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Mild Traumatic Brain Injury in U.S. Soldiers Returning from Iraq

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ABSTRACT

BACKGROUND

An important medical concern of the Iraq war is the potential long-term effect of mild traumatic brain injury, or concussion, particularly from blast explosions. However, the epidemiology of combat-related mild traumatic brain injury is poorly understood.

METHODS

We surveyed 2525 U.S. Army infantry soldiers 3 to 4 months after their return from a year-long deployment to Iraq. Validated clinical instruments were used to compare soldiers reporting mild traumatic brain injury, defined as an injury with loss of consciousness or altered mental status (e.g., dazed or confused), with soldiers who reported other injuries.

RESULTS

Of 2525 soldiers, 124 (4.9%) reported injuries with loss of consciousness, 260 (10.3%) reported injuries with altered mental status, and 435 (17.2%) reported other injuries during deployment. Of those reporting loss of consciousness, 43.9% met criteria for post-traumatic stress disorder (PTSD), as compared with 27.3% of those reporting altered mental status, 16.2% with other injuries, and 9.1% with no injury. Soldiers with mild traumatic brain injury, primarily those who had loss of consciousness, were significantly more likely to report poor general health, missed workdays, medical visits, and a high number of somatic and postconcussive symptoms than were soldiers with other injuries. However, after adjustment for PTSD and depression, mild traumatic brain injury was no longer significantly associated with these physical health outcomes or symptoms, except for headache.

CONCLUSIONS

Mild traumatic brain injury (i.e., concussion) occurring among soldiers deployed in Iraq is strongly associated with PTSD and physical health problems 3 to 4 months after the soldiers return home. PTSD and depression are important mediators of the relationship between mild traumatic brain injury and physical health problems.

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More than 1.5 million U.S. military personnel have deployed to Iraq or Afghanistan since the start of military operations in 2001. Because of improved protective equipment, a higher percentage of soldiers are surviving injuries that would have been fatal in previous wars.[1] Head and neck injuries, including severe brain trauma, have been reported in one quarter of service members who have been evacuated from Iraq and Afghanistan.[1,2] Concern has been emerging about the possible long-term effect of mild traumatic brain injury, or concussion, characterized by brief loss of consciousness or altered mental status, as a result of deployment-related head injuries, particularly those resulting from proximity to blast explosions.[3-5] Traumatic brain injury has been labeled a signature injury of the wars in Iraq and Afghanistan.[4,5]

The exact proportion of troops who have mild traumatic brain injury is not known, although it has been reported to be as high as 18% in news articles citing army medical officials.[6] Many troops reportedly have persistent postconcussive symptoms, such as irritability, memory problems, headache, and difficulty concentrating. As a result, the Department of Defense and the Department of Veterans Affairs are implementing new population-screening procedures for mild traumatic brain injury.[7-9]

Despite these steps, little is known about the epidemiology of mild traumatic brain injury during deployment and its association with adverse health outcomes after deployment. The bulk of the literature on mild traumatic brain injury has been based on civilian patients treated in clinics or hospitals, has not been population-based, and has lacked adequate comparison groups, such as persons with other types of injuries.[10,11] It is not known whether population screening for mild traumatic brain injury could improve health outcomes,[12] and there are conflicting guidelines for treating mild traumatic brain injury.[13,14]

The case definition of mild traumatic brain injury that is being adopted by the new Department of Defense and Department of Veterans Affairs screening programs[8,9] is consistent with national surveillance definitions.[11,15] However, the use of this definition for clinical screening weeks or months after concussive events, such as during the period after deployment, has not been evaluated. The definition may not be sufficiently specific for the combat environment, where acute signs of concussion, such as alteration of mental status (e.g., being dazed or confused), may overlap with dissociative symptoms of acute stress disorder, or for the postcombat period, during which postconcussive symptoms may overlap with symptoms of post-traumatic stress disorder (PTSD) and other disorders.[16]

This epidemiologic study assesses the prevalence and significance of a self-reported history of combat-related mild traumatic brain injury, based on the accepted case definition, among soldiers after a yearlong deployment to Iraq. The purpose is to provide information to advance prevention and treatment strategies and inform public health policies.

Methods

In 2006, we conducted an anonymous survey of 2714 soldiers from two U.S. Army combat infantry brigades — one Active Component and one Reserve Component (Army National Guard) — 3 to 4 months after their return from a yearlong deployment in Iraq. The units saw high levels of combat, similar to those of other infantry units.[17-19] The 3-to-4-month time point was chosen to minimize recall bias and for its appropriateness for assessing persistent postconcussive symptoms.[20,21]

Recruitment

Unit leaders provided time for all their soldiers who had deployed to Iraq and were on duty to attend a recruitment briefing by study investigators. Written informed consent was obtained under a protocol approved by the institutional review board of the Walter Reed Army Institute of Research. Of 4618 soldiers in the two brigades, 2714 (59%) completed the questionnaire. Lack of availability of soldiers to complete the questionnaire was mostly due to normal transfers to other units, training, or attendance at military schools. More than 98% of soldiers who attended the recruitment briefings agreed to participate. However, up to 7% of the values for some variables were missing.

Injuries and Combat Experience

The questionnaire asked soldiers whether they had been injured during their deployment by a blast or explosion, a bullet, a fragment or shrap-

nel, a fall, a vehicle accident, or other means and whether the injury involved the head. A soldier was considered to have had a mild traumatic brain injury if any of three questions — regarding "losing consciousness (knocked out)," "being dazed, confused, or 'seeing stars,'" or "not remembering the injury" — elicited a positive response. These questions were based on definitions from the Centers for Disease Control and Prevention and the World Health Organization that were adapted by the Defense and Veterans Brain Injury Center working group for military-wide use.[8,9,11] The question regarding loss of consciousness was analyzed separately to determine whether it was a stronger predictor than the two other questions pertaining to altered mental status, the results of which were combined. Soldiers who reported any injury that did not involve altered mental status or losing consciousness served as the reference group for all analyses.

Combat intensity was measured with the use of 17 of the 18 questions from the Combat Experiences Scale[17] (range, 0 to 17, with higher scores indicating a greater number of different combat experiences on one or more occasions). The 18th question, concerning being wounded, was excluded because it was covered in the questions about injuries. Of the 17 experiences, soldiers had a median of 9 (interquartile range, 6 to 11) during the deployment. The Cronbach alpha for the 17 dichotomized questions was 0.85.

MEASURES OF PHYSICAL HEALTH

Soldiers were asked how they rated their overall health (from "poor" to "excellent"), how many primary care ("sick call") appointments they had attended, and how many days of work they had missed in the past month because of illness. Physical symptoms were measured by the Patient Health Questionnaire 15-item somatic symptom severity scale (PHQ-15).[22] This scale normally has a range of 0 to 30, with higher numbers indicating a greater number and severity of symptoms. For this study, the range was 0 to 28 because a question on menstrual cramps was excluded owing to the low number of women. High severity of symptoms was defined as a score of at least 15.[22,23] Five additional questions, which were not part of the PHQ-15, were asked regarding important postconcussive symptoms that concerned memory, balance, concentration, ringing in the ears, and irritability.

MEASURES OF DEPRESSION AND PTSD

Current symptoms (i.e., symptoms during the past month) of major depressive disorder and PTSD were assessed by the 9-question depression-assessment module of the Patient Health Questionnaire[24] and the 17-item National Center for PTSD Checklist, respectively, which are based on well-validated case definitions used in veteran and military populations.[17,25,26] For major depression, subjects had to meet the criteria of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV), and report impairment in work, home, or interpersonal functioning at the "very difficult" level.[17,24] For PTSD, subjects had to meet the DSM-IV criteria (one intrusion symptom, three avoidance symptoms, and two hyperarousal symptoms) and have substantial distress, as measured by a total score of at least 50 (range, 17 to 85, with higher scores indicating a greater number and severity of symptoms).[17,26]

STATISTICAL ANALYSIS

Surveys were scanned with the use of ScanTools (National Computer Systems), with quality control verifying error rates below 0.25%. SPSS software (version 12.0) was used for data analysis, including chi-square and analysis-of-variance testing for univariate analyses. Multivariate analyses were conducted with the use of multiple logistic regression with SPSS software (version 12.0), including goodness-of-fit testing of all models.

RESULTS

SUBJECTS

Of 2714 soldiers, 149 (5.5%) were excluded because of missing data from the questions about injuries, and 40 (1.5%) were excluded because they reported having had a head injury without loss of consciousness or altered mental status. The demographics of the study population were similar to those of infantry soldiers deployed to Iraq[17-19]: 95.5% were male, 55.5% were under the age of 30 years, and 47.5% were of junior enlisted rank.

INJURIES

Of the 2525 soldiers included in the study, 124 (4.9%) reported an injury with loss of consciousness (most often lasting between a few seconds and 2 or 3 minutes), and 260 (10.3%) reported an injury with altered mental status not involving

Table 1. Characteristics of the Study Population.*

Characteristic	Injury with Loss of Consciousness (N=124)	Injury with Altered Mental Status (N=260)	Other Injury (N=435)	No Injury (N=1706)	P Value for Loss of Consciousness vs. Other Injury	P Value for Altered Mental Status vs. Other Injury
Female sex — no./total no. (%)	1/123 (0.8)	3/258 (1.2)	21/431 (4.9)	88/1692 (5.2)	0.04	0.01
Age <30 yr — no./total no. (%)	79/123 (64.2)	149/257 (58.0)	206/431 (47.8)	958/1698 (56.4)	0.001	0.01
High-school education or less — no./total no. (%)	53/122 (43.4)	103/253 (40.7)	172/429 (40.1)	719/1683 (42.7)	0.51	0.87
Rank — no./total no. (%)					0.04	0.86
Junior enlisted (E1–E4)	73/122 (59.8)	127/256 (49.6)	202/426 (47.4)	780/1684 (46.3)		
Midlevel enlisted (E5–E6)	40/122 (32.8)	97/256 (37.9)	168/426 (39.4)	615/1684 (36.5)		
Senior enlisted and officers	9/122 (7.4)	32/256 (12.5)	56/426 (13.1)	289/1684 (17.2)		
Marital status — no./total no. (%)					0.30	0.06
Single	32/108 (29.6)	76/245 (31.0)	100/403 (24.8)	528/1595 (33.1)		
Married	67/108 (62.0)	149/245 (60.8)	250/403 (62.0)	933/1595 (58.5)		
Divorced, separated, or other	9/108 (8.3)	20/245 (8.2)	53/403 (13.2)	134/1595 (8.4)		
Mechanism of injury — no. (%)†					<0.001	<0.001
Blast or explosion	98 (79.0)	189 (72.7)	101 (23.2)			
Bullet	6 (4.8)	2 (0.8)	7 (1.6)			
Fragment or shrapnel	31 (25.0)	48 (18.5)	35 (8.0)			
Fall	38 (30.6)	73 (28.1)	190 (43.7)			
Vehicle accident	38 (30.6)	47 (18.1)	58 (13.3)			
Other	16 (12.9)	23 (8.8)	147 (33.8)			
Improvised explosive device exploded near soldier on ≥2 occasions (with or without injury) — no./total no. (%)	106/122 (86.9)	231/258 (89.5)	281/434 (64.7)	938/1690 (55.5)	<0.001	<0.001
Hospitalized while deployed — no./total no. (%)	50/124 (40.3)	44/259 (17.0)	59/433 (13.6)	89/1701 (5.2)	<0.001	0.23
Quartile of combat intensity — no./total no. (%)‡					<0.001	<0.001
1	2/124 (1.6)	8/259 (3.1)	74/435 (17.0)	452/1705 (26.5)		
2	15/124 (12.1)	29/259 (11.2)	95/435 (21.8)	467/1705 (27.4)		
3	21/124 (16.9)	53/259 (20.5)	97/435 (22.3)	376/1705 (22.1)		
4	86/124 (69.4)	169/259 (65.3)	169/435 (38.9)	410/1705 (24.0)		

Mental health problems						
PTSD — no./total no. (%)§	54/123 (43.9)	71/260 (27.3)	70/433 (16.2)	155/1701 (9.1)	<0.001	<0.001
Major depression — no./total no. (%)¶	27/118 (22.9)	21/250 (8.4)	28/423 (6.6)	55/1673 (3.3)	<0.001	0.39
Score on Post-Traumatic Stress Disorder Checklist§	46.8±19.0	39.8±16.3	35.0±15.0	29.1±13.2	<0.001	<0.001

* Complete data regarding some of the characteristics were not available for all subjects. P values were calculated with the use of the chi-square test except where indicated. PTSD denotes post-traumatic stress disorder.
† Mechanisms of injury are not mutually exclusive.
‡ Combat intensity was measured with a 17-question scale representing the number of different combat experiences. Scores range from 0 to 17, with higher values indicating a greater number of experiences. Scores of 0 to 5 constitute quartile 1, 6 to 8 quartile 2, 9 and 10 quartile 3, and 11 to 17 quartile 4.
§ PTSD was measured with the Post-Traumatic Stress Disorder Checklist, which has a range from 17 to 85, with higher scores indicating a greater number and severity of symptoms. All subjects who met the psychiatric-symptom criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV), and who had a total score on the Post-Traumatic Stress Disorder Checklist of at least 50 were classified as having PTSD. Plus–minus values are means ±SD. P values for the score on the Post-Traumatic Stress Disorder Checklist were calculated with the use of analysis of variance.
¶ Major depression was measured with the Patient Health Questionnaire. Subjects who were classified as having major depression had to meet the psychiatric criteria according to DSM-IV and report functional impairment at the "very difficult" level.

loss of consciousness (253 said they had been "dazed, confused, or seeing stars"). Four soldiers reported loss of consciousness lasting longer than 30 minutes. Although technically they were considered to have had moderate traumatic brain injury, they were not excluded because the number was low and it was not possible to verify the self-reported data from any of the subjects. An additional 435 soldiers (17.2%) reported some other injury during the deployment with no loss of consciousness or altered mental status, most commonly resulting from a fall or other incident (e.g., handling heavy equipment or injuring oneself during training) (Table 1). This was the reference group for all analyses (Tables 1, 2, and 3). Also shown in Tables 1 and 2, for comparison purposes, are the characteristics of the remaining 1706 soldiers who reported no injury.

As compared with soldiers who had other injuries, soldiers who reported mild traumatic brain injuries were significantly more likely to report high combat intensity, a blast mechanism of injury, more than one exposure to an explosion, and hospitalization during deployment (Table 1). Soldiers who reported mild traumatic brain injuries were also significantly younger, more likely to be junior in rank, and more likely to be male than were soldiers who had other injuries.

PTSD AND MILD TRAUMATIC BRAIN INJURY

PTSD was strongly associated with mild traumatic brain injury. Overall, 43.9% of soldiers who reported loss of consciousness met the criteria for PTSD, as compared with 27.3% of those with altered mental status, 16.2% of those with other injuries, and 9.1% of those with no injuries (Table 1). In a logistic-regression model that included age, military rank, sex, hospitalization or no hospitalization, mechanism of injury (blast or other mechanisms), level of combat intensity, exposure or nonexposure to multiple blasts from improvised explosive devices, and type of injury (loss of consciousness vs. other injuries), only loss of consciousness and combat intensity remained significantly associated with PTSD (odds ratio for loss of consciousness, 2.98; 95% confidence interval [CI], 1.70 to 5.24; odds ratio for top quartile of combat intensity vs. lowest quartile, 11.58; 95% CI, 2.99 to 44.83) (see Supplementary Appendix 1, available with the full text of this article at www.nejm.org). Injury with loss of consciousness was also independently associated with ma-

Table 2. Physical Health Status after Deployment According to Type of Injury during Deployment.*

Physical Health during the Past Month	Injury with Loss of Consciousness (N=124)	Injury with Altered Mental Status (N=260)	Other Injury (N=435)	No Injury (N=1706)	P Value for Loss of Consciousness vs. Other Injury	P Value for Altered Mental Status vs. Other Injury
	no./total no. (%)					
Poor overall health	15/119 (12.6)	17/257 (6.6)	29/422 (6.9)	38/1665 (2.3)	0.04	0.90
≥2 Missed workdays due to illness	28/120 (23.3)	40/256 (15.6)	61/419 (14.6)	122/1671 (7.3)	0.02	0.71
≥2 medical visits for physical condition	51/120 (42.5)	84/256 (32.8)	123/426 (28.9)	331/1678 (19.7)	0.005	0.28
PHQ-15 score of ≥15†	30/121 (24.8)	41/254 (16.1)	48/426 (11.3)	85/1683 (5.1)	<0.001	0.07
Physical symptoms included in PHQ-15‡						
Stomach pain	14/120 (11.7)	20/249 (8.0)	37/421 (8.8)	71/1674 (4.2)	0.34	0.73
Back pain	40/121 (33.1)	78/253 (30.8)	122/424 (28.8)	311/1678 (18.5)	0.36	0.57
Arm, leg, or joint pain	45/121 (37.2)	105/252 (41.7)	168/423 (39.7)	387/1673 (23.1)	0.62	0.62
Headache	39/121 (32.2)	45/254 (17.7)	51/421 (12.1)	141/1674 (8.4)	<0.001	0.04
Chest pain	17/121 (14.0)	7/253 (2.8)	20/425 (4.7)	40/1675 (2.4)	<0.001	0.21
Dizziness	10/120 (8.3)	15/254 (5.9)	13/425 (3.1)	31/1680 (1.8)	0.01	0.07
Fainting spells	5/120 (4.2)	2/253 (0.8)	8/423 (1.9)	7/1678 (0.4)	0.17	0.34
Heart pounding or racing	23/120 (19.2)	25/253 (9.9)	21/425 (4.9)	62/1679 (3.7)	<0.001	0.01
Shortness of breath	17/120 (14.2)	19/254 (7.5)	30/421 (7.1)	54/1675 (3.2)	0.02	0.86
Constipation, loose bowels, or diarrhea	26/120 (21.7)	31/253 (12.3)	50/424 (11.8)	115/1681 (6.8)	0.006	0.86
Nausea, gas, or indigestion	22/120 (18.3)	34/253 (13.4)	65/423 (15.4)	132/1677 (7.9)	0.43	0.49
Pain or problems during sexual intercourse	10/120 (8.3)	8/253 (3.2)	16/425 (3.8)	16/1673 (1.0)	0.04	0.68
Fatigue	59/111 (53.2)	92/232 (39.7)	136/393 (34.6)	388/1542 (25.2)	<0.001	0.21
Sleep disturbance	63/117 (53.8)	111/247 (44.9)	157/422 (37.2)	402/1666 (24.1)	0.001	0.05
Other postconcussive symptoms§						
Memory problems	29/118 (24.6)	41/253 (16.2)	58/422 (13.7)	124/1680 (7.4)	0.005	0.38
Balance problems	10/120 (8.3)	17/254 (6.7)	12/424 (2.8)	26/1677 (1.6)	0.02	0.02
Ringing in the ears	28/119 (23.5)	45/251 (17.9)	59/422 (14.0)	99/1675 (5.9)	0.01	0.17
Concentration problems	37/118 (31.4)	65/250 (26.0)	76/420 (18.1)	170/1667 (10.2)	0.002	0.02
Irritability	67/118 (56.8)	118/248 (47.6)	154/419 (36.8)	409/1659 (24.7)	<0.001	0.006

* Complete data regarding the physical health categories were not available for all subjects.
† PHQ-15 refers to the Patient Health Questionnaire 15-item somatic symptom scale (range in this study, 0 to 28, with higher numbers indicating a greater number and severity of symptoms).
‡ The numbers and percentages of persons reporting "bothered a lot" (for all symptoms except fatigue or sleep disturbance) or "more than half the days" (for fatigue and sleep disturbance) are shown. One symptom from the PHQ-15 pertaining to menstrual cramps was not included, since there were so few women in the study.
§ The numbers and percentages of persons reporting "bothered a lot" (for memory problems, balance problems, and ringing in the ears) or "more than half the days" (for concentration problems and irritability) are shown.

jor depression (odds ratio, 3.67; 95% CI, 1.65 to 8.16). Similarly, injuries associated with altered mental status (as compared with other injuries) and combat intensity were significantly associated with PTSD (but not with depression) (odds ratio for injuries with altered mental status, 1.78; 95% CI, 1.13 to 2.81; odds ratio for combat intensity, 6.63; 95% CI, 2.23 to 19.76).

ADJUSTED AND UNADJUSTED ANALYSES OF PHYSICAL HEALTH

Tables 2 and 3 show the association of the type of injury with measures of physical health. Soldiers who had lost consciousness were significantly more likely to report poor general health, more missed workdays, and a higher number of medical visits in the past month than were soldiers with other injuries. Soldiers who had lost consciousness also had significantly higher scores on the PHQ-15 and significantly higher rates of nine of the PHQ-15 physical symptoms and all five of the other postconcussive symptoms (Table 2). Multivariate logistic-regression analysis was then conducted to assess whether PTSD and major depression mediated the relationship between loss of consciousness and physical health outcomes (Table 3).[27] When PTSD and depression were included in the analyses, the associations between loss of consciousness and the multiple physical health outcomes disappeared, except for two symptoms (headache and heart pounding). For example, when loss of consciousness was compared with other injuries, the odds ratio for having a high PHQ-15 score fell from 2.60 (95% CI, 1.56 to 4.33) in the unadjusted comparison to 0.92 (95% CI, 0.46 to 1.82) after adjustment for PTSD and depression (Table 3). In contrast, the odds ratio for having a high PHQ-15 score in this adjusted equation for PTSD was 7.86 (95% CI, 4.09 to 15.10), and the odds ratio for major depression was 7.47 (95% CI, 3.53 to 15.78) (see Supplementary Appendix 2). Further adjustment to include all significant variables from Table 1 did not change the results appreciably; the odds ratio for having a high PHQ-15 score dropped to 0.76 (95% CI, 0.31 to 1.84), and the association with heart pounding became nonsignificant (Table 3). Of all physical health outcomes associated with loss of consciousness in the unadjusted analysis, only headache remained significant after adjusting for PTSD and depression. In contrast, PTSD, depression, or both were strongly associated with all the physical health outcomes in these adjusted models.

A similar analysis compared altered-mental-status injuries with other injuries (Tables 2 and 3). Initially, altered mental status was associated with only three of the physical symptoms and three of the other postconcussive symptoms. The associations disappeared when PTSD was included in the analyses, and there was no change with further adjustment for demographic and combat variables. Depression was not included, since there was no association between altered mental status and depression (Table 1).

The following example illustrates how cases were distributed and why the association between mild traumatic brain injury and high symptom-severity scores did not persist after adjustment for PTSD. The high PHQ-15 scores occurred almost exclusively in soldiers who had PTSD. Of soldiers with PTSD, there were no significant differences in the proportion with a high PHQ-15 score according to type of injury: 27 of 53 with loss of consciousness (50.9%), 28 of 67 with altered mental status (41.8%), and 29 of 69 with other injuries (42.0%) had a high PHQ-15 score. Of soldiers without PTSD, the proportion with a high PHQ-15 score was much lower and also showed no significant differences according to type of injury: 3 of 67 with loss of consciousness (4.5%), 13 of 187 with altered mental status (7.0%), and 19 of 356 with other injuries (5.3%). (The denominators differ slightly from those in the tables because of missing values.)

DISCUSSION

In this study, nearly 15% of soldiers reported an injury during deployment that involved loss of consciousness or altered mental status. These soldiers, defined as having mild traumatic brain injury, were significantly more likely to report high combat exposure and a blast mechanism of injury than were the 17% of soldiers who reported other injuries. Soldiers with mild traumatic brain injury reported significantly higher rates of physical and mental health problems than did soldiers with other injuries. Injuries associated with loss of consciousness carried a much greater risk of health problems than did injuries associated with altered mental status.

Although this study was based on a nonrandom sample from two brigades, the sample is likely to be representative of soldiers serving in ground-combat units in Iraq. The demographic characteristics and rates of combat experience of the subjects are consistent with those in other studies.[17-19] The unavailability of soldiers was mostly due to work schedules, which would be unlikely to introduce bias. One bias is that on the survey days, soldiers who were ill, at medical appointments, or more seriously injured did

Table 3. Unadjusted and Adjusted Odds Ratios for Each Postdeployment Physical Health Outcome According to Type of Injury during Deployment.*

Physical Health during the Past Month†	Injury with Loss of Consciousness vs. Other Injury‡			Injury with Altered Mental Status vs. Other Injury§		
	Unadjusted	Adjusted for PTSD and Depression	Adjusted for PTSD, Depression, and Other Variables	Unadjusted	Adjusted for PTSD	Adjusted for PTSD and Other Variables
	odds ratio (95% confidence interval)					
Poor overall health	1.96 (1.01–3.78)¶	0.92 (0.43–1.99)	1.43 (0.50–4.07)	0.96 (0.52–1.78)	0.76 (0.40–1.44)	0.97 (0.44–2.16)
≥2 Missed workdays due to illness	1.79 (1.08–2.95)¶	1.31 (0.75–2.27)	1.76 (0.85–3.65)	1.09 (0.71–1.68)	1.00 (0.64–1.55)	0.93 (0.54–1.60)
≥2 Medical visits for physical condition	1.82 (1.19–2.77)‖	1.31 (0.82–2.07)	1.28 (0.72–2.28)	1.20 (0.86–1.68)	1.11 (0.79–1.57)	1.08 (0.71–1.63)
PHQ-15 score of ≥15**	2.60 (1.56–4.33)††	0.92 (0.46–1.82)	0.76 (0.31–1.84)	1.52 (0.97–2.38)	1.13 (0.69–1.87)	1.31 (0.71–2.41)
Physical symptoms included in PHQ-15**						
Stomach pain	1.37 (0.72–2.63)	0.70 (0.32–1.50)	0.67 (0.25–1.82)	0.91 (0.51–1.60)	0.78 (0.43–1.40)	1.21 (0.58–2.51)
Back pain	1.22 (0.79–1.89)	0.84 (0.52–1.36)	0.87 (0.48–1.57)	1.10 (0.79–1.55)	0.96 (0.68–1.37)	0.97 (0.64–1.47)
Arm, leg, or joint pain	0.90 (0.59–1.36)	0.62 (0.39–0.98)	0.79 (0.44–1.39)	1.08 (0.79–1.49)	0.97 (0.70–1.35)	1.28 (0.86–1.92)
Headache	3.45 (2.13–5.58)††	2.10 (1.22–3.61)‖	2.38 (1.12–5.07)¶	1.56 (1.01–2.41)¶	1.34 (0.85–2.10)	1.63 (0.92–2.90)
Chest pain	3.31 (1.67–6.54)††	1.58 (0.72–3.49)	1.84 (0.61–5.52)	0.58 (0.24–1.38)	0.48 (0.20–1.17)	0.52 (0.18–1.54)
Dizziness	2.88 (1.23–6.75)¶	1.19 (0.45–3.15)	4.00 (0.96–16.62)	1.99 (0.93–4.25)	1.54 (0.70–3.38)	2.15 (0.83–5.56)
Fainting spells	2.26 (0.72–7.03)	1.02 (0.30–3.52)	1.11 (0.22–5.60)	0.41 (0.09–1.96)	0.31 (0.06–1.50)	0.27 (0.05–1.62)
Heart pounding or racing	4.56 (2.43–8.58)††	2.14 (1.04–4.41)¶	1.90 (0.71–5.09)	2.11 (1.56–3.85)¶	1.64 (0.87–3.10)	1.75 (0.79–3.84)
Shortness of breath	2.15 (1.14–4.05)¶	1.02 (0.49–2.13)	0.77 (0.30–1.99)	1.05 (0.58–1.91)	0.82 (0.44–1.53)	0.72 (0.34–1.54)
Constipation, loose bowels, or diarrhea	2.07 (1.22–3.49)‖	1.42 (0.80–2.53)	1.55 (0.74–3.24)	1.05 (0.65–1.68)	0.88 (0.53–1.44)	1.20 (0.67–2.17)
Nausea, gas, or indigestion	1.24 (0.73–2.11)	0.74 (0.40–1.36)	0.65 (0.31–1.38)	0.86 (0.55–1.34)	0.75 (0.47–1.18)	1.06 (0.60–1.85)
Pain or problems during sexual intercourse	2.32 (1.03–5.26)¶	0.80 (0.31–2.07)	0.98 (0.27–3.51)	0.84 (0.35–1.98)	0.58 (0.24–1.42)	0.81 (0.26–2.54)
Fatigue	2.14 (1.40–3.29)††	1.15 (0.68–1.94)	1.24 (0.66–2.34)	1.24 (0.89–1.74)	1.03 (0.72–1.49)	1.25 (0.79–1.96)
Sleep disturbance	1.97 (1.30–2.98)‖	1.14 (0.70–1.85)	1.13 (0.63–2.03)	1.38 (1.00–1.90)¶	1.19 (0.84–1.67)	1.23 (0.81–1.85)
Other postconcussive symptoms						
Memory problems	2.05 (1.24–3.38)‖	1.06 (0.59–1.90)	1.79 (0.85–3.79)	1.21 (0.79–1.87)	0.97 (0.61–1.54)	1.23 (0.70–2.15)
Balance problems	3.12 (1.31–7.41)¶	1.66 (0.63–4.36)	1.58 (0.41–6.08)	2.46 (1.16–5.25)¶	2.07 (0.96–4.48)	1.40 (0.51–3.82)
Ringing in the ears	1.89 (1.14–3.14)¶	1.30 (0.75–2.26)	0.78 (0.39–1.55)	1.34 (0.88–2.05)	1.19 (0.77–1.83)	0.76 (0.45–1.27)
Concentration problems	2.07 (1.30–3.28)‖	0.83 (0.45–1.55)	0.92 (0.42–2.00)	1.59 (1.09–2.32)¶	1.29 (0.84–1.96)	1.59 (0.94–2.69)
Irritability	2.26 (1.49–3.42)††	1.33 (0.82–2.16)	1.17 (0.65–2.11)	1.56 (1.14–2.15)‖	1.32 (0.93–1.89)	1.46 (0.95–2.24)

* PTSD denotes post-traumatic stress disorder.
† All dependent variables (physical health problems or symptoms 3 to 4 months after deployment) are shown.
‡ Two adjusted analyses were conducted by logistic regression. The first was adjusted for PTSD and depression, and the second was adjusted for PTSD, depression, sex, age, rank, mechanism of injury, exposure or nonexposure to multiple blasts from improvised explosive devices, hospitalization or no hospitalization, and combat intensity.
§ Two adjusted analyses were conducted by logistic regression. The first was adjusted for PTSD, and the second was adjusted for PTSD, sex, age, rank, mechanism of injury, exposure or nonexposure to multiple blasts from improvised explosive devices, hospitalization or no hospitalization, and combat intensity.
¶ P=0.01 to <0.05.
‖ P=0.001 to 0.009.
** PHQ-15 denotes the Patient Health Questionnaire 15-item somatic symptom severity scale (range in this study, 0 to 28, with higher numbers indicating a greater number and severity of symptoms).
†† P<0.001.

not have the opportunity to participate, possibly resulting in an underestimate of prevalence rates.

In this study, mild traumatic brain injury was significantly associated with psychiatric symptoms, notably PTSD, and the association remained significant after combat experiences had been controlled for. More than 40% of soldiers with injuries associated with loss of consciousness met the criteria for PTSD. The data indicate that a history of mild traumatic brain injury in the combat environment, particularly when associated with loss of consciousness, reflects exposure to a very intense traumatic event that threatens loss of life and significantly increases the risk of PTSD.[28]

The principal limitation of the study is the cross-sectional design based on self-reported data, and thus causality can only be inferred and recall bias is possible. However, the consistency of the results obtained with the use of validated clinical instruments supports the validity of the methods. The analyses suggest that the high rates of physical health problems reported by soldiers with mild traumatic brain injury 3 to 4 months after deployment are mediated largely by PTSD or depression. When these mental disorders were included in the analyses, mild traumatic brain injury was no longer associated with any of the physical health problems, except for headache among those who had lost consciousness. Both PTSD and depression have been associated with a wide range of physical health problems,[23,29,30] including persistence of postconcussive symptoms.[31,32]

The mechanisms of these relationships are complex. Studies have not confirmed any direct link between PTSD and injury to brain tissue from the concussion itself, although this is an important area of research that makes use of new technology, such as diffusion tensor imaging.[33,34] There is evidence that implicit processing of traumatic memories and fear conditioning, both mechanisms for the development of PTSD, occur even in persons with severe traumatic brain injury who are amnesic for the traumatic event.[16] Mechanisms that are likely to underlie both the onset of PTSD after traumatic brain injury and the physical symptoms related to PTSD and depression include biologic processes associated with exposure to extreme stress, activation of the hypothalamic–pituitary–adrenal axis, autonomic reactivity, reactive cell–mediated immune responses, disturbed sleep physiology, and altered perception of symptoms.[16,28,29,35]

Despite the complexity associated with attribution of physical health symptoms in the postdeployment period, these data should not be construed as suggesting that mild traumatic brain injury is not a serious medical concern. Soldiers who reported mild traumatic brain injury events, particularly loss of consciousness, were at very high risk for physical and mental health problems. Multiple concussions are associated with a longer recovery period,[36] which increases the risk for soldiers who have more than one episode during deployment. However, the relationship between concussion and persistent postconcussive symptoms is poorly understood. Postconcussive symptoms, which usually resolve rapidly (within several days or weeks),[20,21] are not specific to traumatic brain injury.[37] One recent study showed that the prevalence of postconcussive symptoms after injury was identical among patients with mild traumatic brain injury and patients with non-head traumas.[37] There is a theoretical concern about the neurologic effects of primary-blast overpressure (as distinct from the mechanical injuries caused by secondary or tertiary blast effects).[3,38] However, there is no evidence that a brief period of unconsciousness from a blast explosion is different clinically from an equivalent duration of unconsciousness caused by any other mechanism. With the absence of meaningful data on the effects of primary blast exposure on the brain, speculation by clinicians and the surrounding publicity[39] may unnecessarily increase patients' anxieties about the nature of their symptoms.[40]

From a diagnostic and treatment perspective, postconcussive symptoms are indistinguishable from symptoms of various disorders, including other symptom-based conditions described by soldiers returning from war.[40-42] The persistence of postconcussive symptoms has also been shown to be associated with medical disability and compensation processes, as well as the expectations and beliefs that patients have about their injuries.[10,43] Evidence-based interventions for the treatment of persistent postconcussive symptoms are lacking,[13,14] and the results of diagnostic procedures (neuroimaging or neuropsychological testing) for mild traumatic brain injury or deployment-related cognitive effects are often inconclu-

sive and difficult to interpret.[15,19,44] Management focuses largely on alleviating symptoms, yet the most compelling efficacy data highlight the importance of education to normalize symptoms and provide expectation of rapid recovery.[13,14,43,45] Toward this goal, the use of the term "concussion" is encouraged instead of "mild traumatic brain injury." Validated risk-communication approaches, education strategies, and evaluation procedures are needed.

A public health policy implication of this study relates to the sheer number of service members and veterans likely to be referred for further evaluation after being screened under new Department of Defense and Department of Veterans Affairs policies. This study suggests that a self-reported history of mild traumatic brain injury during deployment, particularly when associated with altered mental status without loss of consciousness, lacks specificity in predicting postdeployment physical health problems among injured soldiers. No empirical validation of the screening questions by means of clinical interviews has been done, with the exception of one widely quoted study that had no control group.[9,46] Almost two thirds of the mild traumatic brain injuries in this study sample were identified on the basis of a question that asked soldiers whether they were dazed or confused at the time of the injury. The question proved to have poor correlation to physical health outcomes, even without adjustment for PTSD. Screening for mild traumatic brain injury months after the injury is likely to result in the referral of a large number of persons for evaluation and treatment of nonspecific health symptoms attributed to brain injuries, with potential unintended iatrogenic consequences.[12,40,47,48] Evaluation of the screening programs for traumatic brain injury is needed to ensure that the risks do not outweigh the benefits and that screening is conducted within an effective structure of care.

The strong associations between mild traumatic brain injury, PTSD, depression, and physical health symptoms in combat veterans reinforce the need for a multidisciplinary approach centered in primary care. Evidence-based studies of the management of symptom-based disorders and collaborative care approaches to the evaluation and treatment of coexisting mental disorders in primary care settings are important in designing intervention strategies.[30,40,41,45,48-51]

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