Original Investigation

Association Between Traumatic Brain Injury and Risk of Posttraumatic Stress Disorder in Active-Duty Marines

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IMPORTANCE Whether traumatic brain injury (TBI) is a risk factor for posttraumatic stress disorder (PTSD) has been difficult to determine because of the prevalence of comorbid conditions, overlapping symptoms, and cross-sectional samples.

OBJECTIVE To examine the extent to which self-reported predeployment and deployment-related TBI confers increased risk of PTSD when accounting for combat intensity and predeployment mental health symptoms.

DESIGN, SETTING, AND PARTICIPANTS As part of the prospective, longitudinal Marine Resiliency Study (June 2008 to May 2012), structured clinical interviews and self-report assessments were administered approximately 1 month before a 7-month deployment to Iraq or Afghanistan and again 3 to 6 months after deployment. The study was conducted at training areas on a Marine Corps base in southern California or at Veterans Affairs San Diego Medical Center. Participants for the final analytic sample were 1648 active-duty Marine and Navy servicemen who completed predeployment and postdeployment assessments. Reasons for exclusions were nondeployment (n = 34), missing data (n = 181), and rank of noncommissioned and commissioned officers (n = 66).

MAIN OUTCOMES AND MEASURES The primary outcome was the total score on the Clinician-Administered PTSD Scale (CAPS) 3 months after deployment.

RESULTS At the predeployment assessment, 56.8% of the participants reported prior TBI; at postdeployment assessment, 19.8% reported sustaining TBI between predeployment and postdeployment assessments (ie, deployment-related TBI). Approximately 87.2% of deployment-related TBIs were mild; 250 of 287 participants (87.1%) who reported posttraumatic amnesia reported less than 24 hours of posttraumatic amnesia (37 reported ≥24 hours), and 111 of 117 of those who lost consciousness (94.9%) reported less than 30 minutes of unconsciousness. Predeployment CAPS score and combat intensity score raised predicted 3-month postdeployment CAPS scores by factors of 1.02 (P < .001; 95% CI, 1.02-1.02) and 1.02 (P < .001; 95% CI, 1.01-1.02) per unit increase, respectively. Deployment-related mild TBI raised predicted CAPS scores by a factor of 1.23 (P < .001; 95% CI, 1.11-1.36), and moderate/severe TBI raised predicted scores by a factor of 1.71 (P < .001; 95% CI, 1.37-2.12). Probability of PTSD was highest for participants with severe predeployment symptoms, high combat intensity, and deployment-related TBI. Traumatic brain injury doubled or nearly doubled the PTSD rates for participants with less severe predeployment PTSD symptoms.

CONCLUSIONS AND RELEVANCE Even when accounting for predeployment symptoms, prior TBI, and combat intensity, TBI during the most recent deployment is the strongest predictor of postdeployment PTSD symptoms.

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Traumatic brain injury (TBI) is common. According to a 2010 Centers for Disease Control and Prevention report,[1] at least 1.7 million Americans annually sustain TBI. A significant number of injury survivors join more than 5 million (approximately 2%) Americans already living with TBI-related disabilities, which comprise a wide range of medical, cognitive, emotional, and behavioral impairments.[2,3] The estimated economic burden of TBI in the United States in 2000, prior to initiation of the Iraq and Afghanistan conflicts, was approximately $60 billion annually.[4]

Pervasive use of improvised explosive devices (IEDs), rocket-propelled grenades, and land mines in the Iraq and Afghanistan theaters has brought TBI and its effect on health outcomes into public awareness.[5-7] Blast injuries have been deemed signature wounds of these conflicts, with an estimated 52% of deployment-related TBI cases caused by IEDs.[5,8] Of Operations Enduring Freedom, Iraqi Freedom, and New Dawn service members, approximately 10% to 20% reported mild TBI or concussion, and nearly 60% of those reported exposure to more than 1 blast.[9-11]

War-related TBI is not new, having become prevalent during World War I and remaining medically relevant in World War II and beyond.[12,13] Medicine's past attempts to disentangle the pathophysiology of war-related TBI parallels current lines of inquiry and highlights limitations in methods and attribution of the cause of symptoms, be it organic, psychological, or behavioral.[14] Thus far, cross-sectional data from the Operations Enduring Freedom, Iraqi Freedom, and New Dawn conflicts reveal significantly higher rates of psychiatric symptoms, including posttraumatic stress disorder (PTSD), in deployed than in nondeployed service members.[10,15,16] Moreover, self-reported TBI and PTSD symptoms show considerable overlap.[17] Symptoms of PTSD are reported at approximately double the rate by service members who show positive results on screening for mild TBI in comparison with those who report no TBI.[9,18] These cross-sectional studies limit causal inference and stress the need for longitudinal data to define further the contribution of war-related TBI to PTSD. Using data from the Marine Resiliency Study, a prospective, longitudinal study of infantry Marines,[19] we examined whether deployment-related TBI predicts PTSD symptom severity when accounting for combat intensity and predeployment characteristics.

Methods

Study Design and Participants

We extracted data from a longitudinal study of 2600 active-duty Marine and Navy servicemen from 4 infantry battalions of the First Marine Division stationed in southern California. Assessments were conducted between July 14, 2008, and May 24, 2012, and were centered on the deployments of each battalion. Servicemen were evaluated approximately 1 month before a 7-month deployment to Iraq or Afghanistan, 1 week after deployment, and 3 and 6 months after deployment. For this study, we used data collected at predeployment, as well as 1 week and 3 months after deployment. Data from the 6-month postdeployment evaluation were not analyzed because of reduced follow-up rates. This study was approved by the institutional review boards of the University of California, San Diego; the Veterans Affairs San Diego Research Service; and the Naval Health Research Center (University of California, San Diego, and Veterans Affairs San Diego Research Service approval 070533), and written informed consent was obtained from all participants.[19] Participants received financial compensation for each study visit in which a blood draw occurred (ie, predeployment, 3-months, and 6-months postdeployment).

The **Figure** shows the sampling composition and exclusions. Of the 2600 servicemen assessed at predeployment, 34 did not deploy and were excluded a priori as well as 66 officers who were significantly older ($P < .001$) and had lower Combat Experience Scale (CES) scores ($P < .001$) than enlisted participants. Forty-five of the 66 officers (68%) were missing cognitive ability scores on a military enlistment test (Armed Forces Qualification Test [AFQT]), an important variable associated with resilience.[20] The 32% of officers with available AFQT scores scored significantly higher than current enlisted participants ($P < .001$). Of the remaining 2500 individuals, 1829 completed the 3-month postdeployment assessment. Of these, 181 were excluded for missing data on measures used in the present analysis. The final analytic sample included 1648 participants.

Measures

Complete Marine Resiliency Study methods are described elsewhere.[19] Measures relevant to the present study are described here. Posttraumatic stress symptoms were assessed using the Clinician-Administered PTSD Scale (CAPS),[21] a 17-item criterion standard, structured diagnostic interview de-

Figure. Flowchart
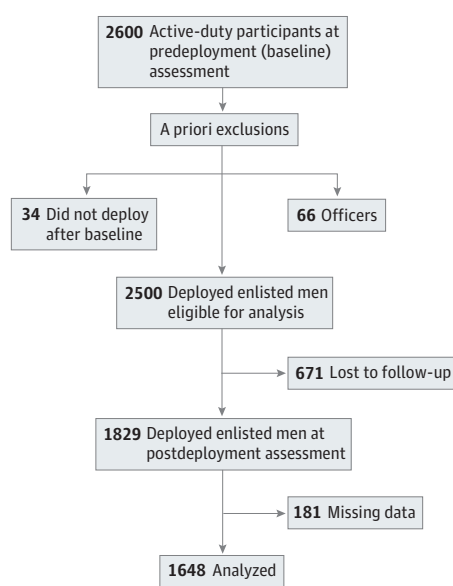
Longitudinal sample composition and reasons for exclusion.

veloped by the National Center for PTSD,[22-24] administered before deployment and 3 months after deployment. We captured the worst lifetime event in 2351 of the 2600 servicemen (90.4%) assessed at predeployment. Interrater reliability for the CAPS total score was high (intraclass correlation coefficient, 0.99).[25] Our outcome variable was 3-month postdeployment CAPS total score (possible range, 0-136), with higher scores indicating greater symptom severity. Posttraumatic stress disorder was defined as a score of 65 or greater,[24] partial PTSD as scores of 40 to 64, healthy/minimally symptomatic as scores of 1 to 39, and no symptoms as a score of 0.[23]

We inquired via face-to-face interview about any lifetime head injuries sustained before the index deployment and injuries sustained between the predeployment and 3-month postdeployment assessments. Participants were asked whether they sustained a head injury from a blast or explosion, vehicular accident, fragment or bullet wound above the shoulder, fall, blunt object, being rendered unconscious by another person, or by any other means. Probable TBI was any head injury resulting in self-reported loss of consciousness (LOC) or altered mental status (ie, dazed, confused, "seeing stars," and/or posttraumatic amnesia [PTA]) immediately afterward or upon regaining consciousness.[26-28] The time between predeployment and postdeployment assessments was broader than the deployment; thus, nondeployment TBIs sustained between assessment dates were included in analyses to account for potential effects on PTSD symptoms.[29] For parsimony, we labeled all TBIs experienced between predeployment and postdeployment assessments as *deployment-related* TBI, realizing that few were experienced outside of deployment and that some TBIs experienced before the study's predeployment assessment were acquired during a prior deployment.

Combat intensity was measured using a modified 16-item, 5-point Likert version of the Deployment Risk and Resilience Inventory[30,31] CES. The CES was administered during a brief session conducted 1 week after deployment. Response items ranged from 0 (never) to 4 (daily or almost daily) and were summed to yield a total score. Possible total CES scores range from 0 to 64, with higher total scores indicating more intense combat.

The AFQT,[20] a military enlistment aptitude test of general cognitive ability, has been negatively associated with PTSD outcomes.[32] The AFQT scores were obtained from the Career History Archival Medical and Personnel System database maintained by the Naval Health Research Center and were included as a covariate along with battalion, age, and rank. Self-reported race and ethnicity have been shown to vary with PTSD and were also entered as covariates.[33,34]

Statistical Analysis

All continuous predictors, except predeployment CAPS scores, were centered before analysis. A priori χ^2 tests showed battalion differences in deployment and TBI characteristics (Supplement [eTable 1]). We corrected for these and other unknown battalion differences, such as training schedules, timing of assessments, group leadership, and cohesion, by including battalion as a covariate. Battalion, TBI, race, and ethnicity were dummy-coded with the following reference groups: battal-

ion 1, no TBI, white, and non-Hispanic. Analyses were conducted using statistical software package R, version 2.15.3.[35]

Predeployment differences between participants in the final sample and nonparticipants (ie, servicemen assessed at predeployment only or excluded otherwise) were tested using a paired, 2-tailed *t* test, exact conditional test of proportions, or χ^2, as appropriate. Differences in predeployment CAPS scores were analyzed using zero-inflated negative binomial regression (ZINBR) because of overdispersion.

The CAPS outcome scores were positively skewed, overdispersed, and had an excess of zero scores (Supplement [eFigure]). Zero-inflated negative binomial regression was the best-fitting model[36] for our data (Supplement [eAppendix and eTable 2]) and was used to test effects of predeployment PTSD symptoms, combat intensity, and prior and deployment-related TBI on 3-month postdeployment PTSD symptoms. The ZINBR model accounts for a positively skewed integer-valued distribution with a high proportion of zero scores.[37] This model assumes that our sample contains a mixture of participants whose CAPS outcome scores are generated by the standard negative binomial distribution and those who have zero probability of a CAPS outcome score greater than zero (eg, resulting from nontraumatic CAPS event and possible genetic or biological resilience). An observed CAPS score of zero could come from either group. Zero-inflated negative binomial regression uses maximum likelihood to model outcomes via 2 component models: logistic regression (the zero model) predicts the probability of a CAPS outcome score of zero, and negative binomial regression (the count model) predicts change in CAPS score. Throughout this article we refer to predicting the odds of a zero vs nonzero outcome as the zero model and predicting nonzero outcomes as the count model.

Model estimates and predeployment symptom severity, combat intensity, and TBI were used to predict postdeployment symptom severity. Additional ZINBR models assessed the effects of TBI-related attributes, including injury severity (mild vs moderate/severe), time since most recent TBI, single vs multiple deployment-related TBIs, and group comparisons among deployment-related TBIs with LOC, TBI without LOC, and no deployment-related TBI.

Results

Sample Characteristics

Predeployment sample characteristics were similar to demographics of other deployed service members (**Table 1**).[38] Participants were younger (mean [SD] age, 22.4 [3.3] vs 23.0 [3.4] years), more likely to be junior enlisted (74.1% vs 62.2%), and were less likely to have had prior deployments (45.3% vs 62.0%) compared with nonparticipants. Approximately 31.8% of participants were married. Participants had lower childhood trauma scores (39.8 [13.2] vs 41.6 [14.8]), and better predeployment 12-item Short-Form Health Survey physical health component scores (53.9 [6.3] vs 52.6 [6.8]) than nonparticipants. Participants and nonparticipants did not differ significantly in other demographic and predeployment factors, including AFQT scores,

Table 1. Comparisons of Predeployment Characteristics Between Participants and Nonparticipants

Predeployment Characteristic	Nonparticipants (n = 852)[a]	Participants (n = 1648)	P Value
Age, mean (SD), y	23.0 (3.4)	22.4 (3.3)	<.001
Race/ethnicity, %[b]			
Hispanic	25.7	22.6	.10
White	82.3	84.9	.13
Educational level ≤high school, %	67.4	69.5	.27
Married, %	40.7	31.8	<.001
Years in military service, mean (SD)	3.3 (2.6)	2.7 (2.7)	<.001
Rank E1-E3 vs E4-E9, %	62.2	74.1	<.001
Prior deployment, %	62.0	45.3	<.001
Prior TBI, %	52.8	56.8	.06
Assessment scale scores, mean (SD)			
AFQT	58.1 (19.1)	59.8 (19.2)	.07
Childhood trauma	41.6 (14.8)	39.8 (13.2)	.003
SF-12 mental health	49.0 (9.4)	49.64 (8.7)	.14
SF-12 physical health	52.6 (6.8)	53.9 (6.3)	<.001
CAPS[c]	15.6 (16.6)	14.9 (14.8)	.38
Beck Anxiety Index Scale[d]	7.2 (8.6)	6.8 (7.6)	.35
Beck Depression Inventory Scale[e]	6.8 (8.2)	6.6 (7.5)	.69

Abbreviations: AFQT, Armed Forces Qualification Test; CAPS, Clinician-Administered PTSD [posttraumatic stress disorder] Scale; E1-E3, junior enlisted; E4-E9, senior enlisted; SF-12, 12-item Short-Form Health Survey; TBI, traumatic brain injury.

[a] Nonparticipants were defined as enlisted servicemen who deployed but completed only the predeployment assessment or were missing data required for the final model.

[b] African Americans constituted approximately 4.3% of participants and 5.7% of nonparticipants.

[c] Predeployment CAPS median score (interquartile range [IQR]) was 11 (21 − 3 = 18) for nonparticipants and 11 (21 − 4 = 17) for participants.

[d] Beck Anxiety Index median score (IQR) was 4 (11 − 1 = 10) for nonparticipants and 4 (10 − 1 = 9) for participants.

[e] Beck Depression Inventory median score (IQR) was 4 (10 − 1 = 9) for both nonparticipants and participants.

depression, anxiety, CAPS scores, 12-item Short-Form Health Survey mental health scores, and predeployment TBI rates.

Table 2 reports the final sample characteristics. Of the total number of respondents, 56.8% reported probable TBI before the index (ie, most recent) deployment. At the 3-month postdeployment assessment, 40 of the participants (2.4%) had CAPS scores of 65 or more, and 327 individuals (19.8%) reported sustaining TBI after predeployment, with 295 (17.9%) reporting TBI during the index deployment. Of the 32 participants reporting nondeployment TBI between predeployment and 3-month postdeployment assessments, 2 sustained TBI after predeployment but before the index deployment, and 24 sustained TBI after their index deployment but before their follow-up assessment; the event timing of 6 TBIs could not be verified. There were no significant differences between deployment TBI and nondeployment TBI sustained between predeployment and postdeployment on model outcomes; thus, nondeployment TBIs were included in the main analysis. Mean time since most recent TBI was 200 (126) days. Of the 327 individuals who sustained TBI after the predeployment assessment, 112 participants (34.3%) reported more than 1 TBI, and 285 TBIs (87.2%) were categorized as probably mild[39]; 208 of 327 individuals (63.6%) reported alteration of consciousness without LOC, 250 of 287 (87.1%) who reported PTA indicated less than 24 hours of PTA (37 reported >24 hours), and 111 of 117 participants (94.9%) who lost consciousness reported less than 30 min-

utes of LOC. Severity of 4 TBIs (1.2%) was unknown. Participants who sustained TBI after the predeployment assessment were more likely than others to have had prior TBI and reported more severe predeployment PTSD symptoms and greater combat intensity during their index deployment.

Zero-Inflated Negative Binomial Regression
Results of ZINBR are reported in Table 3. A significant main effect reflected a predictor's association with postdeployment CAPS scores given a predeployment CAPS score of zero, mean scores on all other continuous predictors, and reference group membership for categorical predictors. Significant interactions out of all possible tested are reported.

Zero Model: Predicting Absence of PTSD Symptoms
Logistic regression was used to predict probability of a 3-month postdeployment CAPS score of zero. Coefficients were exponentiated and interpreted as odds of a zero CAPS score. The zero model intercept reflects a 27.1% base probability of having a postdeployment CAPS score of zero given the participant was white, non-Hispanic, from battalion 1, had no predeployment or deployment TBI, had a predeployment CAPS score of zero, and had average scores on all other continuous predictors.

For the zero model, deployment-related TBIs were collapsed across severity because the small number of moderate/

Table 2. Descriptive Statistics for Participants Reporting TBI vs No TBI Sustained After Predeployment Assessment

	Mean (SD)		
Characteristic	No TBI (n = 1321)	TBI (n = 327)[a]	All Participants (N = 1648)
Predeployment variable, %			
Hispanic	22.0	25.1	22.6
White	84.9	85.0	84.9
Rank E1-E3	74.5	72.2	74.1
Prior TBI	54.5	66.1	56.8
In Battalion 1	15.5	11.9	14.8
Age, y	22.5 (3.4)	22.2 (2.8)	22.4 (3.3)
AFQT	60.4 (19.2)	57.4 (19.3)	59.8 (19.2)
CAPS score[b]	14.3 (14.6)	17.4 (15.2)	14.9 (14.8)
Deployment variable			
Combat experience score[c]	10.5 (8.7)	22.4 (13.4)	12.9 (10.9)
3-mo Postdeployment variable			
CAPS score %[d]			
Asymptomatic, score 0	22.3	4.9	18.8
Minimally symptomatic, scores 1-39	70.2	70.0	70.2
Partial PTSD, scores 40-64	6.1	18.7	8.6
PTSD, scores ≥65	1.4	6.4	2.4

Abbreviations: AFQT, Armed Forces Qualification Test; CAPS, Clinician-Administered PTSD Scale; E1-E3, junior enlisted; PTSD, posttraumatic stress disorder; TBI, traumatic brain injury.

[a] Of the 327 individuals who reported deployment-related TBI, 285 (87.2%) reported mild symptoms; 208 (63.6%) reported alteration without loss of consciousness, 250 of 287 (87.1%) with posttraumatic amnesia reported less than 24 hours of posttraumatic amnesia, and 111 of 117 (94.9%) participants who lost consciousness reported less than 30 minutes' loss of consciousness. Approximately 34.3% reported more than 1 TBI, and mean (SD) time since

most recent TBI was 200 (126) days.

[b] Predeployment CAPS median score (interquartile range [IQR]) was 10 (20 − 4 = 16) for no TBI, 14 (25 − 5 = 20) for TBI, and 11 (21 − 4 = 17) for all participants.

[c] Combat experience median score (IQR) was 8 (14 − 4 = 10) for no TBI, 20 (32 − 11 =21) for TBI, and 10 (17 − 5 = 12) for all participants.

[d] Postdeployment CAPS median score (IQR) was 10 (21 − 2 = 19) for no TBI, 24 (40 − 12 = 28) for TBI, and 12 (26 − 4 = 22) for all participants.

severe TBIs caused problems with model convergence. Unit increases in predeployment CAPS scores decreased the odds of an outcome (ie, postdeployment) CAPS score of zero by a factor of 0.92 (7.7%; $P < .001$). Unit increases in combat intensity reduced the odds by a factor of 0.96 (3.6%; $P < .001$). Prior TBI reduced the odds of having an outcome CAPS score of zero by a factor of 0.65 (35.5%; $P < .01$), and deployment-related TBI reduced the odds by a factor of 0.34 (66.1%; $P < .01$). There were no effects of TBI with vs without LOC, time since most recent TBI, or single vs multiple deployment-related TBI on the absence of postdeployment symptoms.

Count Model: Predicting PTSD Symptom Severity

The count model predicted the postdeployment CAPS scores being generated from a negative binomial distribution. Exponentiated coefficients of the counts model represent multiplicative change in predicted CAPS score per unit change in a given predictor. The intercept reflects a predicted postdeployment CAPS score of 12.54 given the participant was white, non-Hispanic, from battalion 1, had no TBI, had a predeployment CAPS score of zero, and had average scores on all other continuous predictors.

Predeployment CAPS score and combat intensity score raised the predicted 3-month postdeployment CAPS score by factors of 1.02 (1.9%; $P < .001$) and 1.02 (1.5%; $P < .001$) per unit increase, respectively. Prior (ie, pre–index deployment) TBI

raised the predicted CAPS outcome score by a factor of 1.08 (7.5%), but the effect was not significant ($P < .08$). Deployment-related mild TBI raised the predicted CAPS score by a factor of 1.23 (22.6%; $P < .001$), and deployment-related moderate/severe TBI raised the predicted CAPS score by a factor of 1.71 (70.5%; $P < .001$). Dividing the estimated coefficients for deployment-related TBI by combat intensity yielded the equivalent of a 14.0-point increase in combat intensity for participants reporting mild TBI, and a 36.6-point increase for those reporting moderate/severe TBI. There were no effects of deployment-related TBI with vs without LOC, time since recent TBI, or single vs multiple TBI on postdeployment symptom severity.

There was a relatively small interaction effect that accounted for less than 1% change in 3-month postdeployment CAPS score. Unit increases in AFQT increased the predicted CAPS score by 0.8% ($P < .001$), but this effect was reduced by roughly two-thirds in participants with predeployment TBI ($P < .02$).

The overall effects of predeployment symptoms, combat intensity, and TBI on postdeployment PTSD symptoms were confirmed using logistic regression to determine the effects of the same predictors as in the final ZINBR model on the categorical outcome of PTSD vs no PTSD at 3-month postdeployment assessment (Supplement [eMethods, eResults, and eTable 3]).

Table 3. Zero-Inflated Negative Binomial Regression Predicting Postdeployment PTSD Symptoms

Model	Variable	Estimate (SE)	P Value	Predicted CAPS Total[a]	Ratio (95% CI)
Count	(Intercept)	2.53 (0.06)	<.001	12.54	(11.10-14.17)
	Battalion 2	−0.03 (0.06)	.65		0.97 (0.86-1.00)
	Battalion 3	−0.05 (0.06)	.46		0.96 (0.85-1.08)
	Battalion 4	0.13 (0.07)	.06		1.14 (0.10-1.31)
	CAPS score, predeployment	0.02 (0.00)	<.001		1.02 (1.02 -1.02)
	AFQT	0.01 (0.00)	<.001		1.01 (1.01-1.01)
	TBI, predeployment	0.07 (0.04)	.07		1.08 (0.99-1.16)
	AFQT × TBI, predeployment	−0.0 (0.00)	.02		1.00 (0.99-1.00)
	Combat Experience Score	0.01 (0.00)	<.001		1.02 (1.01-1.02)
	Mild TBI, deployment[b]	0.20 (0.05)	<.001		1.23 (1.11-1.36)
	Moderate/severe TBI, deployment	0.53 (0.11)	<.001		1.71 (1.37-2.12)
Zero	(Intercept)	−0.10 (0.25)	<.001	27.10%	(18.60%-37.69%)
	Battalion 2	0.93 (0.24)	<.001		2.52 (1.60-4.06)
	Battalion 3	0.63 (0.25)	.01		1.87 (1.14-3.07)
	Battalion 4	0.33 (0.29)	.26		1.39 (0.79-2.45)
	CAPS score, predeployment	−0.08 (0.01)	<.001		0.92 (0.90-0.94)
	TBI, predeployment	−0.44 (0.15)	.003		0.64 (0.48-0.86)
	Combat Experience Score	−0.04 (0.01)	<.001		0.96 (0.94-0.98)
	TBI, deployment[b,c]	−1.08 (0.30)	<.001		0.34 (0.19-0.62)

Abbreviations: AFQT, Armed Forces Qualification Test; CAPS, Clinician-Administered PTSD Scale; PTSD, posttraumatic stress disorder; TBI, traumatic brain injury.

[a] For the zero model, base probability (%) of a predicted CAPS total score, 0.

[b] There were no significant differences between deployment and nondeployment TBI sustained between predeployment and postdeployment assessments (n = 32). Thus, nondeployment TBI was included in the analysis to account for any potential effects on PTSD outcomes.[27]

[c] For the zero model, deployment-related TBIs were collapsed across severity because of the small number of moderate/severe TBIs causing problems with model convergence.

Predictions

Predeployment CAPS scores, combat intensity, and deployment-related mild TBI were used to predict the probability that 3-month postdeployment CAPS scores would fall within defined symptom ranges for partial PTSD and PTSD while holding all other variables constant (Table 4). Predeployment CAPS scores used for prediction were 0 (no symptoms), 19 (healthy/minimally symptomatic; range, 1-39), 52 (partial PTSD; range, 40-64), and 65 (PTSD; scores ≥65).[23] Low and high combat intensity were defined as CES scores of 5 (25th percentile) and 19 (75th percentile), respectively.

Based on study outcomes, participants with no predeployment symptoms, low combat intensity, and no deployment-related TBI were ascertained to have a predicted 3-month postdeployment CAPS score of 7.23, with less than 1% probability of partial PTSD or PTSD. Deployment-related mild TBI raised the predicted CAPS score slightly to 11.45, with 1.5% probability of partial PTSD.

Participants who were minimally symptomatic before deployment had low combat intensity, and those with no TBI had less than 4% predicted probability of postdeployment partial PTSD (3.2%) and PTSD (0.2%). High combat intensity increased predicted rates to 6.9% for partial PTSD and 0.8% for PTSD. In addition, deployment-related mild TBI nearly doubled outcome rates to 12.4% for partial PTSD and 2.4% for PTSD.

Compared with the minimally symptomatic group, participants whose predeployment CAPS scores met the criteria for partial PTSD or PTSD had higher predicted probabilities of postdeployment PTSD at 3 months, even with low combat intensity (>6%). Higher combat intensity increased predicted PTSD rates for those who reported partial symptoms before deployment (12.3%), and deployment-related mild TBI further increased predicted PTSD rates for this group (21.1%).

Discussion

As expected, both predeployment psychiatric symptoms and combat intensity significantly predicted postdeployment PTSD symptoms. Predeployment psychiatric conditions have been deemed a risk factor for PTSD and other mental health problems during deployment.[40] Likewise, prior psychological trauma[16,41] and extensive combat exposure[15,16,42,43] may increase PTSD risk after combat deployment.

Independent of the above effects, TBI sustained before the index deployment was associated with more severe postdeployment PTSD symptoms. According to our model, deployment-related TBIs nearly double the likelihood of postdeployment PTSD for participants who reported minimal to no symptoms before deployment. Probability of postdeployment PTSD was greatest for participants reporting prior psychiatric symptoms and deployment-related TBI. However, of the 16 participants with predeployment PTSD, 8 considerably improved (postdeployment CAPS range, 0-35) and 3 slightly improved (range, 50-78), whereas 3 worsened (range, 78-94). In contrast to those with improved symptoms, participants with persistent symptoms reported higher combat intensity (mean score, 22.7 vs 8.4) and 2 of the 3 reported deployment-related TBI. These findings parallel reported symptom trajectories for deployed service members in which 8% showed improvement in PTSD symptoms and 2.2% showed continuation of severe symptoms.[44]

Prior cross-sectional studies have also reported associations between TBI and PTSD,[45,46] although injury severity may govern the association.[47,48] Higher morbidity and use of medical services are associated with severe TBI, whereas mental health diagnoses, including PTSD, are more frequent in pa-

Table 4. Predictions of Postdeployment CAPS Scores and Outcome Probabilities

Predeployment Symptom Severity (N = 1648)[a]	Combat Intensity[b]	Mild Deployment TBI	Predicted Mean Postdeployment CAPS Score (95% CI)	% Predicted Probability of Partial PTSD (95% CI)[c]	% Predicted Probability of PTSD (95% CI)[c]
No symptoms (n = 243)	Low	No	7.23 (6.10-8.36)	0.38 (0.27-0.51)	0.01 (0.00-0.02)
		Yes	11.45 (10.18-12.72)	1.50 (1.28-1.75)	0.05 (0.01-0.10)
	High	No	10.29 (9.00-11.58)	1.35 (1.13-1.58)	0.04 (0.01-0.09)
		Yes	14.95 (13.90-16.00)	3.88 (3.51-4.27)	0.26 (0.16-0.36)
Minimally symptomatic (n = 1283)	Low	No	14.17 (13.43-14.91)	3.22 (2.87-3.57)	0.18 (0.10-0.27)
		Yes	18.63 (18.09-19.18)	7.12 (6.63-7.63)	0.77 (0.61-0.95)
	High	No	18.13 (17.47-18.80)	6.93 (6.43-7.43)	0.75 (0.59-0.93)
		Yes	23.21 (22.79-23.63)	12.44 (11.80-13.11)	2.37 (2.08-2.68)
Partial PTSD (n = 106)	Low	No	29.40 (29.13-29.67)	19.01 (18.27-19.79)	6.21 (5.74-6.69)
		Yes	36.25 (36.05-36.45)	24.13 (23.30-24.96)	12.35 (11.72-13.01)
	High	No	36.19 (35.96-36.42)	24.09 (23.25-24.92)	12.33 (11.70-12.98)
		Yes	44.52 (44.34-44.71)	27.12 (26.25-27.99)	21.08 (20.30-21.88)
PTSD (n = 16)[d]	Low	No	37.89 (37.68-38.09)	24.97 (24.10-25.83)	14.02 (13.35-14.96)
		Yes	46.55 (46.36-46.75)	27.44 (26.57-28.32)	23.27 (22.47-24.11)
	High	No	46.54 (46.34-46.73)	27.42 (26.54-28.29)	23.27 (22.44-24.09)
		Yes	57.14 (56.95-57.33)	27.32 (26.45-28.19)	34.36 (33.44-35.29)

Abbreviations: CAPS, Clinician-Administered PTSD Scale; PTSD, posttraumatic stress disorder; TBI, traumatic brain injury.

[a] CAPS scores used for prediction were no symptoms (score, 0), healthy/minimally symptomatic (median score, 19; range, 1-39), partial PTSD (median score, 52; range, 40-64), and PTSD scores ≥65.[23]

[b] Low and high combat intensity were Combat Experience Scale scores 5 (25th percentile) and 19 (75th percentile), respectively.

[c] Predicted probability of a continuous outcome CAPS score that falls within

defined symptoms ranges for partial PTSD and PTSD.

[d] Of the 16 participants with predeployment PTSD, 8 improved considerably (postdeployment CAPS range, 0-35) and 3 improved slightly (range, 50-78). Symptoms of 3 worsened (range, 78-94); these participants had higher combat intensity (Combat Experience Scale mean score, 22.7 vs 8.4), and 2 of the 3 sustained deployment-related TBI compared with those whose symptoms improved.

tients with mild TBI.[5] In the present study, however, postdeployment CAPS scores increased with TBI severity. More severe TBI in our participants may reflect more severe physical injury, which has been shown to increase the risk of PTSD.[49] Higher CAPS scores may also reflect nonspecific symptoms that overlap with TBI sequelae. Alternatively, perhaps the overall contexts surrounding severe TBI were more emotionally traumatic than contexts surrounding milder injuries. Although we adjusted for overall combat intensity, that adjustment would not account for the characteristics of any particular traumatic event.

A possible contributor to the overlap of TBI and PTSD symptoms might be that the emotional salience of the event contiguous with TBI may exceed that of the typical civilian or combat-related traumatic event, thereby increasing PTSD risk. Structural and functional brain changes following TBI are likely additional contributors to PTSD outcomes. Prefrontal cortical networks implicated in PTSD[50-52] may be damaged during the course of mild TBI, consequently affecting fear memory processing.[53] Correlations between white matter integrity, cortical function, and postconcussive symptoms provide initial evidence that brain changes associated with mild TBI are distinct from those associated with PTSD or depression.[54-57] Ultimately, high-resolution neuroimaging may help to clarify whether TBI severity reflects neural tissue injury that impedes emotional recovery from stressful events.

There is growing interest in the persistence of postconcussive symptoms and the extensive overlap with anxiety dis-

orders, including PTSD.[58-60] Brain injuries also have been linked to increased suicidality, particularly for individuals with comorbid psychiatric and emotional disturbances, such as PTSD and depression.[61-63] Comorbidity of TBI and PTSD is not unique to deployed service members; motor vehicle accidents and interpersonal assault are 2 common causes of TBI and PTSD in civilians.[64-66] Furthermore, recurrent TBI from contact sports has, as with repeated blast exposure, been linked to greater mental health problems and neurologic abnormalities.[67,68]

Several study limitations should be addressed. As in prior studies,[9,29,69,70] we used retrospective self-report measures, including TBI accounts, which limit causal inference and reflect potentially inconsistent documentation of in-theater events. Furthermore, TBI may be a marker for a traumatic event not otherwise captured by the CES.

In addition, results from the present study may not be generalizable to other populations. Demographic differences between participants and nonparticipants likely reflect the older age and greater military experience of nonparticipants, most of whom were lost to follow-up, possibly resulting from reassignment or discharge. Participation bias likely accounts for mental and physical health differences between participants and nonparticipants. Similar findings have been documented[29] previously and have not been shown to affect study outcomes. Finally, PTSD symptoms were positively skewed, and CAPS threshold scores for partial PTSD and PTSD that were validated in civilians may be conservative for diagnosis in a military population.

Despite these limitations, the present study's prospective design and inclusion of prior psychological and physical trauma are unique contributions to the study of TBI and PTSD.

Results suggest that deployment-related TBI may be an important risk factor for PTSD, particularly for individuals with symptoms related to a prior traumatic event.

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