17.9	18.2
Healthcare	13.2	12.8
Other	50.7	51.1
Demographic characteristics at T1	%	%
Age, y		
<25	6.9	6.7
25-34	45.4	43.0
35-44	21.1	21.3
45+	26.6	29.0
Sex		
Male	70.3	71.0
Female	29.8	29.0
Race/ethnicity		
White	78.5	78.0
Black	8.5	9.0
Other	12.9	13.0
Marital status		
Single	20.1	19.3
Married	67.1	68.0
Separated/divorced/widowed	12.8	12.8
Education level		
Associates degree or less	51.6	51.9
Bachelor's degree or higher	48.4	48.2

OSA, obstructive sleep apnea; PTSD, post-traumatic stress disorder; T1, Time 1 (2011-2013); T2, Time 2 (2014-2016).
All military and demographic characteristics are assessed at T1 unless otherwise specified.
[a] Average deployment lengths for each branch: Army = 9 months, Navy/Coast Guard = 6 months, Marine Corps = 8 months, Air Force = 4 months. No (less than branch average) category also includes individuals who did not deploy during the time frame.

(Table 2). Over half the sample deployed before T1 and were separated from military service before the end of the study, and most did not deploy between T1 and T2. The majority of both samples were active duty (vs. Reserve/Guard), serving in the Army or Air Force, enlisted members, and serving in occupations other than combat specialist, functional support/administrative, or healthcare. This sample was predominantly younger (<35 years), male, non-Hispanic White and married (Table 2). The mean length of follow-up for participants between T1 and T2 was 3.4 years (SD: 0.6, range: 1.0-5.4).

Adjusted models: PTSD at T1 predicting new-onset OSA/insomnia at T2

In adjusted models examining whether PTSD at T1 predicted new-onset OSA and/or insomnia at T2 (Table 3), participants with a PTSD diagnosis at T1 were significantly more likely to develop OSA only or both OSA and insomnia at T2 compared with those who did not have PTSD symptoms or diagnosis at T1. Those with current PTSD symptoms, a diagnosis, or both were more likely to develop insomnia without OSA compared with individuals without PTSD symptoms or

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Table 3
Adjusted associations for new-onset OSA and insomnia symptoms at T1 among Millennium Cohort Study participants without OSA or insomnia at T1, N = 65,915

Variables at T1[a]	Adjusted ORs of new-onset OSA/insomnia at T2 (ref: Neither)		
	New-onset OSA only, n = 3382 OR (95% CI)	New-onset insomnia only, n = 2686 OR (95% CI)	New-onset OSA and insomnia, n = 593 OR (95% CI)
PTSD			
PTSD at T1			
No symptoms or diagnosis	Ref	Ref	Ref
Symptoms (PCL) only	1.09 (0.85-1.39)	**1.27 (1.06-1.54)**	1.34 (0.90-1.99)
Diagnosis (self-reported) only	**1.50 (1.26-1.79)**	**1.71 (1.46-2.01)**	**1.67 (1.21-2.30)**
Symptoms and diagnosis	1.26 (0.94-1.70)	**1.41 (1.12-1.78)**	1.39 (0.88-2.19)
Military experiences			
Combat deployment before T1			
Never deployed	Ref	Ref	Ref
Deployed, no combat	**1.14 (1.04-1.25)**	0.94 (0.85-1.04)	1.02 (0.81-1.27)
Deployed, low combat	1.11 (0.97-1.26)	1.02 (0.89-1.18)	1.20 (0.89-1.62)
Deployed, medium-to-high combat	**1.26 (1.11-1.43)**	**1.40 (1.24-1.59)**	**1.62 (1.25-2.11)**
Separation status			
On active service at T2	Ref	Ref	Ref
Separated before T1	**0.88 (0.79-0.99)**	1.01 (0.90-1.13)	**0.77 (0.59-1.00)**
Separated between T1 and T2	**2.41 (2.18-2.66)**	**1.61 (1.44-1.80)**	**3.18 (2.59-3.92)**
No. of deployments, T1-T2			
0	Ref	Ref	Ref
1	1.03 (0.89-1.19)	1.06 (0.91-1.24)	1.00 (0.73-1.37)
2 or more	0.94 (0.79-1.12)	1.13 (0.93-1.38)	0.90 (0.59-1.39)
Deployed equal to or longer branch average from T1 to T2[b]			
No	0.93 (0.77-1.12)	**0.78 (0.64-0.96)**	0.76 (0.51-1.15)
Yes	Ref	Ref	Ref
Military characteristics			
Service component			
Reserve/Guard	**0.66 (0.61-0.72)**	**0.89 (0.82-0.98)**	0.87 (0.73-1.05)
Active duty	Ref	Ref	Ref
Service branch			
Army	**1.12 (1.02-1.22)**	**1.44 (1.29-1.61)**	**1.56 (1.24-1.96)**
Navy/Coast Guard	1.07 (0.96-1.19)	**1.28 (1.12-1.46)**	1.30 (0.98-1.72)
Marine Corps	0.96 (0.81-1.14)	**1.63 (1.38-1.91)**	1.18 (0.81-1.72)
Air Force	Ref	Ref	Ref
Pay grade			
Enlisted	Ref	Ref	Ref
Officer	**0.77 (0.69-0.85)**	**0.60 (0.52-0.69)**	**0.63 (0.48-0.83)**
Occupation			
Combat specialist	Ref	Ref	Ref
Functional support/admin	**1.28 (1.13-1.44)**	1.04 (0.90-1.21)	1.16 (0.88-1.54)
Healthcare	**1.38 (1.20-1.59)**	1.00 (0.85-1.17)	0.92 (0.66-1.30)
Other	**1.17 (1.06-1.30)**	1.10 (0.97-1.24)	1.01 (0.80-1.28)

CI, confidence interval; OR, odds ratio; OSA, obstructive sleep apnea; PCL, PTSD Checklist-Civilian Version; PTSD, post-traumatic stress disorder; T1, Time 1 (2011-2013); T2, Time 2 (2014-2016).
Logistic regression model is further adjusted for age, sex, race/ethnicity, marital status, education level, heavy weekly drinking, smoking status, life stressors, diagnosed traumatic brain injury at T2, mental component score, physical component score, time in service at T1, and follow-up time between T1 and T2. All ORs and CIs represent pooled estimates across multiple imputation models.
Bolded values are statistically significant ($p < .05$).
[a] All variables are assessed at T1 unless otherwise specified.
[b] Average deployment lengths for each branch: Army = 9 months, Navy/Coast Guard = 6 months, Marine Corps = 8 months, Air Force = 4 months. No (less than branch average) category also includes individuals who did not deploy during the time frame.

diagnosis at T1. Being deployed with medium-to-high combat exposure (vs. never being deployed), separating from service between T1 and T2 (vs. remaining on active service), and serving in the Army (vs. Air Force) predicted new-onset OSA only, insomnia only, or comorbid conditions at T2. Being an officer (vs. enlisted) was protective against the development of these 3 outcomes. Factors that predicted new-onset OSA only included deployment without combat (vs. not deploying) and serving in non-combat occupations (eg functional support/administration and health care). Factors that predicted new-onset insomnia only included serving in the Navy or Marine Corps (vs. Air Force). Reserve/Guard component (vs. active duty) was protective for new-onset OSA only and insomnia only. Adjusted associations between demographic characteristics at T1 and new-onset OSA and/or insomnia at T2 are presented in Supplemental Table 2.

Adjusted models: OSA/insomnia at T1 predicting new-onset PTSD at T2

In adjusted models examining whether OSA and/or insomnia at T1 predicted new-onset PTSD at T2 (Table 4), participants with OSA only, insomnia only, and both OSA and insomnia were significantly more likely to develop PTSD symptoms, newly report a diagnosis, or both compared with those who had neither OSA nor insomnia at T1. One exception was that the measure of effect for those with insomnia only predicting a PTSD diagnosis was not statistically significant. Being deployed with or without combat exposure before T2 (vs. never deploying), separating from service before T1 *or* between T1 and T2 (vs. remaining on active service), and serving in the Army, Navy, or Marine Corps (vs. Air Force; except Navy was not statistically significant for newly reported PTSD diagnosis only) predicted new-

Table 4
Adjusted associations for new-onset PTSD at T2 among Millennium Cohort Study participants without PTSD at T1 (N = 71,256)

Variables[a]	New-onset PTSD at T2 (ref: No symptoms or diagnosis)		
	Symptoms (PCL) only, n = 2740 OR (95% CI)	Diagnosis (self-reported) only, n = 2052 OR (95% CI)	Symptoms and diagnosis, n = 1477 OR (95% CI)
OSA and insomnia			
OSA/insomnia at T1			
Neither	Ref	Ref	Ref
OSA only	**1.23 (1.02-1.47)**	**1.68 (1.40-2.01)**	**1.29 (1.01-1.65)**
Insomnia only	**1.60 (1.43-1.79)**	1.13 (0.96-1.32)	**1.59 (1.36-1.86)**
OSA and insomnia	**1.31 (1.03-1.67)**	**1.56 (1.17-2.09)**	**1.84 (1.37-2.47)**
Military experiences			
Combat deployment before T1			
Never deployed	Ref	Ref	Ref
Deployed, no combat	**1.15 (1.04-1.27)**	**1.76 (1.55-2.00)**	**1.49 (1.28-1.73)**
Deployed, low combat	1.04 (0.91-1.21)	**2.28 (1.95-2.68)**	**1.46 (1.20-1.79)**
Deployed, medium-to-high combat	**1.54 (1.36-1.76)**	**4.31 (3.74-4.97)**	**3.54 (3.01-4.17)**
Separation status			
On active service at T2	Ref	Ref	Ref
Separated before T1	**1.17 (1.04-1.31)**	**1.29 (1.13-1.48)**	**1.33 (1.12-1.57)**
Separated between T1 and T2	**1.76 (1.57-1.97)**	**2.66 (2.36-2.99)**	**3.29 (2.86-3.78)**
No. of deployments, T1-T2			
0	Ref	Ref	Ref
1	1.14 (0.97-1.33)	**1.40 (1.19-1.64)**	**1.42 (1.17-1.72)**
2 or more	0.86 (0.69-1.07)	**1.38 (1.12-1.70)**	1.21 (0.91-1.59)
Deployed equal to or longer than branch average from T1 to T2[b]			
No	1.19 (0.95-1.49)	0.94 (0.76-1.17)	1.00 (0.77-1.29)
Yes	Ref	Ref	Ref
Military characteristics			
Service component			
Reserve/Guard	1.00 (0.91-1.09)	**1.21 (1.09-1.34)**	1.09 (0.96-1.23)
Active duty	Ref	Ref	Ref
Service branch			
Army	**1.43 (1.28-1.59)**	**1.82 (1.61-2.05)**	**1.87 (1.60-2.18)**
Navy/Coast Guard	**1.23 (1.08-1.40)**	1.14 (0.97-1.34)	**1.27 (1.04-1.55)**
Marine Corps	**1.55 (1.32-1.82)**	**1.70 (1.40-2.07)**	**1.64 (1.30-2.08)**
Air Force	Ref	Ref	Ref
Pay grade			
Enlisted	Ref	Ref	Ref
Officer	**0.66 (0.57-0.76)**	**0.66 (0.56-0.76)**	**0.53 (0.44-0.65)**
Occupation			
Combat specialist	Ref	Ref	Ref
Functional support/admin	0.93 (0.80-1.08)	**0.82 (0.70-0.96)**	0.85 (0.70-1.04)
Healthcare	0.95 (0.81-1.12)	1.14 (0.96-1.35)	0.99 (0.80-1.23)
Other	1.00 (0.89-1.13)	0.88 (0.77-1.00)	0.95 (0.81-1.11)

CI, confidence interval; OR, odds ratio; OSA, obstructive sleep apnea; PCL, PTSD Checklist-Civilian Version; PTSD, post-traumatic stress disorder; T1, Time 1 (2011-2013), T2: Time 2 (2014-2016).
Logistic regression model is further adjusted for age, sex, race/ethnicity, marital status, education level, heavy weekly drinking, smoking status, life stressors, diagnosed traumatic brain injury at T2, mental component score, physical component score, time in service at T1, and follow-up time between T1 and T2. All ORs and CIs represent pooled estimates across multiple imputation models.
Bolded values are statistically significant ($p < .05$).
[a] All variables are assessed at T1 unless otherwise specified.
[b] Average deployment lengths for each branch: Army = 9 months, Navy/Coast Guard = 6 months, Marine Corps = 8 months, Air Force = 4 months. No (less than branch average) category also includes individuals who did not deploy during the time frame.

onset PTSD symptoms, diagnosis, or both symptoms and diagnosis at T2. Being an officer (vs. enlisted) was protective against the development of these 3 outcomes. Factors that predicted newly reporting a PTSD diagnosis only included deploying either 1 or ≥2 times (vs. 0) and Reserve/Guard component (vs. active duty) (Table 4). Adjusted associations between demographic characteristics at T1 and new-onset PTSD at T2 are presented in Supplemental Table 3.

Sensitivity analyses for OSA classifications

The prevalence and agreement of self-reported and MDR-classified OSA are reported in Table 5. At both T1 and T2, the prevalence of OSA via MDR records was lower than the self-reported prevalence, though the proportion of observed agreement between the methods was high (>90%). The kappa coefficients indicated a substantial level of reliability[43] ($\kappa > 0.61$) between both methods at both time points, and the proportions of specific agreement indicated moderate positive agreement and good negative agreement.[42]

Discussion

In this study, we utilized the largest longitudinal U.S. military cohort to examine whether military-related factors and PTSD predict OSA and/or insomnia at follow-up 3-5 years later, and vice versa. Findings suggested that there were strong bi-directional relationships between new-onset PTSD symptoms and/or diagnosis and OSA and/or insomnia, which was sometimes revealed by health care utilization. In addition, several military-related factors increased the odds

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Table 5
Prevalence and agreement of self-reported and MDR-classified OSA among active duty Millennium Cohort Study participants, T1 and T2 (n = 46,394)

Time point	Prevalence		Proportion of observed agreement	Kappa statistics		Proportions of specific agreement	
	Self-report	MDR		κ	95% CI	Positive agreement	Negative agreement
OSA at T1	9.1%	7.4%	94.8%	0.66	0.65-0.67	68.9%	97.2%
OSA at T2	14.6%	13.3%	92.8%	0.70	0.69-0.71	74.3%	95.9%

CI, confidence interval; MDR, Military Health System Data Repository; OR, odds ratio; OSA, obstructive sleep apnea; T1, Time 1 (2011-2013); T2, Time 2 (2014-2016).

for new-onset cases of both conditions. Specifically, prior deployment (especially with combat exposures), recent separation from the military, and service branch (Army, Navy, Marine Corps) predicted new-onset cases, while higher military rank was protective. Supplemental findings revealed that the prevalence of PTSD among the full Millennium Cohort Study population was higher among those with OSA/insomnia than those without sleep disorders, and vice versa; both PTSD and OSA/insomnia were higher among veterans than active duty or Reserve/Guard members.

The longitudinal analyses showed the strength of associations between PTSD symptoms and/or diagnosis and OSA/insomnia, revealing significant bi-directional relationships. Specifically, only self-reported provider-diagnosed PTSD without current symptoms was associated with greater likelihood of newly reporting OSA or comorbid OSA and insomnia, while having PTSD symptoms, a diagnosis, or both were all associated with new-onset insomnia. This may reflect differences in healthcare-seeking or utilization behavior since OSA and PTSD diagnosis would be reported by those who have received care, while screening positive for PTSD and insomnia symptoms may reflect present conditions among those who do not wish or have yet to seek care. When examining OSA/insomnia predicting PTSD, both OSA and insomnia were associated with the development of PTSD symptoms and/or diagnosis, but having insomnia only was not significantly associated with a newly reported PTSD diagnosis. This may reflect that some individuals with insomnia symptoms alone may not necessarily utilize health care services where they would receive a provider PTSD diagnosis, and also that PTSD is a complex condition with many potential causes that are difficult to disentangle. Prior studies indicate that sleep disorders are comorbid with or increase risk for PTSD.[9,12,14-21] Sleep regulates many key functions in the brain, thus, sleep disorders can cause dysregulated neurophysiology and behavior that may heighten PTSD risk if exposed to significant stressors, and vice versa.[5-8] Despite only examining these associations between 2 surveys 3-5 years apart, our longitudinal findings provide support for bi-directional associations between PTSD and sleep disorders. Studies with more frequent surveys and/or longer follow-up time periods are needed to further explore these associations.

We also examined which military-related factors were associated with new-onset PTSD or OSA/insomnia. Deployment (especially with medium-to-high combat exposure) was a significant risk factor. Deployment conditions can be stressful and, when combined with combat exposures, may be traumatic for some individuals, as previous studies have also reported associations of PTSD, OSA/insomnia, and/or other sleep issues with deployment.[1,4,9,14,16-19] Interestingly, except for increased odds at T2 of new-onset OSA among those having prior deployment with no combat exposure, prior deployment with either no or low combat was not associated with new-onset OSA/insomnia. However, there was increased risk for new-onset PTSD symptoms and/or diagnosis with any level of combat exposure in prior deployments, or with 1 or multiple deployments between T1 and T2 (for new-onset diagnosis or both symptoms and diagnosis). Thus, deployment with medium-to-high combat exposure is a strong risk factor for new-onset OSA/insomnia and PTSD, but lower levels of combat appear to confer risk for only new-onset PTSD. These findings are supportive of targeted screening for sleep issues and PTSD among individuals deploying in conditions with high levels of combat exposure.

Recent separation from the military was another strong risk factor for both new-onset OSA/insomnia and PTSD. Previous Millennium Cohort studies[23,44] also found that recent separation was a risk factor for reported trouble sleeping and new-onset insomnia (using ISI), regardless of prior PTSD status. Thus, our findings indicate a risk of developing sleep disorders after separation, and sleep health promotion interventions should be utilized, especially when military members transition back to civilian life.

Service branch was another risk factor. While service in any military branch presents stressors and sleep challenges, prior studies typically found that PTSD[3,4] and sleep issues[13,23,44] were greatest in the Army and/or Marine Corps, with mixed results for Navy. Thus, while our findings support the associations between OSA/insomnia and PTSD in Army, Navy, and Marine Corps personnel, differing requirements, experiences, combat exposures, and cultures may confer different health risk profiles among the service branches.

The only protective factor we found for both new-onset PTSD and OSA/insomnia was being an officer, compared with enlisted. This also aligns with previous Millennium Cohort findings that officers are protected from other new-onset sleep issues (eg, short sleep duration, insomnia, sleep medication use).[23,44] Thus, higher military rank may confer benefits to sleep and mental health risks. Two factors interestingly showed a mix of risk and protection: being in the Reserve/Guard and separating prior to T1 both increased risk for new-onset PTSD but were protective for new-onset OSA/insomnia. This contrasts with recent separation (ie, between T1 and T2), which was a risk factor for both. These complex findings indicate that the risk for new-onset PTSD is high around the transition period, but those separated from service for longer times are at lower risk after passing through the higher-risk transition period. This may be due in part to service members reporting health issues immediately prior to transition out of the military, even when the condition may have existed earlier but was not reported. Thus, separation has a complex risk timeline that should be further examined. Additionally, all occupations (compared with combat specialist) had increased risk for new-onset OSA only, but being in a functional support/administrative occupation was protective for newly diagnosed PTSD only. Our previous reports[23,44] showed mixed results for military occupations, wherein we found no significant associations for new-onset short sleep duration or insomnia, and only healthcare occupations increased risk for new-onset trouble sleeping and sleep medication use.

There are limitations to this study. First, we used self-reported survey data, which are subject to reporting and recall biases and do not always represent a clinical diagnosis of the outcomes under study. As 2 time points were utilized for the analyses, participants were only eligible if they responded at both points, which may bias the sample. This limitation was alleviated somewhat with the application of multiple imputation models that included characteristics associated with attrition.[40] Also, the ISI cutoff of $\geq$15 has been utilized in several previous military samples[23,25] and is more

conservative than lower cutoffs sometimes used with general population samples[24] that include "sub-threshold" insomnia. Thus, insomnia cases may be underestimated in the current study. Formal validation of the ISI in military samples is needed. Furthermore, OSA and PTSD may be underestimated in this study given that both OSA and PTSD tend to be underdiagnosed in medical settings, and participants actively serving may be motivated to under-report PTSD symptoms. Therefore, even by casting a wider net that included the assessment of both PTSD symptoms on the PCL and self-reported provider-diagnosed PTSD, this condition may still be underrepresented in this sample. In addition, the presence of PTSD, OSA, and insomnia were not assessed prior to T1 and some participants who screened negative for these at T1 may have a previous history that was not accounted for. Likewise, the screening tools for insomnia and PTSD assessed symptoms over the past 2 weeks and month, respectively, so the prevalence of these conditions at T2 may not represent symptomology present between T1 and T2. Also, we were unable to assess possible treatment for PTSD, OSA, or insomnia prior to T1 and/or between T1 and T2. In addition, we were unable to evaluate TBI at T1 since this item was not assessed until the T2 survey, which means we could not disentangle the temporal sequence of TBI in relation to sleep disorders and PTSD. Lastly, we were unable to assess fitness for duty, which may potentially deter self-reporting PTSD or sleep disorders prior to separation from service.

Despite these limitations, a significant strength was the use of a large, representative sample of service members and veterans from all service branches and components. Additionally, longitudinal data allowed us to establish temporality in the development of the outcomes of interest in relation to baseline conditions. Moreover, the measures used for insomnia and PTSD symptoms are derived from widely used and validated measures,[24] lending credibility to the classifications of each outcome. While OSA was assessed through a single self-report item, sensitivity analyses were used to validate this self-report item with OSA diagnoses in medical records among a subpopulation of active duty participants. Though these analyses suggested there was a small potential over-reporting of OSA via self-report compared with medical records, the overall reliability between both methods was good. Results also indicated that while there was higher agreement between both methods in determining negative OSA diagnoses than in determining positive diagnoses, the self-report item provided adequate coverage in capturing the presence of OSA, strengthening our ability to draw conclusions based on this self-reported measure.

Conclusions

In a large, representative U.S. military cohort assessed at 2 time points, 3-5 years apart, longitudinal analyses showed that having either PTSD or OSA/insomnia was bi-directionally predictive for new onset of the other condition, and several military-related factors increased risk, including prior deployment (especially with medium-to-high combat exposure), recent separation, and serving in the Army, Navy, or Marine Corps, while being an officer was a protective factor. Furthermore, the prevalence of PTSD and OSA/insomnia was high, often comorbid, and greatest among veterans. Utilizing the identified risk factors from this study, sleep and mental health screenings and interventions can be better targeted to the military communities and individuals at highest risk for developing PTSD and sleep disorders.

Declaration of conflict of interest

The authors have no conflict of interest to declare.

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Supplementary materials

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