Prevalence and Predictors of Poor Recovery from Mild Traumatic Brain Injury

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Abstract

Although most patients with mild traumatic brain injury (mTBI) recover within 3 months, a subgroup of patients experience persistent symptoms. Yet, the prevalence and predictors of persistent dysfunction in patients with mTBI remain poorly understood. In a longitudinal study, we evaluated predictors of symptomatic and cognitive dysfunction in adolescents and young adults with mTBI, compared with two control groups—patients with orthopedic injuries and healthy uninjured individuals. Outcomes were assessed at 3 months post-injury. Poor symptomatic outcome was defined as exhibiting a symptom score higher than 90% of the orthopedic control (OC) group, and poor cognitive outcome was defined as exhibiting cognitive performance poorer than 90% of the OC group. At 3 months post-injury, more than half of the patients with mTBI (52%) exhibited persistently elevated symptoms, and more than a third (36.4%) exhibited poor cognitive outcome. The rate of high symptom report in mTBI was markedly greater than that of typically developing (13%) and OC (17%) groups; the proportion of those with poor cognitive performance in the mTBI group exceeded that of typically developing controls (15.8%), but was similar to that of the OC group (34.9%). Older age at injury, female sex, and acute symptom report were predictors of poor symptomatic outcome at 3 months. Socioeconomic status was the only significant predictor of poor cognitive outcome at 3 months.

Key words: cognitive function; human studies; recovery; traumatic brain injury

Introduction

MILD TRAUMATIC BRAIN INJURY (mTBI) is extremely prevalent, affecting more than 1 million persons in the United States (US) annually,¹ and accounting for more than 1% of all US emergency department (ED) visits.² Although most patients with mTBI recover within 3 months, a significant minority complains of symptoms that persist longer. Reviews of the neuropsychological effects of mTBI have concluded that the vast majority of patients exhibit full cognitive recovery within days to weeks.^{3–5} Nevertheless, clinically meaningful persistent cognitive dysfunction in a subset of persons may be poorly characterized by summary statistics based on aggregate data.⁶

Studies of athletes with sports-related mTBI have shown that cognitive dysfunction and symptom complaints follow a similar recovery trajectory, with cognitive recovery occasionally preceding but more often following symptomatic recovery.^{7,8} Prospective studies following patients up to 1 year post-injury have shown evidence of

persistent dysfunction in approximately 15–30% of those samples,^{9,10} and recent magnetic resonance imaging data show that structural changes may account for some of the variation in outcomes.¹¹ The accuracy of this estimate has been called into question, however, because sampling biases may lead to an inflated estimated prevalence of prolonged mTBI symptoms.¹²

The causes of protracted recovery are also a point of debate. Both physiological and psychological factors have been put forth as explanations for prolonged symptoms in this subgroup of patients.¹³ Elucidating the etiology of cognitive and somatic complaints is a complicated task. Post-concussion symptoms are nonspecific in nature and can be found across a variety of clinical populations. They can be influenced by post-traumatic stress,¹⁴ pre-injury depression or anxiety,¹⁵ risk factors such as premorbid cognitive problems, substance use, and psychosocial stressors,^{16–18} or external incentives such as involvement in litigation.^{19–21} These confounding factors make it difficult to estimate the true prevalence and correlates of lingering mTBI sequelae.

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The use of trauma patients with orthopedic injuries as a comparison group allows investigators to control for confounding factors that influence the clinical presentation of patients with mTBI, such as post-trauma stress and pre-injury risk factors including behavioral factors that predispose a person to injury. A recent study examined cognitive performance in 123 patients with mTBI and 100 age and sex matched orthopedically injured controls (OC) at presentation to the ED 1 week, and 3 months post-injury.²² The authors found no differences between patients with mTBI and trauma control in cognitive test performance immediately post-injury. The mTBI group, however, had poorer results than controls on tests of visual memory 1 week and 3 months later. This finding suggests that mTBI may produce cognitive dysfunction above and beyond the effects of trauma-related stress.

Other work has examined the course of symptom complaints in mTBI patients compared with orthopedic injury patients. One study including patients with mTBI of mixed etiology (motor vehicle accident, assault, sports related, etc.) found that mTBI, female sex, and premorbid psychiatric history predicted post-concussion symptoms 1 week post-injury.²³ At 3 months post-injury, however, mTBI was not a significant predictor of ongoing concussion symptoms, but pre-injury physical complaints (assessed with the 36-item short form health survey) and psychiatric history were.

Another study compared symptoms of post-concussion syndrome (PCS) between patients with mTBI (predominantly motor vehicle accident related) and patients with orthopedic injury.¹⁵ The investigators found similar rates of PCS at 3 months post-injury within both groups. Furthermore, pre-injury depression or anxiety and acute post-traumatic stress predicted PCS regardless of mTBI. Research from our group has also found that anxiety and depression are risk factors for complicated recovery after mild to moderate TBI.²⁴

Although patients with orthopedic injuries may be similar to patients with mTBI in terms of pre-morbid characteristics and post-traumatic stress,^{15,23} the possibility of occult brain injury in this group could lead to an underestimation of mTBI-related cognitive dysfunction. Furthermore, pain, analgesic medication, and inflammation may depress cognitive function and inflate the post-concussion symptom report.²⁵ Hence, designs using two control groups—patients with orthopedic injuries and healthy uninjured persons—may represent the most prudent way of evaluating mTBI sequelae.

We evaluated predictors of symptomatic and cognitive dysfunction 3 months post-injury in adolescents and young adults with mTBI, orthopedic injuries, and healthy uninjured persons in a longitudinal design. This design allows us to identify levels of symptom report and cognitive performance that are unusual for those with orthopedic injuries. The OC group was used as a reference to detect outcomes specifically related to brain injury and not the general effects of trauma. Reference scores were based on the OC group's 3-month post-injury outcomes. Poor outcome at 3 months post-injury was defined as exhibiting a symptom score higher than 90% of the OC group and cognitive test scores poorer than 10% of the OC group. Demographic and injury characteristics, as well as acute clinical profile, were examined as predictors of prolonged recovery.

Methods

This project was conducted in accordance with the Helsinki Declaration and approved by the Institutional Review Boards of Baylor College of Medicine, Texas Children's Hospital, Memorial-Hermann Hospital, and Ben Taub General Hospital.

Participants

Participants were adolescents and young adults aged 12–30 years. Participants were excluded if they were not fluent English or Spanish speakers, had a pre-existing neurological disorder or severe psychiatric disorder (e.g., bipolar disorder, schizophrenia), blood alcohol level >200 mg/dL, or previous hospitalization for head injury.

Patient groups (mTBI and OC). Patient recruitment took place between 12/15/2008 and 4/30/2012. MTBI and OC patients were recruited as a consecutive series of admissions to EDs of three Level-1 trauma centers: Texas Children's Hospital, Memorial-Hermann Hospital, and Ben Taub General Hospital in Houston, Texas by study personnel according to a rotating schedule. Eligibility was based, in part, on the following measures: Glasgow Coma Scale (GCS²⁶), graded by ED trauma or other medical staff; Abbreviated Injury Scale (AIS²⁷) ratings made by AIS-certified research nurses based on detailed medical record review; and head CT scans read and coded by a board-certified neuroradiologist (JVH).

Although every attempt was made to screen and enroll the patients while in the ED, patients were allowed to go home from the ED and return for the baseline assessment; the target window for this assessment was <96 h post-injury.

The diagnosis of mTBI was made by ED trauma physicians based in part on GCS²⁶ scores between 13 and 15, loss of consciousness (LOC) less than 30 min, and post-traumatic amnesia (PTA) less than 24 h. PTA was assessed using the Galveston Orientation and Amnesia Test (GOAT²⁸). To be eligible for inclusion, all participants must have had negative findings on initial CT scan and had mild or no extracranial injuries demonstrated by AIS scores less than 2 (not including the head region).

Typically developing (TD) group. Forty-four TD control participants who had not sustained any injury but were similar to the injury groups in age, sex, and level of education were recruited using notices on community bulletin boards.

Procedure

Participants were evaluated with a neuropsychological test battery within 96 h post-injury and again at 3 months post-injury. For a complete description of the sample and all study procedures, see Hanten and associates²⁹; only procedures relevant to the present analysis are described below. Neuropsychological measures included the Brief Visual Memory Test-Revised³⁰ immediate recall (BVMT-R Total), the Verbal Selective Reminding Test^{31,32} including the number of words recalled after a delay (VRST Delay) and number of words continuously recalled (VSRT CLTR), and the Symbol-Digit Modalities Test³³ oral (SDMT-O) and written (SDMT-W) administrations.

The Rivermead Post Concussion Symptoms Questionnaire^{34,35} and the Brief Symptom Inventory,³⁶ from which the Global Severity Index (GSI) was calculated, were also collected as self-report symptom measures. Socioeconomic Composite Index (SCI) scores were calculated based on annual family income, level of education (maternal education for participants younger than 18 years old), and occupational prestige. This measure has been associated with cognitive outcomes after pediatric TBI in previous work.³⁷

Statistical analysis

OC patients at 3 months post-injury served as a reference group. Participants were classified as demonstrating poor symptomatic recovery if they obtained at least one score above the 90th percentile for either the Rivermead Post Concussion Symptom Questionnaire or the Brief Symptom Inventory GSI. They were

TABLE 1. OUTCOME VARIABLES BY GROUP

	MTBI (N=66)				OC (N=63)				TD (N=38)			
	96 h		3 mo		96 h		3 mo		96 h		3 mo	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Rivermead	17.0	12.6	10.8	11.1	4.2	4.6	2.3	3.7	2.0	2.8	3.1	7.1
BSI Global Severity Index	56.1	13.5	50.6	14.9	47.6	12.1	45.2	12.5	46.3	11.4	46.2	12.4
SDMT-O	52.4	11.4	61.5	13.1	58.7	11.8	67.4	14.5	64.2	11.4	72.0	12.7
SDMT-W	46.7	9.8	54.7	9.5	49.2	9.3	58.8	12.6	52.9	8.4	61.5	12.0
VSR Delay	8.6	2.3	8.8	1.9	9.3	2.2	9.5	2.1	9.7	2.1	10.4	1.5
VSR CLTR	42.1	11.6	45.0	11.9	47.1	13.0	47.5	11.3	51.8	11.7	53.1	11.2
BVMT Total	23.3	5.4	26.0	5.0	23.5	5.0	25.2	5.2	24.7	4.6	26.6	4.4

MTBI, mild traumatic brain injury; OC, orthopedic controls; SD, standard deviation; BSI, Brief Symptom Inventory; SDMT-O, Symbol Digit Modalities Test – Oral Version; SDMT-W, Symbol Digit Modalities Test – Written Version; VSR Delay, Verbal Selective Reminding Test – Delay; VSR CLTR, Verbal Selective Reminding Test – Words Continuously Recalled; BVMT, Brief Visual Memory Test.

classified as exhibiting poor cognitive outcome if they scored below the 10th percentile on at least one of the following cognitive outcome measures: SDMT-O, SDMT-W, BVMT, VSRT Delay, and VSRT CLTR. The group and subgroup comparisons were performed using the chi-square (χ^2) test or Fisher exact test for categorical variables (e.g., sex, race, litigation) and *t* test for continuous variables.

Prediction models were built up using stepwise logistic regression. First the demographic and injury variables (age, sex, race, SCI, PTA, LOC, litigation, and method of injury) were entered into the model, and only significant predictors (*p* values < 0.05) remained in the model; then the corresponding outcome measures within 96 h post-injury were entered into the model. To assess performance of the prediction models, we used Hosmer-Lemeshow Goodness-of-Fit test, *p* values (< 0.05) and area under the receiver operating characteristic (ROC) curve (≥ 0.8). All statistical models were performed in SAS version 9.3.

Results

Of 87 patients with mTBI screened at 96 h post-injury, 66 returned for follow-up at 3 months (76% retention rate). Of the 75 OC participants recruited, 63 returned for follow-up (84% retention rate), and 38 of 44 TD participants recruited returned for follow-up (88% retention rate). Patients with incomplete data were more likely to be African American ($\chi^2(1)=6.76$, $p=0.0093$). There were no other significant differences on demographic or 96-hour post-injury outcome variables between study completers and non-completers. Only study completers were included in subsequent analyses.

Initial assessments took place a mean of 65.9 h (standard deviation [SD]=27.32) post-injury for patients with MTBI and a mean of 67.5 h (SD=25.27) post-injury for participants in the OC group. Demographic characteristics and summary statistics for cognitive and symptom variables are presented in Table 1. Age ($F=0.39$, $p=0.6758$) and socioeconomic status ($F=2.53$, $p=0.0828$) did not significantly differ across the three groups.

Symptomatic recovery

The criteria used to determine symptomatic and cognitive outcomes are outlined in Table 2. Thirty-four of the 66 (52%) patients with mTBI, 11 of 64 (17%) OC patients, and 5 of 38 (13%) TD participants met the definition of prolonged elevated symptoms. Rates of prolonged elevated symptoms significantly differed across groups ($\chi^2(2)=24.79$, $p=4.134\text{e-}6$) (Fig. 1). *Post-hoc* tests dem-

onstrated that patients in the mTBI group were more likely to meet criteria for prolonged elevated symptoms than participants in either the OC group ($\chi^2(1)=16.92$, $p=3.905\text{e-}05$) or the TD group ($\chi^2(1)=15.14$, $p=9.991\text{e-}05$). Participants in the OC and TD groups did not differ in prevalence of prolonged elevated symptoms ($\chi^2(1)=0.29$, $p=0.5885$).

Within the mTBI group, patients in the prolonged elevated symptoms group were an average of 4.6 years older ($t(64)=-3.78$, $p=0.0003$) and more likely to be female ($\chi^2(1)=8.33$, $p=0.0039$). Among female patients, 75% met the definition for prolonged elevated symptoms, compared with 38% of male patients. Race and socioeconomic status did not significantly distinguish between those patients with and without prolonged elevated symptoms (Table 3). A logistical regression model was constructed to predict membership in the prolonged elevated symptoms group at 3 months post-injury using demographic and injury-related variables, as well as initial clinical profile (symptom report and cognitive test performance at 96 h post-injury).

First, demographic and injury-related variables were entered as predictors—including age, sex, race, SCI, mechanism of injury (motor vehicle crash vs. other), LOC, and PTA. The final model,

TABLE 2. CLASSIFICATION CRITERIA FOR POOR RECOVERY

	<i>Measure</i>	<i>Cutoff</i>
Symptom outcome criteria	Rivermead Post Concussion Questionnaire	Raw score ≥ 8
Cognitive outcome criteria	BSI Global Severity Index	T score ≥ 61
	SDMT-O	Raw score ≤ 48
	SDMT-W	Raw score ≤ 43
	VSR Delay	Raw score ≤ 6
	VSR CLTR	Raw score ≤ 33
	BVMT Total	Raw score ≤ 18

Cutoffs are based on scores that were unusual for the orthopedic control group—scores above the 90th percentile for symptom outcome measures and scores poorer than the 10th percentile for cognitive outcome measures. Participants who fulfilled one or more of the symptom outcome criteria at 3 months post-injury met the definition of Prolonged Elevated Symptom Recovery, and participants who fulfilled one or more of the cognitive outcome criteria at 3 months post-injury met the definition of Poor Cognitive Recovery. BSI, Brief Symptom Inventory; SDMT-O, Symbol Digit Modalities Test – Oral Version; SDMT-W, Symbol Digit Modalities Test – Written Version; VSR Delay, Verbal Selective Reminding Test – Delay; VSR CLTR, Verbal Selective Reminding Test – Words Continuously Recalled; BVMT, Brief Visual Memory Test.

FIG. 1. Prevalence of poor recovery across groups at 3 months post-injury. Rates of poor recovery significantly differed across groups for both symptomatic ($\chi^2(2)=24.79$, $p=4.1e-6$) and cognitive ($\chi^2(2)=8.01$, $p=0.018$) recovery. mTBI, mild traumatic brain injury.

which was the most parsimonious model to maximize prediction, included sex ($\beta=0.92$, $\chi^2(1)=8.04$, $p=0.0046$) and age of injury ($\beta=0.21$, $\chi^2(1)=10.54$, $p=0.0012$). The ROC curve for the final model showed acceptable discrimination with an area under the curve (AUC)=0.81. Of note, LOC and PTA were not significant predictors.

Next, initial symptom report and cognitive performance variables were added to the model to test whether these variables improved prediction. Initial Rivermead score was a significant predictor of prolonged elevated symptoms ($\beta=0.13$, $\chi^2(1)=8.44$, $p=0.0037$), indicating that with one unit increase in the initial Rivermead score, the odds of elevated symptoms at 3 months increased 14.2%. The ROC curve for this model, including sex ($\beta=0.81$, $\chi^2(1)=4.13$, $p=0.0422$), age of injury ($\beta=0.23$, $\chi^2(1)=9.24$, $p=0.0024$), and initial Rivermead score demonstrated good discrimination (AUC=0.90) (Fig. 2), and the model yielded acceptable fit to the data (Hosmer-Lemeshow $\chi^2(8)=5.39$, $p=0.7155$).

Initial GSI score was also a significant predictor of prolonged elevated symptoms ($\beta=0.08$, $\chi^2(1)=7.07$, $p=0.0078$), indicating that with one unit increase in the GSI score, the odds of elevated symptoms at 3 months increased 8.2%. The ROC curve for this model including sex ($\beta=0.98$, $\chi^2(1)=7.53$, $p=0.0061$), age of injury ($\beta=0.13$, $\chi^2(1)=3.46$, $p=0.0630$), and initial GSI score demonstrated good discrimination (AUC=0.86), and the model yielded acceptable fit to the data (Hosmer-Lemeshow $\chi^2(8)=7.12$, $p=0.4164$). Initial performance on cognitive measures, including SDMT-O ($\beta=-0.007$, $\chi^2(1)=0.03$, $p=0.8258$), SDMT-W ($\beta=-0.007$, $\chi^2(1)=0.05$, $p=0.8258$), VSR Delay ($\beta=-0.03$, $\chi^2(1)=0.12$, $p=0.8030$), VSR CLTR ($\beta=0.03$, $\chi^2(1)=1.09$, $p=0.2958$), and BVMT Total ($\beta=-0.01$, $\chi^2(1)=1.30$, $p=0.2541$) did not improve prediction of prolonged elevated symptoms.

Cognitive recovery

For the complete definition of poor cognitive outcome, see Table 2. Twenty-four (36.4%) of the 66 patients with mTBI, 22 (34.4%) of the 64 in the OC group, and 6 (15.8%) of the 38 TD participants met the definition for poor cognitive outcome. The difference between rates of poor cognitive outcome across groups was marginally significant ($\chi^2(2)=5.34$, $p=0.0691$) (Fig. 1). *Post-hoc* tests demonstrated that patients in the mTBI group were more likely to meet criteria for poor cognitive outcome than participants in the TD group ($\chi^2(1)=7.52$, $p=0.0064$). Patients in the OC group were also

more likely to meet criteria for poor cognitive outcome than participants in the TD group ($\chi^2(1)=6.61$, $p=0.0101$). There was no significant difference in the rates of poor cognitive outcome between the mTBI and OC groups ($\chi^2(1)=0.00$, $p=0.95$).

In the mTBI group, SCI significantly differed between patients with mTBI who had good versus poor cognitive outcome ($t(64)=2.79$, $p=0.0070$), but age of injury ($t(64)=-0.43$, $p=0.6706$), sex ($\chi^2(1)=0.46$, $p=0.4984$), and race (African American vs. other; $\chi^2(1)=0.50$, $p=0.4785$) did not. There was no effect of PTA, LOC, or mechanism of injury (motor vehicle crash vs. other) on cognitive outcome (Table 3).

A logistical regression model was constructed to predict membership in the poor cognitive outcome group at 3 months post-injury using demographic and injury-related variables, as well as initial clinical profile (symptom report and cognitive test performance at 96 h post-injury). First, demographic and injury-related variables were entered as predictors—including age, sex, race, SCI, mechanism of injury, LOC, and PTA. The final model, which was the most parsimonious model to maximize prediction, included SCI only ($\beta=-1.2010$, $\chi^2(1)=6.5838$, $p=0.0103$). The ROC curve for the final model showed fair discrimination with an AUC=0.72.

Next, initial symptom report and cognitive performance variables were added to the logistic regression model, controlling for SCI, to test whether these variables improved prediction. None of the initial symptom report or cognitive performance variables were significant predictors of cognitive outcome, including initial Rivermead ($\beta=-0.0188$, $\chi^2(1)=0.68$, $p=0.4097$), SDMT-O ($\beta=-0.031$, $\chi^2(1)=1.36$, $p=0.2432$), SDMT-W ($\beta=-0.0468$, $\chi^2(1)=2.03$, $p=0.1539$), VSR Delay ($\beta=-0.2039$, $\chi^2(1)=2.91$, $p=0.0880$), VSR CLTR ($\beta=-0.0331$, $\chi^2(1)=1.70$, $p=0.1928$), and BVMT Total ($\beta=-0.006$, $\chi^2(1)=0.40$, $p=0.5258$).

Because the rates of poor cognitive outcome were similar for the mTBI and OC groups, we also examined the mean cognitive scores across groups at 3 months (Table 4). Results revealed that the mTBI group had a poorer performance than the OC group on the SDMT-W and SDMT-O, and these effects remained significant after controlling for age at injury and SCI.

Litigation status

Fifteen patients in the mTBI group, and 6 patients in the OC group were pursuing litigation at some point during their participation in the study. Patients with mTBI were more likely to be pursuing litigation than OC patients ($\chi^2(1)=4.4$, $p=0.0351$). Among patients with mTBI, there was a trend toward a greater likelihood for litigants to belong to the persistent elevated symptom group ($\chi^2(1)=3.5$, $p=0.0630$). There was no relationship between litigation status and membership in the poor cognitive outcome group ($\chi^2(1)=0.04$, $p=0.8497$).

Discussion

This study examined the prevalence and predictors of poor recovery at 3 months post-injury in a prospective sample of adolescent and young adult patients with mTBI. Poor outcome was operationalized based on rates of impairment in a group of age-matched orthopedically injured patients. Using the OC group as the reference, symptom scores greater than the 90th percentile and cognitive scores less than the 10th percentile represented poor recovery. Using these criteria, we found substantial rates of poor symptomatic and cognitive recovery in the mTBI group. At 3 months post-injury, more than half (52%) of the patients with mTBI

TABLE 3. RELATION OF DEMOGRAPHIC AND INJURY VARIABLES TO PERSISTENT ELEVATED SYMPTOMS AND POOR COGNITIVE RECOVERY

Group	Demographics	Elevated symptoms	Mean/Freq.	SD/%	Range	p value
<i>Persistent Elevated Symptoms</i>						
mTBI	Age at injury	Yes	22.1	4.9	14.5–30.6	0.0003
N:		No	17.5	5.0	12.2–29.5	
Yes: 34 (51.5%)	SCI	Yes	–0.05	0.81	–1.10–1.98	0.5033
No: 32 (48.5%)		No	–0.18	0.75	–1.41–1.76	
	LOC	Yes	4	4	1–8	0.5507
		No	3.9	4	1–10	
	PTA	Yes	2.2	2	1–4	0.8412
		No	2.2	2	1–4	
	Time to RTW/RTS	Yes	2.7	1.21	1–4	0.059
		No	6.0	9.54	1–30	
	Sex (M)	Yes	16	47.1%	–	0.0039
		No	26	81.3%	–	
	Race (B)	Yes	9	28.1%	–	0.7088
		No	11	32.4%	–	
	MOI (MV)	Yes	20	58.8%	–	0.0467
		No	11	34.4%	–	
Group	Demographics	Poor cog recovery	Mean/Freq.	SD/%	Range	p value
<i>Poor Cognitive Recovery</i>						
mTBI	Age at injury	Yes	20.2	5.8	12.2–29.5	0.6706
N:		No	19.6	5.2	12.2–30.6	
Yes: 24(36.4%)	SCI	Yes	–.44	.62	–1.41–1.06	0.0070
No: 42 (63.6%)		No	.08	.80	–1.17–1.98	
	LOC	Yes	4.2	2.5	1–10	0.9508
		No	3.8	1.6	1–7	
	PTA	Yes	2.0	.8	1–3	0.1067
		No	2.3	.7	1–4	
	Time to RTW/RTS	Yes	7.0	9.81	1–30	0.0206
		No	2	1.15	1–4	
	Sex (M)	Yes	14	58.3%	–	0.4984
		No	28	66.7%	–	
	Race (B)	Yes	6	25.0%	–	0.4785
		No	14	33.3%	–	
	MOI (MV)	Yes	12	50.0%	–	0.7092
		No	19	45.2%	–	
OC	Age at injury	Yes	19.8	6.1	12.2–30.5	0.5904
N:		No	20.6	5.5	12.1–30.8	
Yes: 22 (34.9%)	SCI	Yes	–.24	.56	–1.27–.88	0.1302
No: 41(65.1%)		No	.07	.84	–1.59–2.33	
	Time to RTW/RTS	Yes	2.67	1.53	1–4	0.1692
		No	2.25	.89	1–4	
	Sex (M)	Yes	18	81.8%	–	0.2489
		No	28	68.3%	–	
	Race (B)	Yes	12	54.6%	–	0.1697
		No	15	36.6%	–	
	MOI (MV)	Yes	4	19.1%	–	0.2199
		No	3	7.5%	–	
TD	Age		20.8	5.1	–	
	SCI		0.24	0.84		
	Sex (M)		21	55.26%		
	Race (B)		15	39.5%		

SD, standard deviation; mTBI, mild traumatic brain injury; SCI=socioeconomic composite index; Loc, LOC, loss of consciousness; PTA, post-traumatic amnesia; RTW, return to work; RTS, return to school; MOI, mechanism of injury; MV, motor vehicle; B, black; M, male. The *p* values were from two sample *t* test or chi-square tests (Wilcoxon nonparametric test for PTA and LOC).

exhibited persistently elevated symptoms, and more than a third (36.4%) exhibited poor cognitive recovery.

The rate of high symptom report in patients with mTBI was markedly greater than that of TD control participants (13%) and orthopedically injured patients (17%). The rate of poor cognitive

performance in the mTBI group was greater than that of TD controls (15.8%), but similar to the rate of cognitive dysfunction in the orthopedic injury group (34.9%). Our results differ from previous findings in older samples, suggesting a lack of association between mTBI and poor outcome at 3 months post-injury.^{23,38}

FIG. 2. Receiver operating characteristic (ROC) curve for the prediction of 3-month symptom recovery based on initial (96-h) Rivermead Score, sex, and age at injury.

Although the rate of persistent cognitive dysfunction was similar for both patients with mTBI and orthopedic patients, a comparison of group means revealed that the mTBI group performed more poorly than the OC group on two measures of processing speed. Long-term cognitive changes after mTBI may be relatively specific (affecting primarily processing speed) and subtle (evident by comparison of group means, but not apparent when using more conservative cutoff scores). This may explain why the OC and mTBI groups look similar when examining rates of poor cognitive recovery, but group differences emerge when comparing mean performance on individual tests.

More pronounced cognitive differences between patients with mTBI and healthy controls may be caused by factors that confer risk for injury, pre-existing differences in baseline cognitive level, genetics, or psychological consequences of trauma. Cognitive deficits in the OC group may have been the result of post-injury stress¹⁸ or covert brain injury.³⁹ Of note, the paper and pencil measures used in the present study may have less precision and

sensitivity than timed computerized tasks.⁴⁰ Hence, it is possible that more robust group differences would emerge with different measures of processing speed.

We also evaluated demographic factors, injury characteristics, and early outcomes (96 h post injury) as predictors of poor recovery. We found that female sex, older age of injury, and initial symptom report predicted persistently elevated symptoms. The SCI was the only significant predictor of poor 3-month cognitive recovery. Of note, mechanism of injury, GCS, LOC, and PTA were not significantly related to poor recovery.

Predictors may directly influence outcome, they may be proxies for injury severity, or they could moderate the recovery process. Each predictor could influence outcome via a different combination of mechanisms. For example, the older adolescents and young adults in our sample may have reported more symptoms because of a greater introspective capacity and/or a more forthright reporting style that comes with age. Because adolescence and early adulthood, however, is a time of substantial brain development,⁴¹ age may also have had a moderating effect on recovery from mTBI.

The association between poorer TBI outcome and older age has been reported elsewhere^{42,43}; however, previous studies have focused on geriatric populations, and it is unlikely that similar mechanisms would account for the relationship between age and outcome in our sample of adolescents and young adults.

The association between female sex and prolonged post-concussion symptoms is also consistent with previous research.⁴⁴⁻⁴⁸ Many hypotheses have been put forth to explain the sex difference in elevated and prolonged symptoms. Some have speculated that sex differences in head size or neck musculature may contribute,⁴⁹ while others have argued that the findings can be explained by women's and girls' more forthcoming reporting style.⁵⁰ Current explanations for sex differences remain purely speculative and should be tested in future research.

Regarding the effect of SCI on cognitive recovery, lower socioeconomic status may have had a direct effect on cognitive performance, and/or cognitive recovery processes may have been hindered by lack of socioeconomic resources. Socioeconomic status has been associated with cognitive reserve, and research has shown that persons with higher cognitive reserve are less susceptible to cognitive deficits after TBI.⁵¹⁻⁵³ The theory of cognitive reserve posits that an individual's experiences affect the efficiency of their neural and cognitive networks, such that those with enriching life histories are protected against cognitive decline.⁵⁴

An association between socioeconomic status and better cognitive recovery is consistent with previous research demonstrating that higher level of education predicted better 6-month outcome

TABLE 4. COMPARISON OF 3-MONTH COGNITIVE OUTCOMES FOR MILD TRAUMATIC BRAIN INJURY AND ORTHOPEDIC CONTROL GROUPS

	MTBI (N=66) M (SD)	OC (N=64) M (SD)	t	p value	Adjusted model ^T	
					F	p value
BVMT Total	26 (4.9)	25 (5.2)	0.86	0.39	0.71	0.40
VSR CLTR	45 (11.9)	48 (11.3)	1.19	0.24	1.21	0.27
VSR Delay	8.8 (1.9)	9.5 (2.0)	1.96	0.05	3.54	0.06
SDMT-W	55 (9.5)	59 (12.5)	2.03	0.04*	3.95	0.05*
SDMT-O	61 (13.1)	67 (14.3)	2.43	0.02*	5.69	0.02*

^TControlling for age of injury and SCI. *Test is significant at $p < 0.05$.

MTBI, mild traumatic brain injury; OC, orthopedic controls; SD, standard deviation; BVMT, Brief Visual Memory Test; VSR CLTR, Verbal Selective Reminding Test – Words Continuously Recalled; VSR Delay, Verbal Selective Reminding Test – Delay; SDMT-W, Symbol Digit Modalities Test – Written Version; SDMT-O, Symbol Digit Modalities Test – Oral Version.

from mTBI.⁵⁵ Further, SCI might be related to environmental resources that promote recovery, such as greater flexibility at work to take time off or limit responsibilities directly after an injury.

Similar to other reports in the literature, we found that traditional indicators of injury severity (i.e., LOC and PTA) were not predictive of 3-month mTBI outcome.^{23,55–57} Some authors have interpreted this to mean that persistent mTBI sequelae must have a psychogenic as opposed to physiological origin.⁵⁷ Although we strongly agree that psychological factors contribute to clinical presentation after mTBI, the lack of association between outcomes and LOC/PTA does not, on its own, warrant this conclusion. In our sample, there was a restricted range of LOC and PTA duration, and these indices lose their sensitivity as predictors of outcomes when their range is narrow.

The clinical neuroscience of mTBI is a rapidly developing field, and we now know that mTBI can produce idiosyncratic and diffuse pathology throughout the brain.⁵⁸ LOC and PTA may reflect specific loci of dysfunction (e.g., alterations in consciousness are probably related to transient changes in brainstem function), and their presence is probably not a valid index of total cerebral disturbance.

There are limitations to the present study. We cannot rule out the possibility of latent brain injury in the OC group. Patients in this group may have had concussions that were overshadowed by more apparent orthopedic injuries. The outcome measures were self-reported symptoms and conventional neuropsychological tests. Although these measures are well validated in the mTBI literature, they are subject to biases. Further, without pre-injury measurement of cognitive ability and symptom report, it is difficult to determine whether abnormal scores represent a change from a person's baseline level of functioning. In addition, although persons with a history of serious psychiatric illness were excluded from the study, pre-injury anxiety and depression were not assessed, and these factors have been shown to influence outcomes in previous work.^{15,22,23} Post-injury anxiety, depression, and post-traumatic stress are also likely to impact cognitive function and functional outcome after mTBI. Future research with careful assessment of these conditions would be valuable in elucidating predictors of poor recovery.

It is possible that the cognitive outcome variables included in this study did not fully capture the cognitive sequelae of mTBI. Other tests, such as computerized measures of reaction time may have been more sensitive to mTBI-related cognitive dysfunction. Of note, delayed memory, which was included in the present study, and verbal fluency have been identified as the most sensitive measures of mTBI-related cognitive impairment in a meta-analysis.⁵⁹

Strengths of this study include the use of two comparison groups, which allow us to describe mTBI-related impairment in the context of both typical development and non-brain injury. Further, exclusion of patients with positive CT findings mitigates major confounds from brain lesions, including surgical lesions involving general anesthesia, which have been found to produce outcomes similar to those of patients with GCS scores of 9–12.⁶⁰ Our high rate of follow-up at 3 months is also a considerable strength of the study and enhances the generalizability of these findings.

Finally, adolescents and young adults with mTBI have been relatively understudied. Our findings indicate that there are high rates of persistent dysfunction in younger patients with mTBI, higher than would be expected based on the adult mTBI literature.^{15,22,23} Clinicians should prepare adolescent and young adult patients for the possibility of symptoms and cognitive deficits that

persist at least 3 months post-injury, with awareness that older age at injury, high initial symptom report, female sex, and lower socioeconomic status are risk factors for persistent dysfunction.

Conclusion

We suggest that persistent symptoms and cognitive dysfunction are common in adolescents and young adults 3 months after mTBI, with 52% of patients exhibiting elevated levels of post-concussion symptoms and 36% of patients exhibiting cognitive dysfunction. While post-concussion symptoms distinguished patients with mTBI from both those with orthopedic injuries and healthy controls, the rates of persistent cognitive problems were similar for patients with mTBI and orthopedic injury.

This dissociation between symptomatic and cognitive recovery is similar to previous findings demonstrating that cognitive deficits largely resolve within 1 to 3 months of CT-negative mTBI, but a subset of patients reported residual symptomatic complaints.⁶¹ This pattern of results suggests that (1) prolonged symptoms may be a specific result of brain injury (moderated by various factors outside of the purview of this study, including psychological stress and pre-injury personality factors), whereas prolonged cognitive problems may be a general consequence of trauma, or (2) persistent cognitive deficits related to mTBI may be relatively subtle and specific and, hence, difficult to detect when applying cutoff scores to standard neuropsychological tests.

Older age at injury, female sex, and acute report of psychological and post-concussion symptoms were all predictors of symptomatic recovery; socioeconomic status was the only significant predictor of cognitive recovery. Clinicians could make use of this information to identify patients at risk for long-term problems. Elucidating the relationship between these predictors and mTBI outcome is an important topic that warrants future research.

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