Mild traumatic brain injury increases risk for the development of posttraumatic stress disorder

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BACKGROUND: Traumatic brain injury (TBI) and posttraumatic stress disorder (PTSD) occur in individuals who sustain physical injury and share a significant overlap in symptoms. PTSD rates in the civilian injury population range from 20% to 40%. The current study examined the presence of PTSD symptoms at multiple time points (3 months and 6 months after injury) among individuals with and without TBI after admission to a Level I trauma center.

METHODS: This prospective cohort study included patients 18 years and older admitted to a Level I trauma center for 24 hours or greater. Demographic and injury-related data were gathered in addition to assessments of PTSD during initial hospitalization after injury, as well as 3 months and 6 months later. The Primary Care PTSD Screen and PTSD Checklist–Civilian version were used to determine probable PTSD. International Classification of Diseases, 9th Rev. codes were used to determine mild TBI (MTBI).

RESULTS: A total of 494 patients were enrolled at baseline, 311 (63%) completed 3-month follow-up, and 231 (47%) completed 6-month follow-up at the time of analysis. Preinjury PTSD was reported by 7% of the participants. At 3 months, patients with MTBI evidenced a probable PTSD rate of 18%, compared with a rate of 9% for patients with no MTBI ($p = 0.04$), although this relationship became a nonsignificant trend ($p = 0.06$) when demographics were included. At 6 months, patients with MTBI evidenced a probable PTSD rate of 26%, compared with a rate of 15% for patients with no MTBI ($p = 0.04$), and this relationship remained significant when demographics were included. Preinjury history of TBI did not predict PTSD, but incidence of TBI for the injury in which they were hospitalized did predict PTSD.

CONCLUSION: TBI at time of injury demonstrated a nonsignificant trend toward higher rates of PTSD at 3 months and significantly predicted PTSD at 6 months after injury. This important finding may help clinicians identify patients at high risk for PTSD after injury and target these patients for screening, intervention, and referral for treatment. (J Trauma Acute Care Surg. 2015;79: 1062–1066.)

LEVEL OF EVIDENCE: Prognostic study, level III.

KEY WORDS: Posttraumatic stress disorder; mild traumatic brain injury; Level 1 trauma center.
Cooccurrence rates range from 11% to 24% for MTBI. Furthermore, studies have found that PTSD can develop when TBI is characterized by LOC or no memory of the traumatic event and that a history of MTBI is associated with current diagnosis of PTSD even after controlling for other demographic, psychiatric, and medical variables.

To date, few studies have examined the trajectory of potential cooccurrence of TBI and PTSD. A recent study by Hoffman et al. found that, among individuals admitted to the emergency department with MTBI, incidence of PTSD at 6 months following admission was 17%. In addition, Hoffman et al. identified Hispanic origin, participants' characterization of themselves as less happy at baseline, and negative expectations of outcome following injury as significant predictors of PTSD at follow-up. The current study sought to extend these findings by examining the presence of PTSD symptoms at multiple time points (3 months and 6 months after injury) both among individuals with and without TBI during admission to a Level I trauma center. The current findings are expected to provide insight regarding the relationship between TBI and PTSD, with significant implications for clinical care of patients potentially at risk for PTSD.

PATIENTS AND METHODS

The data for this study are from the Baylor Trauma Outcome Project (BTOP), an ongoing longitudinal study of patients admitted to a large, urban Level I trauma center in the Southwest United States that admits approximately 2,500 patients annually. Approval from the hospital's institutional review board was obtained before enrolling subjects in the current study. Potential participants were 18 years and older admitted to the trauma service for 24 hours or greater. These individuals were identified through the trauma service admission list and biweekly trauma rounds as well as review of the medical record. Patients who met criteria to be included were approached 24 hours after admission and before hospital discharge by trained clinical research assistants for consent and data collection.

Patients were eligible for study participation if they were medically stable, spoke English or Spanish, were able to provide a least one contact number for follow-up, and met the trauma registry injury criteria determined by the Committee on Trauma American College of Surgeons' Resources for Optimal Care of the Injured Patient. Patients were excluded if they did not have the cognitive capacity (either because of premorbid or injury-related condition) to provide informed consent. Cognition was assessed through chart review before visiting patients and orientation questions from the Cognistat screening tool. Demographic and injury-related data were obtained, and study measures were completed at the time of hospitalization (baseline), 3 months and 6 months later.

Measures

During acute hospitalization after initial injury, methods of data collection included (1) self-identification by participants for demographic-related questions (e.g., age, sex, race, marital status, and education); (2) extraction of injury-related variables from the trauma registry including Injury Severity Score (ISS), cause of injury, and any injury-related TBI; as well as (3) history of preinjury PTSD and history of TBI.

Assessment of PTSD

Primary Care PTSD Screen

Based on the criteria for PTSD in the DSM-IV, symptoms of PTSD were measured using the Primary Care PTSD (PC-PTSD) screen. Designed for use in medical settings, the PC-PTSD is currently used as the screening instrument for Veterans Affairs centers. It has been used specifically in trauma patients and has been shown to be comparable with longer assessments of PTSD in the trauma center setting, with a sensitivity of 72.4% and specificity of 93.4% when compared with the PTSD Checklist–Civilian version (PCL-C) 17-item screen. The PC-PTSD consists of four yes or no items, with scores ranging from 0 to 4. Because of the early time point of the first symptom assessment in the current study (acute hospital admission), a score of 3 or higher on the PC-PTSD was considered a positive screen result for clinical levels of PTSD symptoms. With a cutoff score of 3 for diagnosis, the PC-PTSD has shown 85% diagnostic efficiency, 78% sensitivity, and 87% specificity among Veterans Affairs clinic patients.

PTSD Checklist, Civilian Version

The PCL-C consists of 17 questions that correlate with the DSM-IV-TR criteria for PTSD. On a 5-point severity scale, respondents are asked how often they have been bothered by each symptom of PTSD in the past month, with questions worded generically to refer to “stressful experiences in the past.” Participants whose total scores were 50 or higher were considered positive for PTSD. Patients were coded as having probable PTSD if they indicated three or more primary symptoms on the PC-PTSD and evidenced a score of 50 or higher on the PCL-C.

Mild TBI

A participant was considered positive for MTBI based on ICD-9 coding. According to the Centers for Disease Control and Prevention, the ICD-9 is designed to promote international comparability in the collection, processing, classification, and presentation of mortality statistics.

Data Analysis

We first examined whether a variety of demographic variables were associated with PTSD at 3 months and 6 months after hospitalization. Univariate comparisons were conducted with t-tests or Mann-Whitney U-tests for continuous measures, and χ² tests or Fisher’s exact tests for categorical measures. We next examined whether MTBI for the injury that resulted in hospitalization was associated with higher rates of PTSD at 3 months and 6 months after hospitalization using χ² tests. Lastly, we examined whether MTBI for the injury that resulted in hospitalization would continue to predict PTSD at 3 months and 6 months after including relevant demographic variables. The goal of these analyses was to test the ability of MTBI to predict subsequent PTSD, adjusting for demographic variables. Two separate logistic regression models were conducted—the first model predicted PTSD at 3 months; the second model...
predicted PTSD at 6 months. For each model, predictor variables included MTBI and any demographic variable that correlated with the outcome variable at $\alpha < 0.05$ in Table 1. The criterion for exit/stay in the model was $\alpha < 0.05$. For both models, interaction and polynomial terms were examined. None of these terms were significant and thus are not included in the reported analyses later.

RESULTS

Active data collection was occurring at the time of the analysis. Of the 494 enrolled participants, 311 (63%) completed 3-month follow-up, and 231 (47%) completed 6-month follow-up at the time of analysis. A total of 34 enrolled participants (7%) reported preinjury PTSD. A total of 92 enrolled participants (19%) reported at least one occurrence of preinjury TBI.

PTSD and Demographics

As can be seen in Table 1, PTSD at 3 months was significantly predicted by race (blacks had higher rates of PTSD) and history of PTSD. PTSD at 6 months was significantly predicted by cause of injury (falls had lower rates of PTSD) and age (those with PTSD had lower average age). Sex, educational level, marital status, previous TBI, and ISS failed to significa-cantly predict PTSD at either 3 months or 6 months.

PTSD and MTBI

Participants were divided into those with and without MTBI at the time of injury. At the 3-month follow-up, 90 participants (29%) had MTBI at the time of injury, while 221 (71%) did not. A $\chi^2$ analysis revealed that participants with MTBI evidenced probable PTSD at a significantly higher rate (16 of 90 or 18%) than did participants without MTBI (21 of 221 or 10%) ($p = 0.04$). This same pattern of results was observed at 6 months after hospitalization. At the 6-month follow-up, 66 participants (29%) had MTBI at time of injury, while 165 (71%) did not. Participants with MTBI evidenced probable PTSD at a significantly higher rate (17 of 66 or 26%) than did participants without MTBI (24 of 165 or 15%) ($p = 0.04$). Thus preinjury history of TBI did not significantly predict probable PTSD, but incidence of TBI for the injury in which they were hospitalized did significantly predict PTSD at both 3 months and 6 months after hospitalization.

PTSD and MTBI—Multivariate

For the first model, we conducted a logistic regression in which PTSD at 3 months was the outcome and the predictor variables were MTBI and the two demographic variables that significantly correlated with PTSD at 3 months, namely, race and previous PTSD. There was a general lack of multicolinearity among the predictor variables, as none of the predictor variables were significantly associated with each other (all $p’s > 0.2$). As can be seen in Table 2, the area under the receiver operating characteristic curve (AUROC) and Hosmer-Lemeshow test indicated fair model fit. Only previous PTSD was a significant predictor. However, MTBI evidenced a nonsignificant trend. We then conducted a similar logistic regression model in which PTSD at 6 months was the outcome and the predictors were MTBI and the two demographic variables that significantly

<table>
<thead>
<tr>
<th>Variable</th>
<th>3 mo PTSD, No (n = 279)</th>
<th>3 mo PTSD, Yes (n = 33)</th>
<th>p</th>
<th>6 mo PTSD, No (n = 190)</th>
<th>6 mo PTSD, Yes (n = 41)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>46.8 (17.9)</td>
<td>42.2 (14.7)</td>
<td>0.13</td>
<td>48.0 (18.1)</td>
<td>40.8 (14.7)</td>
<td>0.01</td>
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<td>Sex, male, n (%)</td>
<td>173 (62)</td>
<td>25 (78)</td>
<td>0.51</td>
<td>110 (58)</td>
<td>30 (73)</td>
<td>0.07</td>
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<tr>
<td>Education, n (%)</td>
<td></td>
<td></td>
<td>0.35</td>
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<td>0.45</td>
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<td>High school or higher</td>
<td>105 (38)</td>
<td>11 (30)</td>
<td></td>
<td>77 (59)</td>
<td>14 (34)</td>
<td></td>
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<tr>
<td>Lower than high school</td>
<td>174 (63)</td>
<td>26 (70)</td>
<td></td>
<td>113 (41)</td>
<td>27 (66)</td>
<td></td>
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<tr>
<td>Cause of injury, n (%)</td>
<td></td>
<td></td>
<td>0.12</td>
<td></td>
<td></td>
<td>0.001</td>
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<td>Fall</td>
<td>78 (28)</td>
<td>5 (14)</td>
<td></td>
<td>59 (31)</td>
<td>3 (7)</td>
<td></td>
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<td>Moving vehicle</td>
<td>100 (36)</td>
<td>14 (38)</td>
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<td>71 (37)</td>
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<td>Assault</td>
<td>16 (6)</td>
<td>5 (14)</td>
<td></td>
<td>11 (6)</td>
<td>5 (12)</td>
<td></td>
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<tr>
<td>Other</td>
<td>85 (30)</td>
<td>13 (35)</td>
<td></td>
<td>49 (26)</td>
<td>20 (49)</td>
<td></td>
</tr>
<tr>
<td>Marital status, n (%)</td>
<td></td>
<td></td>
<td>0.26</td>
<td></td>
<td></td>
<td>0.24</td>
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<tr>
<td>Never married</td>
<td>95 (34)</td>
<td>17 (46)</td>
<td></td>
<td>64 (34)</td>
<td>18 (44)</td>
<td></td>
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<tr>
<td>Married</td>
<td>101 (36)</td>
<td>8 (22)</td>
<td></td>
<td>73 (38)</td>
<td>9 (22)</td>
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<tr>
<td>Divorced</td>
<td>53 (19)</td>
<td>9 (24)</td>
<td></td>
<td>33 (17)</td>
<td>8 (20)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>30 (11)</td>
<td>3 (8)</td>
<td></td>
<td>20 (11)</td>
<td>6 (15)</td>
<td></td>
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<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td>0.002</td>
<td></td>
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<td>0.13</td>
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<tr>
<td>White</td>
<td>210 (76)</td>
<td>19 (51)</td>
<td></td>
<td>149 (78)</td>
<td>26 (63)</td>
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<tr>
<td>Black</td>
<td>57 (21)</td>
<td>17 (46)</td>
<td></td>
<td>36 (19)</td>
<td>13 (32)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>11 (4)</td>
<td>1 (3)</td>
<td></td>
<td>5 (3)</td>
<td>2 (5)</td>
<td></td>
</tr>
<tr>
<td>Previous PTSD, n (%)</td>
<td>15 (6)</td>
<td>8 (25)</td>
<td>0.0001</td>
<td>12 (7)</td>
<td>6 (16)</td>
<td>0.07</td>
</tr>
<tr>
<td>Previous TBI</td>
<td>41 (15)</td>
<td>8 (22)</td>
<td>0.27</td>
<td>24 (13)</td>
<td>5 (12)</td>
<td>0.94</td>
</tr>
<tr>
<td>ISS, mean (SD)</td>
<td>11.2 (8.3)</td>
<td>12.5 (8.2)</td>
<td>0.48</td>
<td>11.7 (8.6)</td>
<td>13.4 (8.4)</td>
<td>0.33</td>
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</tbody>
</table>
correlated with PTSD at 6 months, namely, cause of injury and age. There was some multicollinearity among the predictor variables. Although age and MTBI were unrelated \((p = 0.8)\), cause of injury was significantly related to age \((p < 0.0001)\) and TBI \((p < 0.0001)\). As can be seen in Table 2, the AUROC and Hosmer-Lemeshow indicated fair model fit. Only MTBI was a significant predictor. Hence, after accounting for the variance accounted for by demographic variables, MTBI demonstrated a nonsignificant trend toward predicting PTSD at 3 months and did significantly predict PTSD at 6 months.

### DISCUSSION

While much attention has been placed on investigation of military populations with MTBI who are at additional high risk of PTSD, significantly less attention has been given to the consequences of MTBI in a civilian population with regard to later psychological outcome. The natural history of MTBI after civilian injury has not been fully elucidated, and we believe the results of this study add an important contribution to our understanding of the psychological complications of MTBI.

Our results show that patients who sustain an MTBI at the time of injury are at increased risk for the development of later PTSD at both 3 months and 6 months. PTSD was found in those with MTBI at a rate of 18\% at 3 months and 26\% at 6 months, which was statistically significant compared with those without an MTBI, whose rates were at 10\% and 15\%, respectively. When demographic variables were also considered in a regression model, MTBI evidenced a nonsignificant trend \((p = 0.06)\) of predicting PTSD at 3 months and significantly predicted PTSD at 6 months. The rates of PTSD in our sample for both individuals with and without MTBI were higher than those of the general US noninjury population (6.8\%). This pattern of results suggests that sustaining an injury that results in hospitalization in a Level 1 trauma unit puts the individual at an increased risk of developing PTSD and this risk is increased if the injury involves MTBI. This important finding supported and extends the work of Hoffman and Harrison.9 While Hoffman and Harrison showed that individuals with MTBI were at increased risk for later PTSD, our study demonstrated consistent findings with the added strength of using a comparison group of injured individuals without MTBI. This finding is also consistent with that of Bryant et al.,25 who examined individuals with and without an MTBI at 3 months after injury and found that those with MTBI were more likely to develop PTSD. Our study extends these findings to 6 months. We believe that this contributes to the growing evidence that MTBI is a significant contributor to the development of later PTSD.

In our study, demographic factors, including younger age, black race, and history of PTSD were predictive of later PTSD, and this has been observed in other studies in a civilian injury population.26 ISS failed to predict PTSD symptoms in our sample, a finding that, although may be counterintuitive, is nevertheless consistent with recent findings that severity of traumatic events as measured by ISS does not predict PTSD.27 When demographic factors were accounted for, MTBI demonstrated a nonsignificant trend for PTSD at 3 months, with previous PTSD accounting for the difference. However, at 6 months, MTBI predicted later PTSD despite demographic and preinjury factors. This finding suggests that having a MTBI is a critical difference in the development of later PTSD at 6 months.

Other factors that may be assumed to be of significance, such as ISS, did not prove to be associated with later PTSD. ISS means were not significantly different among those with or without PTSD at 3 months or 6 months. This finding suggests that while there may be a clinical bias to attribute more psychopathology to more severe injury, the ISS did not predict later negative psychological consequences such as PTSD. Cause of injury did seem to be a factor, with injuries caused by falls having the least predictive impact on later PTSD. Falls may have resulted in lower rates of PTSD because this type of injury is rarely interpersonal in nature, which can affect likelihood of PTSD outcomes.28 Additional research is needed to better understand the implications of injury cause in those who develop PTSD.

Perhaps, the most important clinical implication from this study is that identification of MTBI when a patient is admitted to the trauma center should be strongly considered. MTBI is often overlooked following injury, especially in the context of more severe and life-threatening injuries that may take understandable medical importance when the patient first presents to the trauma center. However, the results of this study suggest that MTBI could have potential negative psychological ramifications long after other injuries sustained by an individual have healed. Thus, identification of MTBI should occur routinely, and those with MTBI should be provided education regarding MTBI and potential psychological consequences including PTSD. In a similar context, history of PTSD in the

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**TABLE 2. Results From Multivariate Analyses**

<table>
<thead>
<tr>
<th></th>
<th>AUROC (95% CI)</th>
<th>p</th>
<th>HL</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTSD at 3 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>MTBI</td>
<td>0.67 (0.58–0.78)</td>
<td>0.0004</td>
<td>2.25</td>
<td>0.48 (0.22–1.03)</td>
<td>0.06</td>
</tr>
<tr>
<td>Race</td>
<td>0.62 (0.33–1.16)</td>
<td>0.13</td>
<td>0.62</td>
<td>0.62 (0.33–1.16)</td>
<td>0.13</td>
</tr>
<tr>
<td>Previous PTSD</td>
<td>0.17 (0.06–0.45)</td>
<td>&lt;0.001</td>
<td>0.17</td>
<td>0.17 (0.06–0.45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PTSD at 6 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTBI</td>
<td>0.73 (0.65–0.80)</td>
<td>&lt;0.0001</td>
<td>9.68</td>
<td>0.47 (0.23–0.98)</td>
<td>0.01</td>
</tr>
<tr>
<td>Cause of injury</td>
<td>0.91 (0.81–1.02)</td>
<td>0.10</td>
<td>0.91</td>
<td>0.91 (0.81–1.02)</td>
<td>0.10</td>
</tr>
<tr>
<td>Age</td>
<td>1.02 (1.00–1.04)</td>
<td>0.10</td>
<td>1.02</td>
<td>1.02 (1.00–1.04)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

CI, confidence interval; HL, Hosmer-Lemeshow; OR, odds ratio.
injury population continues to emerge as an important factor. Trauma centers should screen patients for past and current mental health history to facilitate early intervention and treatment as needed.

**Study Limitations**

The results of this study are obtained from a single Level I trauma center, and therefore, the results may not be generalized to others who sustain trauma in the civilian injury population. However, our rates of PTSD after injury are consistent with the literature, and we would anticipate that similar trends would be observed in those with and without MTBI who present to other trauma centers. An additional limitation in this study is that those who qualified for the study were conscious and able to provide informed consent very soon after their injury to participate, excluding patients with more severe TBI. A related limitation is that we did not control for the presence of other injuries, and it is possible that the presence of other injuries could be a predictor of PTSD.

Another inherent study limitation is the use of self-report in the measurement of PTSD by both the PC-PTSD and the PCL-C. A more definitive diagnosis of PTSD could have made use of a structured clinical interview. However, PC-PTSD and the PCL-C have been used in similar studies in individuals who sustain physical injury to assess the presence or absence of PTSD.

Interestingly, our population was not at a higher risk of developing PTSD with a history of TBI despite the fact that those with MTBI at time of injury were at increased risk. Additional research should explore the impact of a remote TBI in the context of current MTBI on the development of later PTSD.

**AUTHORSHIP**

A.M.W. was responsible for the study conceptualization and oversight, study design, data interpretation, writing, and critical revisions. T.R.E. was responsible for the study conceptualization and oversight, study design, data interpretation, writing, and critical revisions. A.B. was responsible for the critical revisions. M.L.F. was responsible for the data collection and interpretation. T.R.E. was responsible for the data analysis and interpretation. A.M.W. was responsible for the study conceptualization and oversight. A.B. was responsible for the data collection and writing. R.J.W. was responsible for the writing and critical revisions. P.H. was responsible for the data collection and writing. Z.T. was responsible for the critical revisions. M.L.F. was responsible for the study conceptualization.

**DISCLOSURE**

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**REFERENCES**