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Prospective Associations Between Traumatic Brain Injury and Postdeployment Tinnitus in Active-Duty Marines

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Objective: To examine whether cause, severity, and frequency of traumatic brain injury (TBI) increase risk of postdeployment tinnitus when accounting for comorbid posttraumatic stress disorder. **Design:** Self-report and clinical assessments were done before and after an "index" deployment to Iraq or Afghanistan. **Setting, Participants, and Measures:** Assessments took place on Marine Corps bases in southern California and the VA San Diego Medical Center. Participants were 1647 active-duty enlisted Marine and Navy servicemen who completed pre- and postdeployment assessments of the Marine Resiliency Study. The main outcome was the presence of tinnitus at 3 months postdeployment. **Results:** Predeployment TBI increased the likelihood of new-onset postdeployment tinnitus (odds ratio [OR] = 1.86; 95% confidence interval [CI], 1.28-2.70). Deployment-related TBIs increased the likelihood of postdeployment tinnitus (OR = 2.65; 95% CI, 1.19-5.89). Likelihood of new-onset postdeployment tinnitus was highest for those who were blast-exposed (OR = 2.93; 95% CI, 1.82-6.17), who reported moderate-severe TBI symptoms (OR = 2.22; 95% CI, 1.22-3.40), and who sustained multiple TBIs across study visits (OR = 2.27; 95% CI, 1.44-4.24). Posttraumatic stress disorder had no effect on tinnitus outcome. **Conclusions:** Participants who were blast-exposed, sustained multiple TBIs, and reported moderate-severe TBI symptoms were most at risk for new-onset tinnitus. **Key words:** *blast*, *combat*, *military*, *posttraumatic stress disorder*, *PTSD*, *TBI*, *tinnitus*, *traumatic brain injury*

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TINNITUS, defined as the perception of sound in the absence of an external auditory source,[1] is the number one service-related Veterans Affairs (VA) disability.[2] Tinnitus and hearing loss combined cost more than $1 billion annually in disability benefits, excluding treatment and hearing aid expenditures.[2] In 2012, roughly a quarter of VA beneficiaries received disability payments for tinnitus including 115 638 new cases, an increase of 12% over the previous year.[2] This 12% yearly rise has been consistent since the early 2000s. In addition, 1% to 3% of patients with tinnitus experience long-term health consequences, including sleep disturbance,[3] depression,[4,5] anxiety,[6–10] somatoform disorders,[11] and suicide.[12,13]

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Although typically associated with hearing loss, tinnitus may occur in the absence of hearing difficulty.[14] In the general population, 20.7% of those with high exposure to noise complain of tinnitus compared with 7.5% of adults with little or no noise exposure.[15] In the US military population, more than 60% report tinnitus several months following a blast event.[16] Contact with detonations caused by improvised explosive devices has been one of the leading causes of traumatic brain injury (TBI) in the Iraq and Afghanistan battle zones.[17–19] Rates of blast-related hearing loss and tinnitus have risen significantly since the onset of the war in Iraq.[20] Patients with blast injuries are at least 2.5 times more likely to sustain tinnitus than those with a TBI from nondetonation incidents,[21] and at least 60% to 75% of veterans with a history of mild TBI report tinnitus.[22] Roughly 1.4 million civilians sustain TBI per year in the United States,[23] and a separate survey from Oregon noted that 5% of those with tinnitus list an explosion as the proximate cause of tinnitus.[24] Thus, it may be prudent to screen for tinnitus among US civilians as well as military personnel.

Although the intracranial mechanism of blast-related tinnitus is unclear, the initial cochlear injury may be traced to a generalized central neural syndrome. The cochlea is uniquely vulnerable to primary blast injury since the air-liquid interface of the round window can be subject to direct overpressure through the exquisitely thin and elastic tympanic membrane. In contrast, the brain is somewhat protected by absorption of the pressure wave by the skull. The initial shock wave from a blast leads to shearing of tissues due to differential pressures acting on liquid versus more rigid structures such as blood vessels.[25] This shearing force directly injures the brain and cochlea, causing an inflammatory response, oxidative stress–induced neural degeneration,[26] and subsequent neural alteration both within the cochlea and its auditory pathway.[27]

Establishing a direct, causal link between blast exposure and tinnitus has been limited by the retrospective, cross-sectional nature of available accounts[28–30] and the existence of comorbid psychiatric disorders such as posttraumatic stress disorder (PTSD).[31,32] Failure to differentiate tinnitus symptoms from these comorbidities further hinders the identification of tinnitus-specific treatment modalities. This prospective study examines the effects of blast-related TBI and injury severity on tinnitus while accounting for comorbid and preexisting symptoms, including PTSD symptoms, prior TBI, and tinnitus.

METHODS

Approval for human participants was obtained from University of California San Diego, VA San Diego Research Service, and Naval Health Research Center (VA R&D and UCSD institutional review board approval #070533). All participants gave written informed consent before participation.[33]

Study design and participants

Participants were a subset of the 2600 active-duty Marine and Navy servicemen enrolled in the Marine Resiliency Study (MRS),[33] a prospective, longitudinal investigation of 4 infantry battalions stationed in southern California. Servicemen were deployed to Iraq or Afghanistan between July 2008 and May 2012 for approximately 7 months (the "index deployment") and were assessed approximately 1 month before deployment, 1 week postdeployment (only self-report questionnaires), and 3 and 6 months postdeployment. Data collected at 6 months postdeployment were not analyzed here because of reduced follow-up rates and insufficient number of symptom cases. A priori exclusions were 34 participants without an index deployment and 66 officers who were significantly older ($P < .001$) and had lower combat experience scores ($P < .001$) than enlisted participants. Of the remaining 2500, 1829 completed the 3-month postdeployment assessment and were eligible for analysis.

Data from these remaining participants were examined for any hearing difficulty at 3 months postdeployment. Tones of 500, 1000, 3000, and 6000 Hz were presented at 35 dB (Grayson Stadler Audiometer, Eden Prairie, Minnesota). This screening test was performed to ensure participants would be able to hear and understand study assessments. Preliminary analyses showed that the 6000-Hz frequency was most commonly missed; however, χ^2 tests revealed no difference in rates of tinnitus for this group compared with those who missed other frequencies. To ensure our sample included only those with serviceable hearing within *conversational frequency range*, we excluded 116 participants who failed to hear frequencies at or below 3000 Hz at 3 months postdeployment. Of the remaining 1713, 66 were missing relevant data and were excluded from analysis. The final sample for this study included 1647 participants.

Measures

Complete MRS methodology has been reported previously.[33] Descriptions of measures relevant to this study follow. Demographic information (age, ethnicity, race, battalion) was collected via self-report surveys before deployment and was included in analysis as potential covariates.[34,35]

Presence of tinnitus was assessed before deployment and 3 months postdeployment with a single "yes/no" item on an interview-assisted questionnaire, "Do you

have ringing in the ears?" Participants who responded "yes" as having ringing in the ears at the time of assessment were categorized as having tinnitus. Participants were also asked whether or not they had an ear infection at the time of assessment. To account for any influence on tinnitus outcome, the presence of an ear infection at the 3-month postdeployment assessment was tested for any significant univariate associations with postdeployment tinnitus.

Head injury events were assessed via interview before deployment and 3 months postdeployment. Interviewers gathered details of each reported injury, including injury cause or mechanism and symptom severity. Traumatic brain injury was defined as any head injury that resulted in loss of consciousness or altered mental status (ie, dazed, confused, or seeing stars, and/or posttraumatic amnesia).[36–38] Mild TBI was any TBI resulting in a loss of consciousness of less than 30 minutes and posttraumatic amnesia for less than 24 hours.[39] Because the time between predeployment and postdeployment assessments was broader than the duration of the deployment, nondeployment TBIs sustained between assessment visits ($n = 34$) were included in analyses to account for potential effects on tinnitus.[40,41] As these were a small minority, for succinct communication, all TBIs sustained between predeployment and 3-month postdeployment assessments are labeled "deployment-related" for this article.

Posttraumatic stress symptoms were assessed before deployment and 3 months postdeployment using the Clinician-Administered PTSD Scale[42] in accordance with symptom criteria from the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition, Text Revision).[43] PTSD/partial PTSD group classification required exposure to a traumatic event (ie, actual or threatened death or serious injury, or threat to physical integrity to self or others) but did not require a response of extreme fear, helplessness, or horror.[44,45] In addition, PTSD classification required at least 1 reexperiencing symptom, 3 avoidance symptoms, and 2 hyperarousal symptoms; partial PTSD classification required at least 1 reexperiencing symptom and either 3 avoidance symptoms or 2 hyperarousal symptoms.[46] Symptoms must have occurred at least once within the past month (frequency $\geq$1), causing at least moderate distress (intensity $\geq$2).[47] Participants with partial PTSD and PTSD were evaluated together ($n = 200$ at predeployment; $n = 341$ at postdeployment) to examine the effects of clinically significant symptoms on tinnitus.

A modified 16-item version of the Combat Experiences Scale from the Deployment Risk and Resilience Inventory[48,49] was used to assess combat intensity 1 week after deployment. Item responses were measured on a 5-point Likert scale, ranging from 0 (never) to 4 (daily or almost daily). Total scores ranged from 0 to 64, with higher scores indicating greater combat intensity.

Analysis

Continuous predictors were centered prior to analysis. A priori analysis of variance and χ^2 tests revealed battalion differences in predeployment demographic and psychological characteristics, shown in Table 1. Thus, we included battalion as a covariate to correct for these and any other unknown battalion differences such as training schedules, battalion leadership and cohesion, and timing of study assessments. Categorical demographic predictors were dummy-coded with the following reference groups: battalion 1, white, and non-Hispanic. Reference groups for categorical diagnostic predictors were participants with no prior tinnitus, no PTSD, and no TBI.

Presence of tinnitus at 3 months postdeployment was the dependent variable for all analyses. Predictor variable selection was conducted via univariate logistic regression analysis of each predictor variable.[50] Variables with $P < .2$ associations were included as predictors in the full multivariate analysis. The multivariate analysis tested all main effects and all 2-way interactions between clinical diagnostic and combat exposure variables. Sensitivity analyses tested effects of TBI characteristics, including injury mechanism (blast vs nonblast), severity (mild vs moderate/severe), and frequency (single vs multiple). Significance levels for 3 sensitivity analyses were Bonferroni adjusted with an α level of .017. All data analyses were performed using Statistical Package for Social Sciences (SPSS; version 21.0).[51]

RESULTS

Sample characteristics

Battalion differences in demographic and psychosocial variables have been published previously.[33] Mean (SD) age of participants was 22.4 (3.36) years. Roughly 84.7% of participants were white, 4.5% were African American, and 10.9% were of mixed or other racial descent. The majority (78.5%) was non-Hispanic. Approximately 74.3% were junior enlisted (E1-E3), and 44.6% were deployed prior to the index deployment. Mean (SD) combat intensity score was 13.0 (11.1).

Of the 1647 participants, 219 (13.2%) had tinnitus before the index deployment and 250 (15.1%) had tinnitus after deployment. Of the 250 participants with postdeployment tinnitus, 141 (56.4%) had new-onset tinnitus and 109 (43.6%) had tinnitus both before and after the index deployment. Observed prevalence of deployment-related TBI was 34.8% for those with new-onset postdeployment tinnitus compared with 17.4% for those with no pre- or postdeployment tinnitus

TABLE 1 *Battalion differences in predeployment characteristics*

	Battalion 1 ($n = 232$)	Battalion 2 ($n = 469$)	Battalion 3 ($n = 501$)	Battalion 4 ($n = 445$)
Predeployment characteristic[a]				
Age, mean (SD), y	21.4 (2.6)	22.1 (3.5)	22.9 (3.3)	22.8 (3.5)
% Non-Hispanic	78	81.4	73.3	76.3
% White	84.5	87.4	83.4	83.2
% Rank E1-E3	81.5	81.8	73.6	62.5
% Prior deployed	50.4	43.9	42.9	43.6
% TBI	62.9	60.3	55.9	48.5
% Tinnitus	3.9	16.2	22.0	5.4
Assessment scores, mean (SD)				
CAPS	15.8 (14.8)	15.0 (13.6)	14.7 (15.3)	13.6 (14.6)
Childhood trauma	40.0 (13.0)	38.9 (12.5)	38.4 (12.0)	42.1 (14.8)
SF-12 Physical Health	54.6 (5.6)	53.7 (6.8)	54.2 (6.0)	53.7 (6.2)
SF-12 Mental Health	49.2 (8.4)	48.9 (9.4)	49.9 (8.4)	50.5 (8.1)

Abbreviations: CAPS, Clinician-Administered PTSD Scale; E1-E3, junior enlisted; PTSD, posttraumatic stress disorder; SF-12, 12-item Short Form Health Survey; TBI, traumatic brain injury.
[a]Small but significant differences in age ($F_3 = 13.5$; $P < .001$; $\eta p^2 = 0.02$), ethnicity ($\chi^2_3 = 9.4$; $P < .05$; $\varphi = 0.08$), rank ($\chi^2_3 = 52.1$; $P < .001$; $\varphi = 0.12$), predeployment TBI ($\chi^2_3 = 18.2$; $P < .001$; $\varphi = 0.10$), predeployment tinnitus ($\chi^2_3 = 78.0$; $P < .001$; $\varphi = 0.22$), childhood trauma score ($F_3 = 7.4$; $P < .001$; $\eta p^2 = 0.01$), and SF-12 Physical Health score ($F_3 = 1.5$; $P < .01$; $\eta p^2 = 0.003$) and Mental Health score ($F_3 = 2.9$; $P < .05$; $\eta p^2 = 0.005$). There were no significant battalion differences for the current sample in race, prior deployments, or predeployment CAPS total symptom score.

($\chi^2_1 = 24.7$; $P < .0001$; $\varphi = 0.13$). Before deployment, 195 (11.8%) had partial PTSD or PTSD and 907 (55.1%) had previously sustained TBI. After predeployment, 336 (20.4%) had partial PTSD or PTSD at their 3-month postdeployment assessment and 316 (19.2%) sustained deployment-related TBI. Prevalence of TBI-related characteristics before and after the index deployment is shown in Table 2. Of the 1015 participants who reported TBI at either assessment visit, 825 (81.3%) had mild TBI, 648 (63.8%) sustained injuries from nonblast events, and 415 (40.9%) sustained only 1 TBI across assessment visits.

Univariate predictor selection

Univariate test results are shown in Table 3. Postdeployment tinnitus was significantly associated with battalion membership ($P < .01$), and those with tinnitus were more likely to be non-Hispanic (81.2% vs 76.4%) and white (88.6% vs 84%) than those without tinnitus. Participants with postdeployment tinnitus were more likely to have had prior tinnitus (43.6% vs 7.9%), prior TBI (63.6% vs 54.8%), and prior partial PTSD or PTSD (9.6% vs 5.4%). Those with postdeployment tinnitus also had higher combat intensity scores (mean [SD] = 15.9 [12.7] vs 12.5 [10.7]) and had higher rates of

TABLE 2 *Rates of TBI reported pre- and postdeployment*

TBI characteristic	Predeployment ($n = 907$)	Postdeployment[a] ($n = 316$)	Total[b] ($N = 1015$)
% Mechanism			
Nonblast	82.4	20.9	63.8
Blast	17.6	79.1	36.2
% Severity[c]			
Mild	82.2	88.0	81.3
Moderate/severe	13.8	11.1	15.5
% Frequency			
Single	44.7	66.8	40.9
Multiple	55.3	33.2	59.1

Abbreviation: TBI, traumatic brain injury.
[a]Postdeployment reports of TBI include all deployment-related TBIs ($n = 282$) and nondeployment TBIs sustained between pre- and postdeployment assessments ($n = 34$). There were no significant differences between deployment and nondeployment TBIs; thus, nondeployment TBIs were included in the analysis to account for any potential effects on tinnitus.
[b]Total number of participants with TBI characteristic across pre- and postdeployment visits.
[c]Percentages may not sum to 100% due to missing data.

TABLE 3 *Variable selection via univariate logistic regression*

Variable	3 mo postdeployment		
	No tinnitus ($n = 1397$)	Tinnitus ($n = 250$)	*P*
Demographic			
Age, mean (SD), y	22.5 (3.4)	22.3 (3.1)	.620
% Battalion[a]			.002
Battalion 1	15.1	8.4	
Battalion 2	27.0	36.8	
Battalion 3	31.1	26.8	
Battalion 4	26.8	28.0	
% Non-Hispanic	76.4	81.2	.095
% White[b]	84.0	88.6	.064
% Rank E1-E3	74.3	72.8	.618
Predeployment			
% Tinnitus	7.9	43.6	.000
% Partial PTSD or PTSD[c]	5.4	9.6	.070
% History of TBI	54.8	63.6	.010
Deployment			
Combat intensity,[d] mean (SD)	12.5 (10.7)	15.9 (12.7)	.000
% TBI	17.5	31.6	.000
Postdeployment			
% Partial PTSD or PTSD[e]	18.6	32.4	.000
% Ear infection	1.4	1.2	.774

Abbreviations: E1-E3, junior enlisted; PTSD, posttraumatic stress disorder; TBI, traumatic brain injury.
[a]Cohort sizes are 232 in battalion 1, 469 in battalion 2, 501 in battalion 3, and 445 in battalion 4. Demographic and psychiatric differences across battalions have been published previously.[33]
[b]African Americans constituted roughly 5.0% of participants with no postdeployment tinnitus, 1.6% of those with postdeployment tinnitus, and 4.5% of all participants.
[c]Of the participants *without* postdeployment tinnitus, approximately 7.5% had partial PTSD before deployment and 4.2% had PTSD. Of the participants *with* postdeployment tinnitus, 9.6% had partial PTSD before deployment and 6.0% had PTSD.
[d]Mean (SD) combat intensity score across all participants in this sample was 13.0 (11.1).
[e]Of the participants *without* postdeployment tinnitus, approximately 13.2% had partial PTSD after deployment and 5.4% had PTSD. Of the participants *with* postdeployment tinnitus, 22.8% had partial PTSD after deployment and 9.6% had PTSD.

deployment TBI (31.6% vs 17.5%) and postdeployment partial PTSD or PTSD (32.4% vs 18.6%). Participants with and without postdeployment tinnitus did not differ as a function of age, rank, or ear infection.

Multivariate analysis

Variables with univariate associations with postdeployment tinnitus ($P < .2$) were selected for the multivariate model. Demographic variables were battalion, ethnicity, and race; clinical diagnostic and deployment-related variables were prior tinnitus, prior and deployment-related TBI, combat intensity, and prior and postdeployment partial PTSD/PTSD.

Results of the multivariate model are shown in Table 4. There was a significant association between battalion and postdeployment tinnitus ($P < .01$), with battalion 2 increasing the likelihood of postdeployment tinnitus by a factor of 2.01 ($P < .02$) compared with battalion 1. Prior tinnitus and prior TBI independently increased the likelihood of postdeployment tinnitus by factors of 27.44 ($P < .001$) and 1.86 ($P < .02$), respectively, and showed significant interaction ($P < .01$). Post hoc comparisons revealed that prior TBI significantly increased the likelihood of postdeployment tinnitus for those *without* prior tinnitus (odds ratio = 1.86; 95% confidence interval [CI], 1.28-2.70) but not for those *with* prior tinnitus (odds ratio = 0.59; 95% CI, 0.34-1.02). Deployment-related TBIs increased the likelihood of postdeployment tinnitus by a factor of 2.65 ($P < .02$). As expected, there was no significant interaction between deployment-related TBI and prior tinnitus.

Neither combat intensity nor partial PTSD/PTSD was significantly associated with postdeployment tinnitus. The nonsignificant effect of PTSD was confirmed via 2 post hoc analyses that tested (1) the combined effects of pre- and postdeployment partial PTSD/PTSD as a single diagnostic predictor, and (2) the effects of pre- and postdeployment PTSD, excluding participants with partial PTSD. Furthermore, 2 additional post hoc analyses (3) including participants with any hearing difficulty within the 500- to 3000-Hz range ($n = 116$), and (4) excluding

Table 4 *Multivariate logistic regression predicting postdeployment tinnitus*

Variable	Coef.	SE	*P*	OR	95% CI for OR
Intercept	−2.96	0.33			
Battalion, *main effect*			.000		
Battalion 2	0.70	0.29	.014	2.01	1.15-3.51
Battalion 3	−0.48	0.31	.129	0.62	0.34-1.15
Battalion 4	0.07	0.33	.838	1.07	0.56-2.04
Ethnicity[a]	−0.40	0.21	.051	0.67	0.39-1.14
Race[b]	−0.12	0.24	.609	0.89	0.48-1.63
Predeployment partial PTSD	0.76	0.51	.138	2.13	0.78-5.77
Predeployment tinnitus	3.31	0.32	.000	27.44	14.55-51.75
Predeployment TBI	0.62	0.25	.013	1.86	1.14-3.04
Predeployment TBI × predeployment tinnitus	−1.15	0.37	.002	0.32	0.15-0.65
TBI without predeployment tinnitus	0.62	0.19	.001	1.86	1.28-2.70
TBI with predeployment tinnitus	−0.53	0.28	.057	0.59	0.34-1.02
Combat intensity, *centered*	0.01	0.02	.424	1.01	0.98-1.05
Deployment TBI[c]	0.97	0.41	.017	2.65	1.19-5.89
Postdeployment partial PTSD	0.44	0.41	.285	1.55	0.70-3.44

Abbreviations: CI, confidence interval; OR, odds ratio; PTSD, posttraumatic stress disorder; SE, standard error; TBI, traumatic brain injury.

[a]Results are reported for Hispanics compared with non-Hispanics (reference group).

[b]Results are reported for non-whites compared with whites (reference group).

[c]There were no significant differences between deployment and nondeployment TBIs sustained between pre- and postdeployment assessments ($n = 35$). Nondeployment TBIs were included in the analysis to account for any potential effects on tinnitus.[40,41]

participants with any hearing difficulty within the full 500- to 6000-Hz range ($n = 209$) did not alter model outcomes.

Sensitivity analyses

Table 5 shows results of sensitivity analyses of TBI mechanism (blast vs nonblast), severity (mild vs moderate/severe), and frequency (single vs multiple) on the likelihood of postdeployment tinnitus. Variables for TBI were collapsed across pre- and postdeployment because the small number of nonblast and moderate-severe TBIs caused problems with model convergence.

There was a main effect of TBI mechanism on postdeployment tinnitus ($P < .01$) as well as an interaction with prior tinnitus ($P < .01$). For those with no prior tinnitus, nonblast and blast TBIs significantly increased the likelihood of postdeployment tinnitus by factors of 1.91 (95% CI, 1.20-3.32) and 2.93 (95% CI, 1.82-6.17), respectively. For those with prior tinnitus, TBI mechanism had no effect on postdeployment tinnitus.

There was a significant interaction between TBI severity and prior tinnitus ($P < .01$). For those with no prior tinnitus, mild and moderate/severe TBIs significantly increased the likelihood of postdeployment tinnitus by factors of 1.99 (95% CI, 1.29-3.62) and 2.22 (95% CI, 1.22-3.40), respectively. For those with prior tinnitus, TBI severity had no effect on postdeployment tinnitus.

Finally, there was a main effect of TBI frequency ($P < .02$) and a significant interaction between frequency and prior tinnitus ($P < .01$). For those with no prior tinnitus, a single TBI increased the likelihood of tinnitus outcome by a factor of 1.79 (95% CI, 1.09-2.97) and multiple TBIs increased the likelihood by a factor of 2.27 (95% CI, 1.44-4.24). For those with prior tinnitus, TBI frequency had no effect on postdeployment tinnitus.

DISCUSSION

In our model, prior tinnitus and TBI were each independently associated with postdeployment tinnitus. Prevalence of tinnitus was 13.2% before deployment and 15.1% after deployment, with 8.6% new-onset postdeployment tinnitus. Rates of pre- and postdeployment tinnitus are consistent with prior reports of a prevalence of 15.6% in soldiers deployed to Iraq.[52] Prior tinnitus occurred in roughly 43.6% of participants with postdeployment tinnitus. Interestingly, not all those with prior tinnitus sustained the symptom postdeployment. Of the 219 participants with prior tinnitus, 110 (50.2%) were asymptomatic after the index deployment. Of these, 67.3% sustained TBI prior to the index deployment. Tinnitus for these participants may be an acute symptom from prior TBIs that diminished over time. In addition, those who were asymptomatic after deployment had lower rates of deployment-related TBI (19.1% vs 27.5%) and lower mean combat intensity (11.5 vs 14.5) than

TABLE 5 *Sensitivity analyses of TBI characteristics[a] on postdeployment tinnitus*

TBI characteristic	Prior tinnitus	Coef.	SE	OR	95% CI for OR
Mechanism					
Nonblast	No	0.65	0.24	1.91	1.20-3.32
Nonblast	Yes	−0.88	0.33	0.42	0.22-1.24
Blast	No	1.07	0.24	2.93	1.82-6.17
Blast	Yes	−0.09	0.35	0.92	0.46-1.59
Severity					
Mild	No	0.69	0.22	1.99	1.29-3.62
Mild	Yes	−0.61	0.30	0.54	0.30-1.35
Moderate/severe	No	0.80	0.30	2.22	1.22-3.40
Moderate/severe	Yes	−0.26	0.50	0.77	0.29-1.34
Frequency					
Single	No	0.58	0.25	1.79	1.09-2.97
Single	Yes	−0.97	0.39	0.38	0.18-1.20
Multiple	No	0.82	0.23	2.27	1.44-4.24
Multiple	Yes	−0.46	0.31	0.63	0.34-1.41

Abbreviations: CI, confidence interval; OR, odds ratio; SE, standard error; TBI, traumatic brain injury.
[a]For all sensitivity analyses, TBIs were collapsed across pre- and postdeployment visits because of the small number of deployment-related nonblast TBIs and moderate/severe TBIs causing problems with model convergence.

those with both pre- and postdeployment tinnitus. Alternatively, some participants may have had intermittent tinnitus that was not present after the index deployment.

Traumatic brain injury sustained before the index deployment increased the likelihood of new-onset postdeployment tinnitus, suggesting that a history of TBI may be a risk factor for tinnitus for those with no prior symptoms. As 44.6% of our participants were deployed prior to their index deployment, tinnitus and TBI symptoms reported at the predeployment assessment may be attributable to prior deployments. Independent of any prior tinnitus, those with deployment-related TBI were 2.7 times as likely to report tinnitus after deployment compared with those with no TBI. Furthermore, prevalence of deployment-related TBI was significantly higher for those with new-onset postdeployment tinnitus than those with no pre- or postdeployment tinnitus. These findings are consistent with those of previous cross-sectional studies that show associations between TBI and tinnitus and/or hearing difficulty.[29,30,53,54]

Tinnitus was associated with TBI characteristics. Consistent with prior cross-sectional studies showing higher rates of tinnitus[20] and hearing problems[28] following blast versus nonblast injuries, postdeployment tinnitus was nearly twice as likely for those with nonblast TBI and nearly 3 times as likely for those with blast TBI compared with those with no TBI. In addition, tinnitus was 1.8 times as likely after a single TBI and 2.3 times as likely after multiple TBIs compared with tinnitus occurrence in those with no TBI. Furthermore, new-onset postdeployment tinnitus was 1.9 times as likely for those with mild TBI and 2.2 times as likely for those with moderate/severe TBI. These results suggest a dose-response relationship between TBI characteristics and tinnitus such that more numerous and more severe injuries increase the risk of tinnitus.

This study found no associations between tinnitus and PTSD or combat intensity; thus, associations of TBI with tinnitus cannot be attributed to psychiatric symptoms or other environmental factors. These results are contrary to previous findings that suggest that tinnitus may be associated with exposure to harsh sounds from firearms, artillery, and mechanized equipment during deployment,[16] as well as long-term stress including emotional exhaustion,[55] fatigue,[56] and PTSD.[57] In one study,[58] 75% of participants with PTSD had tinnitus whereas only 15.9% of those without PTSD reported tinnitus. However, this was a retrospective study and there was a large cultural overlay in which tinnitus was thought to indicate "soul loss." Causes of the onset of tinnitus, such as head trauma, noise-induced hearing loss, or prior ear infections, were not addressed in that study.[58] Nevertheless, neural pathways damaged in TBI-related tinnitus may differ from those impacted by psychological stress. Emotional or psychological distress associated with tinnitus has been shown to activate a neural network involving the anterior cingulate cortex, insula, hypothalamus, and amygdala.[59] This same network has been implicated in other perceptual disorders such as phantom limb pain and may reflect the nonspecific influence of psychological distress.[59] Further investigation is needed to determine whether neural networks associated with stress-related tinnitus are distinct from TBI-induced tinnitus.

Neural changes following cochlear trauma have been demonstrated using acoustically evoked discharge, otoacoustic emissions, protein expression, and neuroimaging.[27,60–65] The initial shock wave from a blast leads to shearing of tissues,[25] directly injuring the cochlea and leading to an inflammatory response with subsequent neural degeneration.[26] Animal models of TBI demonstrate loss of ribbon synapses from inner hair cells to the auditory nerve in mild cases and then deterioration of outer hair cells of the cochlea, leading to altered auditory nerve activity.[66] Upregulation of BDNF (brain-derived nerve growth factor), a modulator of neuronal plasticity, is noted in spiral ganglion neurons and intracranially, and the spontaneous discharge rate of auditory fibers increases as a result of acoustic trauma.[62] These changes accompany enhanced subcortical disinhibition in the brainstem and inferior colliculus.[67] Disinhibition and prolonged excitation occur along the tonotopic map of the auditory cortex immediately following a loud sound.[68] Neural activity of the central auditory system, including reorganization of the cortical tonotopic map, is associated with an imbalance between excitation and inhibition in the auditory pathway.[64] These studies suggest immediate changes in expression of excitatory and inhibitory neurotransmitters and increased spontaneous signal transmission to the dorsal cochlear nucleus in the brainstem. Along with multiple biomarkers of neural plasticity in the cochlea and auditory tract and nuclei, there is a reorganization of frequency representation in the dorsal cochlear nuclei and inferior colliculus and a long-term change in the temporal pattern of neural activity. In animal studies, these neural alterations continue for at least 1 month following acute noise injury.[27,67]

In addition, functional magnetic resonance imaging and positron emission tomography studies show that tinnitus is associated with increased activity in the frontal lobe, limbic system, and auditory association cortex and show asymmetry in the primary auditory cortex and metabolic asymmetry between hemispheres.[64] Magnetoencephalography, which measures spatial and temporal neural activity, has identified activity between the anterior cingulum and right frontal cortex correlating with tinnitus distress,[69] although it is unclear whether differences in patterns are more related to hearing loss or tinnitus.[70] Future studies should address the specific pathophysiology of TBI-induced tinnitus to ascertain any differences from noise-induced injury.

Several study limitations warrant consideration. Self-reported symptoms, including reports of TBI, PTSD, and tinnitus, are subject to bias and misclassification errors, thus limiting causal inference. Our tinnitus measurement did not capture symptom severity, duration, or functional impact, all of which may have important clinical implications[24] and should be explored in future studies. Although it was made clear to participants that their individual responses and data would be kept confidential and would not be reported to their command, participants may still have had concerns regarding the impact of reporting PTSD and tinnitus symptoms on their careers or future disabilities compensation. It should be noted that information obtained via self-report and interview was not relevant for research study compensation. A post hoc analysis that excluded those with partial PTSD did not alter study findings; therefore, it is unlikely that the inclusion of partial PTSD diluted any potential effects of PTSD on tinnitus.

In addition, our hearing evaluation was not intended to detect hearing loss above 6000 Hz but ensured that participants had normal hearing within conversational frequency range (500-3000 Hz at 35 dB). A more thorough audiometric examination was not possible due to ethical constraints. Finally, our data are from an all-male cohort of military service members, many of whom experienced repeated blast exposure; thus, results may not be generalizable to civilian populations, although they are likely generalizable to other military groups.

Despite these limitations, our prospective, longitudinal data suggest that TBI may be a significant risk factor for new-onset tinnitus. Furthermore, risk of tinnitus is higher for blast TBIs than for nonblast TBIs and increases with injury severity and frequency. Our findings provide support for the use of TBI assessments as potential screening tools for tinnitus, particularly for those exposed to explosive devices. Blast head trauma may be a different clinical entity than tinnitus from blunt head trauma and should be treated differently. In the closely related vestibular system, military service members with blast head injury demonstrated longer latency times on motor control testing than those with mild TBI post–blunt head trauma. Blast exposure appears to produce a more global injury pattern, whereas closed blunt head injury in the mouse model shows more focal brain injury.[71,72]

Notably, this study did not find an association between PTSD and tinnitus. Traumatic brain injury–induced tinnitus in this population may be a nonsomatoform diagnosis with distinct pathophysiology and should be addressed by referral from primary care early in the treatment of TBI. Early treatment may influence the neural alterations noted in cochlear and cranial studies immediately following injury. Although treatment modalities are beyond the scope of this article, both medications and cognitive therapy have shown promise in taking advantage of neuroplasticity to "redirect" neural circuits during the repair phase after injury.[27,66] Imaging studies that measure spatial and temporal neural activity may lead to a better understanding and ultimately treatment of this ubiquitous symptom.

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