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Prospective Longitudinal Evaluation of the Effect of Deployment-Acquired Traumatic Brain Injury on Posttraumatic Stress and Related Disorders: Results From the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS)

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Abstract

Objective—Traumatic brain injury (TBI) is increasingly recognized as a risk factor for deleterious mental health and functional outcomes. The purpose of this study was to examine the strength and specificity of the association between deployment-acquired TBI and subsequent posttraumatic stress and related disorders among U.S. Army personnel.

Method—A prospective, longitudinal survey of soldiers in three Brigade Combat Teams was conducted 1–2 months prior to an average 10-month deployment to Afghanistan (T0), upon redeployment to the United States (T1), approximately 3 months later (T2), and approximately 9 months later (T3). Outcomes of interest were 30-day prevalence postdeployment of posttraumatic stress disorder (PTSD), major depressive episode, generalized anxiety disorder, and suicidality, as well as presence and severity of postdeployment PTSD symptoms.

Results—Complete information was available for 4,645 soldiers. Approximately one in five soldiers reported exposure to mild (18.0%) or more-than-mild (1.2%) TBI(s) during the index deployment. Even after adjusting for other risk factors (e.g., predeployment mental health status, severity of deployment stress, prior TBI history), deployment-acquired TBI was associated with elevated adjusted odds of PTSD and generalized anxiety disorder at T2 and T3 and of major depressive episode at T2. Suicidality risk at T2 appeared similarly elevated, but this association did not reach statistical significance.

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Conclusions—The findings highlight the importance of surveillance efforts to identify soldiers who have sustained TBIs and are therefore at risk for an array of postdeployment adverse mental health outcomes, including but not limited to PTSD. The mechanism(s) accounting for these associations need to be elucidated to inform development of effective preventive and early intervention programs.

Mild traumatic brain injury (mild TBI; also known as concussion), previously believed to be an almost uniformly benign event, has garnered increased attention as a potential source of adverse neuropsychological outcomes in civilians (e.g., athletes who play contact sports) and military personnel alike (1–4). With respect to mental health outcomes, many observational studies—the earliest from military settings (5, 6)—have established an association between mild TBI and posttraumatic stress disorder (PTSD) (7–15). Although most of these studies have been cross-sectional and/or retrospective in design, or have relied on hospitalized, treatment-seeking or other potentially nonrepresentative samples, a few studies of longitudinal prospective cohorts have clearly demonstrated an association between TBI and subsequent PTSD (15, 16).

Numerous questions about the association between TBI and PTSD remain unanswered. Among them are uncertainties about the specificity of this association. Is PTSD a unique or particularly prevalent outcome of TBI, or is risk of developing (certain) other mental disorders comparable? A civilian study of 1,084 traumatically injured individuals found that TBI was a strong risk factor not only for PTSD but also for a wide range of depressive and anxiety disorders (16). Another area of controversy pertains to the importance of the severity of TBI, particularly with regard to whether “very mild” (i.e., dazed but no loss of consciousness or amnesia) TBIs have a salient impact on subsequent mental health. To the best of our knowledge, neither of these questions has been addressed in a large, prospective longitudinal cohort and never in a military setting. The present study uses data from the Pre/Post Deployment Study (PPDS), a prospective, longitudinal component of the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS) (17), to examine the relationships of deployment-acquired TBI with postdeployment PTSD and related disorders, controlling for a range of other known and hypothesized pre- and peri-deployment predictors of these outcomes.

METHOD

Overview of the PPDS of Army STARRS

Detailed information about the design and conduct of Army STARRS is available in a separate report (17). The PPDS of Army STARRS is a multiwave panel survey that collected baseline data (T0; self-administered questionnaire) from U.S. Army soldiers in three Brigade Combat Teams during the first quarter of 2012, within approximately 6 weeks of their deployment to Afghanistan. Follow-up data were collected from these same respondents at three times after they returned from deployment: within 1 month of their return (T1; self-administered questionnaire and blood samples), approximately 3 months later (T2; self-administered questionnaire), and 9 months later (T3; self-administered questionnaire). The baseline (T0) questionnaire was an extensive survey of socio-demographic characteristics, lifetime and past-30-day mental disorders, and a panoply of potential risk and resilience

factors, including but not limited to past civilian and military experiences. The T1 follow-up questionnaire included only a brief assessment of experiences that occurred during deployment (including deployment stressors and TBI). The T2 and T3 questionnaires, which were virtually identical, were more extensive, covering mainly intercurrent experiences subsequent to the prior assessments.

The PPDS study population consisted of all soldiers in three Brigade Combat Teams that deployed to Afghanistan (average duration of deployment was 10 months) shortly after completing the baseline (T0) PPDS data collection. All participants gave their informed, written consent to participate. Baseline PPDS respondents were additionally asked for consent to provide blood samples, to link their Army and Department of Defense administrative records to their survey responses, and to participate in future assessments. Similar informed consent procedures were used in the postdeployment data collections. These procedures were approved by the human subjects committees of all collaborating organizations.

At the baseline (T0), a total of 9,949 soldiers were present for duty in the three Brigade Combat Teams. Of these, a total of 9,488 (95.3%) consented to participate in the survey with 8,558 (86.0%) providing complete T0 survey responses and consent to link their survey responses to their administrative records. The T0 longitudinal analysis cohort for this investigation was restricted to the subpopulation (N=7,742) of these T0 study participants who subsequently deployed to Afghanistan. A total of 4,645 (60.0%) of the 7,742 T0 study participants that deployed to Afghanistan provided complete data at all three postdeployment assessments (i.e., T1, T2, and T3). To compensate for T1, T2, and/or T3 attrition losses from the eligible baseline sample of 7,742 participants, response propensity (based on T0 measures available for all baseline respondents) and poststratification (based on comparisons of distributions for key socio-demographic and Army career variables from administrative data available for the entire Army as well as for survey respondents) weighting factors (18) were developed and applied in all analyses of the multiwave data.

Measures

Diagnostic assessment—At baseline (T0), PPDS respondents self-administered a computerized version of the Composite International Diagnostic Interview screening scales (CIDI-SC) (19) and a 6-item screening version of the PTSD Checklist (20) to assess 10 lifetime DSM-IV mental disorders. Diagnoses were made without DSM-IV diagnostic hierarchy or organic exclusion rules. The sum of all past-30-day depression, anxiety, and irritability items from the screening scales (24 items, each ranging 0–4) was also used to create a general distress score (range: 0–96). As reported in detail elsewhere (21), an Army STARRS clinical reappraisal study found satisfactory concordance between CIDI-SC and modified PTSD Checklist diagnoses and independent clinical diagnoses based on blinded Structured Clinical Interviews for DSM-IV (area under receiver operating characteristic curve=0.70–0.79; κ=0.4–0.6).

These measures were repeated approximately 3 months (T2) and 9 months (T3) after redeployment to the United States. The full 17-item PTSD Checklist was administered at T2

and T3. In this sample, 6-item PTSD Checklist scores correlated highly (T2: r=0.96; T3: r=0.96) with PTSD Checklist (i.e., 17-item) scores.

Suicidality—Suicidal behaviors were assessed using a modified version of the Columbia-Suicide Severity Rating Scale (22) assessing lifetime occurrence and age at onset of suicide ideation and, among respondents who reported lifetime ideation, suicide plans and attempts. Lifetime (or past-30-day) suicidality was determined at T0 as endorsing lifetime (or past-30-day) suicidal ideation, plans, and/or attempt(s). Past-30-day suicidality was assessed at T2 and T3 using the same questions.

Deployment stress—The T1 survey included 15 questions that assessed the frequency of stressful deployment experiences (e.g., During your deployment how many times did you …. Go on combat patrols or have other dangerous duty? [e.g., route clearance, clearing buildings, disarming civilians, working in areas that had IEDs] or …. Fire rounds at the enemy or take enemy fire? [either direct or indirect fire]). Responses to these questions were discretized (yes/no), and positive responses were summed to create a total (0–15) deployment stress severity score.

TBI status—Probable TBI was determined by the probe (How many times during your recent deployment did you have a head, neck, or blast injury that…?) followed by a series of questions pertaining to subsequent alteration or loss of consciousness and lapse of memory. We used the highest level of severity of response(s) to characterize each respondent as having had one of the following: 1) No TBI; 2) probable “very mild” TBI (alteration but no loss of consciousness [“didn’t knock you out but caused you to be dazed or ‘see stars’”] and no lapse of memory); 3) probable “mild TBI” (loss of consciousness [“knocked you out”] for less than 30 minutes and/or lapse of memory for less than 30 minutes); or 4) probable “more-than-mild TBI” (loss of consciousness for 30 minutes or more or lapse in memory lasting 30 minutes or more). Using these criteria, TBIs classified as “very mild” or “mild” would match up with most standard and widely used definitions of mild TBI (e.g., http://tbilaw.com/acrm-brain-injury-definition.html). The majority of TBIs classified as “more-than-mild” would fall into a higher category of clinical severity, although cases in this category defined by loss of consciousness <30 minutes and posttraumatic amnesia <24 hours could fall within standard definitions of mild TBI (hence our labeling of this category as probable “more-than-mild”). We evaluated the effects of the various levels of severity, as well as “any” deployment-acquired TBI (or lifetime TBI prior to the index deployment) compared with none.

We also attempted to corroborate our survey reporting of TBIs with the Army’s own TBI surveillance as a component of the Pre- or Post-Deployment Health Reassessment (http://www.armyg1.army.mil/hr/pdhra/), which, it should be noted, is also based on self-report. Data showing the concordance between these two modes of self-assessment are presented in the online data supplement accompanying this article.

Socio-demographic variables—Socio-demographic variables considered here were age, sex, ethnicity, and race.

Analysis methods—We conducted a series of logistic regression analyses where deployment-acquired TBI (1=any, 0=none, assessed at T1) or severity of deployment-acquired TBI (none versus very mild versus mild versus more-than-mild) was the predictor of primary interest and past 30-day, postdeployment mental health disorders or indicators (assessed at T2 and T3) were the outcome(s). Models adjusted for factors that we thought might influence risk for TBI as well as have independent associations with the outcomes, including age (≤30 versus older), sex, ethnicity, race, Brigade Combat Team, predeployment (T0) mental health status, number of prior deployments (none versus one versus two or more), and severity of deployment stress. Duration of index deployment was included in earlier models but found to be entirely nonpredictive, and thus it was excluded from the final models. We also conducted zero-inflated negative binomial regression analyses to jointly model the effect of deployment-acquired TBI on presence (yes/no) and severity (for nonzero scores) of PTSD symptoms as measured by the PTSD Checklist.

All analyses were weighted to account for T1, T2, and T3 survey attrition from the eligible T0 soldier cohort. Since the PPDS data are both clustered by Brigade Combat Team and administration session and weighted, the design-based Taylor series linearization method was used to produce standard errors. Multivariate significance was examined using design-based Wald chi-square tests. All statistical analyses were conducted using the software R (version 3.0.2, R Development Core Team, 2011). Additionally, p values <0.05 (two-tailed) were considered statistically significant.

RESULTS

Participant Characteristics at Predeployment Baseline (T0)

All reported percentages and means are weight-adjusted. The sample was predominantly male (94.7% [SE=0.6%]) and less than 30 years of age (71.6% [SE=1.4%]). The majority of participants were White (71.8% [SE=0.8%]), with smaller proportions identifying their race as Other (12.2% [SE=0.6%]), Black (12.0% [SE=0.7%]), and Asian (4.0% [SE=0.3%]), and 16.1% (SE=0.6%) identifying their ethnicity as Hispanic. For 44.8% (SE=1.2%) of soldiers, the index deployment to Afghanistan was their first, with others reporting one (23.3% [SE=0.7%]) or multiple (31.8% [SE=1.1%]) previous deployments.

Estimated lifetime prevalence of mental disorders at the baseline (T0) interview was 12.0% (SE=0.6%) for PTSD, 9.3% (SE=0.6%) for major depressive episode, 8.3% (SE=0.4%) for generalized anxiety disorder, and 10.7% (SE=0.5%) for suicidality. Prior to deployment, mean PTSD symptom severity as measured by the 6-item PTSD Checklist was 7.87 (SD=3.49; median=6, range=6–30, interquartile range=6–8), and mean general distress was 11.03 (SD=14.51; median=6, range=0–96, interquartile range=2–13).

Approximately one-third of soldiers reported having sustained TBI(s) prior to the index deployment (T0), with 14.8% (SE=0.6%) endorsing one and 19.5% (SE=0.8%) endorsing two or more lifetime TBIs.

Deployment Stress and Deployment-Acquired TBI

The mean number of deployment stressors in the index deployment endorsed by respondents at T1 was 4.02 (SD=2.76; median=4, range=0–15, interquartile range=2–6). Approximately 1 in 5 soldiers reported exposure to TBI(s) during the index deployment, with 13.2% (SE=0.6%) endorsing probable very mild TBI (i.e., dazed only, no loss of consciousness or amnesia), 4.8% (SE=0.4%) endorsing probable mild TBI, and 1.2% (SE=0.2%) endorsing probable more-than-mild TBI.

Mental Health Outcomes at 3 Months Postdeployment (T2)

At the T2 follow-up, approximately 3 months postredeployment to the United States from Afghanistan, past-30-day DSM-IV PTSD was reported by 7.8% (SE=0.5%) of soldiers. The mean PTSD Checklist score at T2 was 24.80 (SD=10.78; median=21, range=17–85, interquartile range=17–28).

Past-30-day prevalence of other mental disorders at T2 was 6.8% (SE=0.4%) for major depressive episode, 4.8% (SE=0.3%) for generalized anxiety disorder, and 2.9% (SE=0.2%) for suicidality. The combined prevalence of any past-30-day PTSD, major depressive episode, generalized anxiety disorder, or suicidality at T2 was 12.9% (SE=0.6%; see Figure 1 for depiction of comorbidity rates). The mean general distress score at T2 was 11.97 (SD=16.02; median=6, interquartile range=1–15).

Association of deployment-acquired TBI with posttraumatic stress outcomes

—In a logistic regression analysis adjusting for age group, sex, ethnicity, race, Brigade Combat Team, number of prior deployments, predeployment TBI history, lifetime PTSD predeployment, PTSD symptoms at baseline (6-item PTSD Checklist score at T0), and deployment stress severity, deployment-acquired TBI was strongly associated with increased odds of postdeployment (T2) past-30-day PTSD (adjusted odds ratio=1.81, 95% CI=1.32–2.46, $p<0.0005$; see Table 1).

The above model was rerun stratifying TBI-positive subjects into those with probable “very mild,” “mild,” and “more than mild” concussions. Whereas all TBI-positive groups displayed increased odds for past 30-day PTSD at T2, a dose-response relationship was observed whereby odds of PTSD increased as TBI severity worsened (adjusted odds ratios=1.66, 1.76, and 3.90 for “very mild,” “mild,” and “more-than-mild,” respectively; $p<0.0005$).

Whereas the previous models evaluated presence or absence of PTSD as a dichotomous outcome, we also evaluated whether deployment-acquired TBI was associated with increased PTSD symptoms at T2. Having sustained a TBI during the index deployment was associated with increased odds of a nonzero score on the PTSD Checklist (i.e., having some PTSD symptoms versus none; adjusted odds ratio=1.47, 95% CI=1.03–2.08, $p=0.04$) and a 1.35-fold increase in PTSD Checklist score when symptoms were present (i.e., when the PTSD Checklist score was nonzero; fold change=1.35, 95% CI=1.21–1.51, $p<0.001$; see Table 2).

Association of deployment-acquired TBI with other mental health outcomes— In logistic regression analyses adjusting for age group, sex, ethnicity, race, Brigade Combat Team, number of prior deployments, lifetime history of the outcome in question (major depressive episode, generalized anxiety disorder, or suicidality) predeployment (T0), general distress predeployment (T0), and deployment stress severity, deployment-acquired TBI was associated with postdeployment (T2) risk of past-30-day major depressive episode (adjusted odds ratio=1.45, 95% CI=1.02–2.04, p=0.037) and generalized anxiety disorder (adjusted odds ratio=1.81, 95% CI=1.21–2.70, p=0.004). The association between deployment-acquired TBI and past-30-day suicidality did not reach the threshold for statistical significance (adjusted odds ratio=1.39, 95% CI=0.97–2.01, p=0.076).

Deployment-acquired TBI was associated with increased odds of the composite of any of these past-30-day outcomes (adjusted odds ratio=1.74, 95% CI=1.33–2.27, p<0.0005; see Table 3). When the composite outcome was rerun stratifying TBI-positive subjects into those with probable “very mild,” “mild,” and “more than mild” concussions, a dose-response relationship between severity of TBI and odds of the composite outcome was observed (adjusted odds ratios=1.57, 1.78, and 4.28 for “very mild,” “mild,” and “more than mild,” respectively; p<0.0005).

Mental Health Outcomes at 9 Months Postdeployment (T3)

At the T3 follow-up, approximately 9 months postredeployment to the United States from Afghanistan, past-30-day DSM-IV PTSD was reported by 11.7% (SE=0.5%) of soldiers. The mean PTSD Checklist score at T3 was 25.79 (SD=12.70; median=19, interquartile range=17–30).

Past-30-day prevalence of other mental disorders at T3 was 6.7% (SE=0.3%) for major depressive episode, 6.2% (SE=0.4%) for generalized anxiety disorder, and 5.7% (SE=0.4%) for suicidality. The combined prevalence of any past-30-day PTSD, major depressive episode, generalized anxiety disorder, or suicidality at T3 was 16.8% (SE=0.6%; see Figure 2 for depiction of comorbidity rates). The mean general distress score at T3 was 14.32 (SD=18.12; median=6, interquartile range=2–21).

Association of deployment-acquired TBI with posttraumatic stress outcomes—In a logistic regression analysis adjusting for age group, sex, ethnicity, race, Brigade Combat Team, number of prior deployments, predeployment TBI history, lifetime PTSD predeployment, PTSD symptoms at baseline (6-item PTSD Checklist score at T0), and deployment stress severity, deployment-acquired TBI was strongly associated with increased odds of past-30-day PTSD at 9 months postdeployment (T3) (adjusted odds ratio=1.48, 95% CI=1.21–1.83, p<0.0005; see Table 1).

When the above model was rerun stratifying TBI-positive subjects into those with probable “very mild,” “mild,” and “more-than-mild” concussions, a dose-response relationship with TBI severity was seen such that increasing severity of TBI was associated with increasing odds of T3 past-30-day PTSD (adjusted odds ratios=1.21, 1.78, and 4.49 for “very mild,” “mild,” and “more than mild,” respectively; p<0.0005). However, the adjusted odds ratio for

"very mild TBI" (1.21) was not significantly elevated relative to the "no TBI" reference group (p=0.13).

Whereas the previous models evaluated presence or absence of PTSD as a dichotomous outcome, we also evaluated whether deployment-acquired TBI was associated with increased PTSD symptoms at T3. Having sustained a TBI during the index deployment was associated with increased odds of a nonzero score on the PTSD Checklist (i.e., having some PTSD symptoms versus none; adjusted odds ratio=1.82, 95% CI=1.22–2.70, p=0.005) and a 1.20-fold increase in PTSD Checklist score when symptoms were present (i.e., when the PTSD Checklist score was nonzero; fold change=1.20, 95% CI=1.10–1.31, p<0.001; see Table 2).

Association of deployment-acquired TBI with other mental health outcomes— In logistic regression analyses adjusting for age group, sex, ethnicity, race, Brigade Combat Team, number of prior deployments, lifetime history of the outcome in question (major depressive episode, generalized anxiety disorder, or suicidality) predeployment (T0), general distress predeployment (T0), and deployment stress severity, deployment-acquired TBI was associated with postdeployment (T3) risk of past-30-day generalized anxiety disorder (adjusted odds ratio=1.81, 95% CI=1.21–2.70, p<0.0005). The association of deployment-acquired TBI with T3 past-30-day major depressive episode did not reach statistical significance (adjusted odds ratio=1.28, 95% CI=0.97–1.69, p=0.08), nor was its association with T3 past-30-day suicidality significant (adjusted odds ratio=1.12, 95% CI=0.86–1.46, p=0.40).

Deployment-acquired TBI was associated with the composite of any of these outcomes at T3 (adjusted odds ratio=1.53, 95% CI=1.29–1.82, p<0.0005; see Table 3). When the composite outcome was rerun stratifying TBI-positive subjects into those with probable "very mild," "mild," and "more-than-mild" concussions, a dose-response relationship with TBI severity was seen such that increasing severity of TBI was associated with increasing odds of T3 past-30-day composite of these outcomes (adjusted odds ratios=1.28, 1.87, and 4.22, p<0.0005, for "very mild," "mild," and "more than mild," respectively).

DISCUSSION

Consistent with studies of individuals who sustained traumatic injury in civilian settings (16, 23, 24), we found evidence from this large, prospective military cohort study that deployment-acquired TBI is associated with substantially increased risk for having PTSD at 3 and 9 months postdeployment. This association was robust across models that adjusted for multiple concurrent risk factors (particularly lifetime PTSD, baseline PTSD symptoms, prior TBI history and deployment stress severity) and that considered multiple indicators of the outcome of interest (PTSD diagnosis; presence and severity of PTSD symptoms). These findings converge with results of considerable observational research that has shown mild TBI to be among the most salient risk factors for the development of PTSD (3, 14, 15).

Few studies have attempted to investigate the impact of TBI severity on subsequent mental health outcomes. However, a recent study of military personnel found that blast-related mild

TBI with loss of consciousness (versus no loss of consciousness) was associated with increased risk for PTSD (25). An Israeli study of civilian motor vehicle collision survivors with head injuries similarly found that the risk of PTSD was increased if the injury included loss of consciousness (26). We found a dose-response relationship between “very mild” (dazed but no loss of consciousness or amnesia), “mild” (some loss of consciousness or amnesia), and “more-than-mild” TBI and the observed outcomes. More-than-mild TBI was associated with the greatest elevations of risk for PTSD and the composite outcome of any PTSD, major depressive episode, generalized anxiety disorder, or suicidality, with odds ratios reflecting approximately 4 times greater risk relative to those without deployment-acquired TBI. Mild TBI conveyed an intermediate elevation of risk for the same outcomes, with odds ratios suggesting a near-doubling of risk relative to those without deployment-acquired TBI. Very mild TBI was also associated with increased odds of PTSD and the composite outcome; however, the elevation of risk was smaller in magnitude (range of adjusted odds ratios=1.21–1.66) and, in the case of PTSD, was only statistically significant at T2.

Some TBI studies suggest that memory of the traumatic event increases risk for PTSD (27). Our results stand in contrast with that observation, in that risk for PTSD became more elevated as TBI severity (including extent of amnesia) increased. The impact of trauma memory on PTSD risk merits further study; however, it seems clear that PTSD can, indeed, occur after TBI characterized by incomplete or partial memories of the injury or postinjury period (including dis-orienting and painful medical procedures, such as those that may occur during intensive care unit stays) (28).

The present findings related to TBI severity further suggest that extent of injury to the brain moderates the likelihood of the development of mental health sequelae. This is hardly a radical notion, as considerable neuroimaging and neuropsychological research supports a model wherein TBI impairs functioning of prefrontocortical and networked systems that are believed to be integral for inhibiting fear responses and promoting fear extinction (29). But there also exists a contrarian view that concussions increase risk for mental disorders not by virtue of their mechanical impact on the brain, per se, but rather by their emotional impact on the individual’s psyche as a result of their occurrence within a potentially life-threatening and otherwise stressful context (i.e., military combat) (30). Which of these accounts is most true—and it is likely that both have explanatory power—remains to be determined by future studies that can more accurately gauge these factors (i.e., extent of physical and emotional injury) and disaggregate their effects.

Another important finding from the present study is the observation that whereas PTSD is, indeed, a frequent consequence of deployment-acquired TBI, so are other mental disorders. In addition to PTSD, postdeployment major depressive episode and generalized anxiety disorder were both significantly associated with deployment-acquired TBI. These data are again consistent with the aforementioned study of civilian traumatic injury survivors (16), where TBI was associated with increased incidence of multiple psychiatric disorders. These observations highlight the myriad mental health sequelae of TBI (29) and indicate that surveillance must extend beyond the relatively narrow framework of PTSD. It is evident that mental disorder incidence following TBI is sufficiently high that routine screening might be

worth implementing (7), but precisely if, how, and when to conduct such screening remains to be empirically determined. Moreover, researchers have begun to recognize that symptoms and impairment post-TBI do not neatly fall into any one diagnostic psychiatric or neurologic (including postconcussive syndrome) category (23) and that much additional work will be needed to characterize and classify the full and complex range of cognitive, emotional, and behavioral symptoms that can occur.

Suicidality has until very recently been an understudied potential consequence of TBI. A large Swedish population-based study found that TBI was associated with a threefold increased risk of suicide compared with the adjusted risk in the general population (31). A study of 161 U.S. military personnel referred to a TBI clinic in Iraq for suspected head injury found that multiple episodes of TBI, which were common among U.S. military personnel, were associated with increased risk for lifetime suicidal thoughts and behaviors, as well as for current suicidal ideation (11). Baseline assessment of the Veterans After-Discharge Longitudinal Registry (Project VALOR), an observational registry of over 1,600 veterans with and without PTSD who deployed in support of the wars in Iraq and Afghanistan and were enrolled in the Veterans Affairs health care system, found that a history of TBI was associated with increased risk for current suicidal ideation, though only in men (9). The present longitudinal cohort study failed to clearly demonstrate an increase in risk for suicidality in individuals who sustained TBI during deployment. Whereas a modest, nearly significant association was seen at 3 months postdeployment, by the 9-month follow-up this association was no longer evident. It may be that suicidality should be a greater concern for the first few months postconcussion but that this risk may wane with time. Additional longitudinal research will be required to resolve this question. Thus, although inconclusive, these data call for increased attention to TBI, along with what is already known about other susceptibility factors such as pre-existing mental disorders (32, 33), as a potentially modifiable risk factor for suicide among military personnel.

Strengths of this study are its large sample size and its detailed, systematic longitudinal prospective assessment of three Army Brigade Combat Teams about to be deployed to Afghanistan. A limitation is that diagnostic data were collected by self-report rather than by direct clinical interviews, but this is mitigated by the extensive testing and clinical calibration of our diagnostic measures (21). A second limitation is that information about the main exposure of interest, TBI, was obtained by self-report and further lacked specification about presumed mechanism of injury (e.g., blast versus impact). Studies show, however, that mild TBIs are often medically undiagnosed (1, 34) or underreported (35), and our own attempts to corroborate TBI self-reports with military medical records revealed poor concordance (data not shown). The presence of a dose-response relationship between severity of self-reported TBI—even within the mild spectrum—and the outcomes of interest provides some re-assurance that the observed associations are valid. Nonetheless, future studies that can more deliberately and deeply debrief participants about the circumstances of their TBI(s) are needed. A third limitation is that the nature of our survey, wherein we tracked soldiers within their Brigade Combat Teams, would have resulted in very few cases of moderate or severe TBI being included, as many if not most of those soldiers would have been hospitalized and probably inaccessible to us for the follow-up assessments. Accordingly, it is important to recognize that this study is, essentially, a study of persons

with a range of TBI severity within the mild spectrum. A fourth limitation is the unavailability of survey data about other concurrent physical injury that respondents may have sustained. It is well established that extent and severity of physical injury increases risk for PTSD (36). It is therefore possible that those with TBIs may have also had more serious nonhead injuries than other soldiers and that an increased aggregate burden of injury may have contributed to the observed increase in PTSD and related disorders in those individuals. This hypothesis can be tested in future studies with access to more granular data about the type, timing, and extent of physical injuries sustained.

In summary, we found in this large, prospective cohort study of military personnel about to be deployed to Afghanistan that mild TBI is common during deployment and that it is associated with substantially increased risk for PTSD observed 3 and 9 months after redeployment to the United States. We also found that the risk for mental health problems following mild TBI is not restricted to PTSD, implying that the focus on surveillance and intervention needs to be broadened to include other anxiety and depressive disorders. Finally, the process(es) by which mild TBI increases risk for these disorders, which may include inflammatory or other neurodegenerative etiologies that impair brain network function (37–39), perhaps especially involving systems that mediate executive functioning (40), should be further studied in order to arrive at more mechanistic approaches to prevention and treatment.

Appendix

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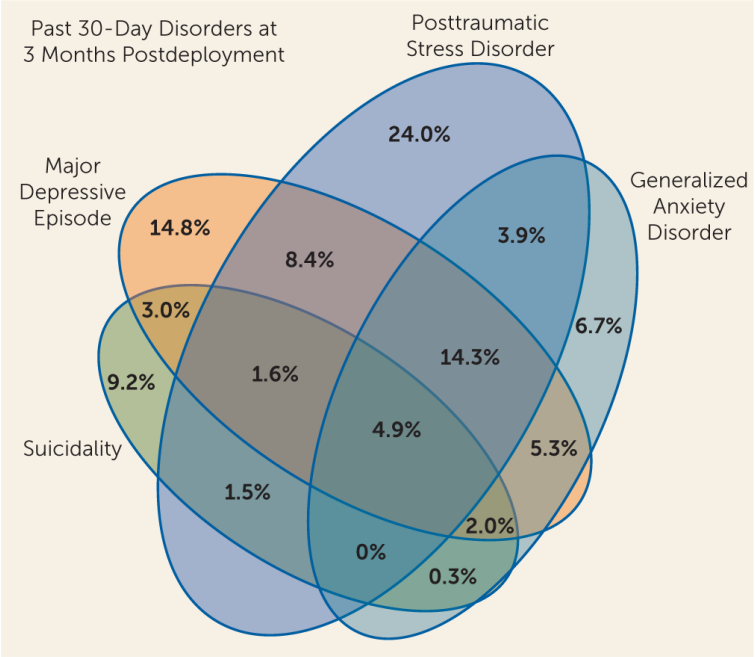

FIGURE 1. Comorbidity of Disorders Among Soldiers Classified at T2 (3 Months Postdeployment) as Experiencing Major Depressive Episode, Posttraumatic Stress Disorder, Generalized Anxiety Disorder, or Suicidality in the Past 30 Days[a]

[a] Prevalence of any of these four outcomes at T2 was 12.9%.

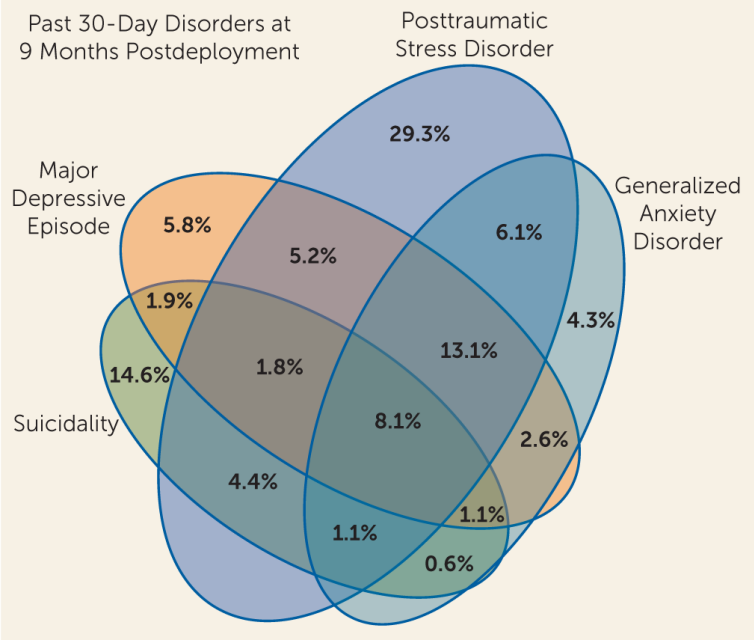

FIGURE 2. Comorbidity of Disorders Among Soldiers Classified at T3 (9 Months Postdeployment) as Experiencing Major Depressive Episode, Posttraumatic Stress Disorder, Generalized Anxiety Disorder, or Suicidality in the Past 30 Days[a]

[a] Prevalence of any of these four outcomes at T3 was 16.8%.

TABLE 1

Results of Weighted Logistic Regression Evaluating Effects of Deployment-Acquired Traumatic Brain Injury (TBI) on Posttraumatic Stress Disorder (PTSD) Diagnosis at 3 Months (T2) and 9 Months (T3) Postdeployment[a]

	3 Months Postdeployment (T2)				9 Months Postdeployment (T3)			
Variable	**Adjusted Odds Ratio**	**95% CI**	**χ^2**	**p**	**Adjusted Odds Ratio**	**95% CI**	**χ^2**	**p**
Age (years)			0.51	0.48			0.56	0.45
≥30	1.00				1.00			
<30	0.90	0.66–1.21			1.10	0.86–1.40		
Sex			2.73	0.10			11.69	0.001
Male	1.00				1.00			
Female	1.58	0.92–2.72			2.11	1.37–3.23		
Race			6.14	0.11			3.43	0.33
White	1.00				1.00			
Black	0.97	0.60–1.58			1.06	0.67–1.66		
Asian	1.74	1.01–2.99			0.97	0.50–1.89		
Other	1.53	0.94–2.51			1.39	0.94–2.08		
Ethnicity			0.79	0.37			0.48	0.49
Non-Hispanic	1.00				1.00			
Hispanic	1.20	0.80–1.81			1.13	0.80–1.61		
Brigade Combat Team			6.97	0.03			1.33	0.51
Fort #1	1.00				1.00			
Fort #2	1.11	0.81–1.52			1.09	0.87–1.37		
Fort #3	1.55	1.11–2.18			0.98	0.75–1.27		
Prior deployments			3.62	0.16			0.57	0.75
None	1.00				1.00			
One	1.24	0.93–1.67			0.93	0.70–1.24		
Two or more	0.99	0.67–1.48			1.05	0.82–1.34		
Lifetime PTSD (predeployment)			4.95	0.03			16.47	<0.0005
No	1.00				1.00			
Yes	1.58	1.06–2.35			1.97	1.42–2.73		
Past-month PTSD Checklist score (predeployment)	1.15	1.12–1.19	71.31	<0.0005	1.12	1.09–1.16	48.77	<0.0005
Deployment stress severity	1.28	1.20–1.36	63.95	<0.0005	1.19	1.15–1.23	113.10	<0.0005
Lifetime TBI (predeployment)			0.60	0.44			3.69	0.06
None reported	1.00				1.00			
One or more reported	1.12	0.84–1.51			1.22	1.00–1.50		
Deployment-acquired TBI			13.82	<0.0005			13.92	<0.0005
None reported	1.00				1.00			
One or more reported	1.81	1.32–2.46			1.48	1.21–1.83		

[a]Multivariate significance was evaluated using design-based Wald chi-square tests. The significance test for race had 3 degrees of freedom; the significance tests for Brigade Combat Team and prior deployments had 2 degrees of freedom; and the significance tests for all other independent variables had 1 degree of freedom.

TABLE 2

Results of Weighted Zero-Inflated Negative Binomial Regression Evaluating Effects of Deployment-Acquired Traumatic Brain Injury (TBI) on Presence (Yes/No; Adjusted Odds Ratio) and Severity (for Nonzero Scores; Fold Change) of Postdeployment Posttraumatic Stress Symptoms (PTSD Checklist score[a]) at T2 and T3

	3 Months Postdeployment (T2)						9 Months Postdeployment (T3)					
Variable	**Adjusted Odds Ratio[b]**	**95% CI**	**p**	**Fold Change[c]**	**95% CI**	**p**	**Adjusted Odds Ratio[b]**	**95% CI**	**p**	**Fold Change[c]**	**95% CI**	**p**
Age												
≥30	1.00			1.00			1.00			1.00		
<30	1.26	0.99–1.61	0.06	1.03	0.94–1.14	0.50	1.24	0.95–1.60	0.11	1.03	0.93–1.14	0.59
Sex												
Male	1.00			1.00			1.00			1.00		
Female	0.99	0.66–1.46	0.94	1.27	1.07–1.49	0.006	0.71	0.49–1.03	0.07	1.19	0.97–1.46	0.10
Race												
White	1.00			1.00			1.00			1.00		
Black	1.43	1.05–1.96	0.02	1.01	0.88–1.16	0.91	1.34	1.01–1.78	0.05	1.03	0.90–1.19	0.66
Asian	0.98	0.66–1.44	0.91	1.19	0.99–1.45	0.07	1.12	0.76–1.67	0.56	0.95	0.76–1.19	0.66
Other	0.99	0.69–1.40	0.93	1.20	1.04–1.38	0.01	0.90	0.70–1.17	0.42	1.22	1.00–1.50	0.06
Ethnicity												
Non-Hispanic	1.00			1.00			1.00			1.00		
Hispanic	1.21	0.93–1.57	0.15	1.02	0.92–1.13	0.74	1.00	0.73–1.39	0.98	1.05	0.86–1.29	0.60
Brigade Combat Team												
Fort #1	1.00			1.00			1.00			1.00		
Fort #2	0.60	0.47–0.78	<0.001	1.07	0.96–1.18	0.22	0.85	0.70–1.03	0.09	1.06	0.96–1.17	0.24
Fort #3	0.60	0.45–0.78	0.001	1.18	1.08–1.30	0.001	1.03	0.84–1.27	0.75	1.02	0.92–1.14	0.68
Prior deployments												
None	1.00			1.00			1.00			1.00		
One	0.71	0.54–0.93	0.02	1.01	0.92–1.11	0.89	0.82	0.66–1.01	0.06	0.92	0.82–1.03	0.16
Two or more	1.00	0.74–1.35	0.99	0.99	0.90–1.10	0.82	0.96	0.74–1.26	0.77	0.95	0.85–1.05	0.27
Lifetime PTSD (predeployment)												

Variable	3 Months Postdeployment (T2)						9 Months Postdeployment (T3)					
	Adjusted Odds Ratio[b]	95% CI	p	Fold Change[c]	95% CI	p	Adjusted Odds Ratio[b]	95% CI	p	Fold Change[c]	95% CI	p
No	1.00			1.00			1.00			1.00		
Yes	0.99	0.60–1.63	0.97	1.19	1.06–1.34	0.004	0.50	0.25–0.99	0.05	1.23	1.06–1.42	0.007
Past-month PTSD Checklist score (predeployment)	0.86	0.79–0.94	0.001	1.08	1.06–1.09	<0.001	0.79	0.70–0.89	<0.001	1.05	1.04–1.07	<0.001
Deployment stress severity	0.84	0.80–0.87	<0.001	1.11	1.08–1.13	<0.001	0.88	0.84–0.91	<0.001	1.07	1.06–1.08	<0.001
Lifetime TBI												
None	1.00			1.00			1.00			1.00		
One or more	0.67	0.53–0.85	0.002	1.04	0.95–1.13	0.43	0.79	0.68–0.93	0.005	1.08	0.99–1.17	0.08
Deployment-acquired TBI												
None	1.00			1.00			1.00			1.00		
One or more	0.68[d]	0.48–0.97	0.04	1.35	1.21–1.51	<0.001	0.55[d]	0.37–0.82	0.005	1.20	1.10–1.31	<0.001

[a] PTSD Checklist scores were shifted from 17–85 to 0–68 before analysis to fit for the models.

[b] Adjusted odds ratio indicates odds of a zero score on the 17-item PTSD Checklist associated with each predictor; inverse of adjusted odds ratio (not shown) represents odds of a nonzero score (i.e., reporting any symptoms on the PTSD Checklist).

[c] Fold changes indicate the fold increase or decrease in PTSD Checklist score associated with each predictor when any symptoms are present (i.e., when the PTSD Checklist score is nonzero).

[d] For ease of interpretation, the inverse of the adjusted odds ratios for PTSD symptoms at T2 and T3 are reported in the article text. The adjusted odds ratios reported here indicate that deployment-acquired TBI was associated with lower odds (0.68 at T2 and 0.55 at T3) of having a zero score on the PTSD Checklist. The inverse of these adjusted odds ratios (1/0.68=1.47;1/0.55=1.82) conveys that TBI was associated with increased odds of endorsing any PTSD symptoms at both follow-up points (i.e., having a nonzero PTSD Checklist score at T2 and T3).

TABLE 3

Results of Weighted Logistic Regression Evaluating Effects of Deployment-Acquired Traumatic Brain Injury (TBI) on the Composite Outcome of Any Postdeployment Posttraumatic Stress Disorder (PTSD), Major Depressive Episode, Generalized Anxiety Disorder, or Suicidality at 3 Months (T2) and 9 Months (T3) Postdeployment[a]

	3 Months Postdeployment (T2)				9 Months Postdeployment (T3)			
Variable	**Adjusted Odds Ratio**	**95% CI**	**χ^2**	**p**	**Adjusted Odds Ratio**	**95% CI**	**χ^2**	**p**
Age (years)								
≥30	1.00				1.00			
<30	0.93	0.71–1.20	0.35	0.55	0.89	0.74–1.07	1.44	0.23
Sex								
Male	1.00				1.00			
Female	1.48	1.01–2.16	4.08	0.04	1.70	1.25–2.31	11.32	0.001
Race			4.55	0.21			4.44	0.22
White	1.00				1.00			
Black	1.20	0.85–1.70			1.14	0.80–1.64		
Asian	1.17	0.73–1.87			0.67	0.40–1.11		
Other	1.36	0.94–1.97			1.21	0.88–1.65		
Ethnicity			0.17	0.68			0.36	0.55
Non-Hispanic	1.00				1.00			
Hispanic	1.08	0.75–1.55			1.09	0.82–1.45		
Brigade Combat Team			17.63	<0.0005			8.25	0.02
Fort #1	1.00				1.00			
Fort #2	1.30	0.98–1.72			1.25	1.04–1.49		
Fort #3	1.86	1.39–2.49			1.04	0.84–1.28		
Prior deployments			1.69	0.43			1.21	0.55
None	1.00				1.00			
One	1.07	0.87–1.31			0.93	0.77–1.14		
Two or more	0.90	0.67–1.21			0.90	0.74–1.11		
Lifetime Diagnostic Composite (predeployment)[b]			37.35	<0.0005			55.13	<0.0005
No	1.00				1.00			
Yes	2.42	1.82–3.21			2.43	1.92–3.06		
Past-month general distress (predeployment)	1.04	1.03–1.05	121.96	<0.0005	1.02	1.02–1.03	58.60	<0.0005
Deployment stress severity	1.22	1.16–1.27	77.61	<0.0005	1.14	1.11–1.18	86.53	<0.0005
Lifetime TBI (predeployment)			0.04	0.85			4.21	0.04
None reported	1.00				1.00			
One or more reported	1.02	0.82–1.28			1.22	1.01–1.47		
Deployment-acquired TBI			16.67	<0.0005			24.13	<0.0005
None reported	1.00				1.00			
One or more reported	1.74	1.33–2.27			1.53	1.29–1.82		

[a]Multivariate significance was evaluated using design-based Wald chi-square tests. The significance test for race had 3 degrees of freedom; the significance tests for Brigade Combat Team and prior deployments had 2 degrees of freedom; and the significance tests for all other independent variables had 1 degree of freedom.

[b]Diagnostic Composite refers to whether criteria were met for any of the following: PTSD, major depressive episode, generalized anxiety disorder, or suicidality.