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Mild Traumatic Brain Injury: Longitudinal Study of Cognition, Functional Status, and Post-Traumatic Symptoms

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Abstract

More than 75% of traumatic brain injuries (TBIs) seeking medical attention are mild, and outcome in that group is heterogeneous. Until sensitive and valid biomarkers are identified, methods are needed to classify mild TBI into more homogeneous subgroups. Four hundred twenty-one adults with mild TBI were divided into groups based on Glasgow Coma Scale (GCS) 13–15 without computed tomography (CT) abnormalities, GCS 15 with CT abnormalities, and GCS 13–14 with CT abnormalities, and were compared with 120 trauma controls on 1-month and 1-year outcomes. At 1 month post-injury, almost all neuropsychological variables differed significantly among the groups. Compared with trauma controls, the GCS 13–15 CT normal group showed no significant differences on any neuropsychological measure or Glasgow Outcome Scale (GOS). The GCS 15 CT abnormal group performed significantly worse on only a measure of episodic memory and learning (Selective Reminding Recall [SRCL]) and GOS, and the GCS 13–14 CT abnormal group performed significantly worse on most neuropsychological measures and GOS. At 1 year post-injury, except for an isolated difficulty on SRCL in the GCS 13–14 CT abnormal group, no differences were observed on any neuropsychological measures nor on GOS. Mean percent of total post-traumatic symptoms endorsed as new or worse and percent endorsing three or more symptoms differed significantly ($p < 0.001$), with each TBI subgroup reporting significantly more symptoms than the trauma controls at both 1 month and 1 year. In conclusion, this subgrouping improves granularity within mild TBI. While most neuropsychological and functional differences abate by 1 year, reporting three or more post-traumatic symptoms remain for about half of individuals.

Keywords: cognition; control group; Glasgow Outcome Scale; mild traumatic brain injury; post-traumatic symptoms

Introduction

More than 75% of traumatic brain injuries (TBIs) seeking medical attention are mild—that is, have a score of 13 to 15 on the Glasgow Coma Scale (GCS).[1–3] Factors that influence outcome include severity of TBI, time since injury reflecting recovery, and the type of function or outcome of interest. While the effects of moderate-to-severe TBI are relatively well established, those of the milder injuries are less clear.

Until sensitive and valid biomarkers are identified, there is a need for more sensitive methods to classify mild TBI that may assist in future treatment planning in individual cases, and improve the design of clinical trials aimed at minimizing sequelae and preventing secondary complications. The earliest study to address this question of subgrouping mild TBI was a study by Williams and colleagues.[4] They divided the mild TBI subjects into complicated mild (GCS 13–15 with intracranial abnormalities on computed tomography [CT]) and uncomplicated mild (GCS 13–15 with no intracranial abnormalities visible on CT), and examined neuropsychological outcome at 1 to 3 months post-injury and global functional outcome at 6 months post-injury. They found that the complicated mild TBI group had similar performance to those with moderate injuries (GCS 9–12) and had worse outcome than those with uncomplicated mild TBI.

Perhaps a more critical comparison is whether complicated and uncomplicated mild TBI groups show difficulties, compared with non–brain injured subjects, on outcome measures early and late after the injury. Well-controlled studies of mild uncomplicated civilian TBIs[5–7] and sports concussions that allow comparisons with pre-injury baseline[8] have reported good recoveries on cognitive and functional status measures following uncomplicated mild TBI. Based on a meta-analysis of the literature, Belanger and colleagues[9] concluded that cognition in mild TBI subjects recovers by 3 months post-injury.

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Outcome studies of complicated mild TBI have mostly reported worse neuropsychological outcome.[10–12] However, the findings have not been consistent.[13] The studies have differed in sample selection criteria, definition of complicated mild TBI, type of outcome measures used, type of comparison group used, and the timing of the outcome assessment, making it difficult to draw firm conclusions about the relevance of radiological findings to outcome in those with GCS of 13–15.

Findings regarding self-reported post-traumatic symptoms in milder injuries has received a fair amount of attention. Based on review of the literature, the International Collaboration on Mild Traumatic Brain Injury Prognosis Group noted the weaknesses of the existing studies and based on the available information, concluded that post-traumatic symptoms are not specific to mild TBI and that they occur after other injuries, as well. Further, they recommended that such symptoms be assessed in light of pre-morbid psychosocial factors, early emotional reactions to the injury, and litigation, and not be automatically attributed to brain injury per se.[14,15]

The purpose of the present study is to provide a comprehensive examination of the effect of complicated and uncomplicated mild TBI on outcome at 1 month and 12 months after injury in a prospectively followed group of subjects identified on the basis of their initial presentation for medical services following injury. Cognitive abilities, functional status, and post-traumatic symptoms in uncomplicated and complicated mild TBI are compared with a trauma control group at 1 and 12 months post-injury. Initial GCS score, presence of CT abnormalities, and time since injury are examined in relation to these outcomes.

Methods

Subjects with traumatic brain injuries

The subjects of this study participated in one of four prospective longitudinal investigations: Behavioral Outcome,[16] Patient Characteristics,[17] and studies of Dilantin[18,19] and Valproate[20,21] to prevent post-traumatic seizures. Subjects were enrolled from 1980 to 1994. The selection criteria varied across the studies but all subjects met the following minimum entrance criteria: positive evidence of TBI (e.g., any period of loss of consciousness, post-traumatic amnesia of at least 1 h, or CT evidence of an acute brain lesion), injury serious enough to require hospitalization, and willingness to participate in the study. More detailed information about the selection criteria for these studies has been published. [20–22] Some aspects of outcome have been published on subsets of these cases, but only one small study concentrated on mild TBI.[5]

The present study included 463 participants with mild traumatic brain injury represented by an initial post-resuscitation GCS score of 13–15 in the emergency department (ED) who survived and agreed to participate in an assessment at 1 and 12 months after injury. Participants were excluded if they had penetrating brain injury ($n = 18$) or questionable CT abnormalities due to poor scan quality or abnormalities due to a neurologic condition such as stroke or tumor that predated the traumatic brain injury ($n = 24$), resulting in a group of 421 participants. Subjects were followed to 1 year post-injury with an 80% follow-up rate.

General trauma comparison subjects

One hundred twenty comparison subjects were enrolled from the Patient Characteristics Study. These subjects sustained traumatic injury to the body but not to the head. Seventy percent were hospitalized for their injury. They were carefully questioned about disturbance of consciousness or post-traumatic amnesia to exclude people whose TBI had been missed in the routine medical evaluation.[23,24] Demographically, these subjects were similar to the participants with traumatic brain injury. They were evaluated at 1 month and 1 year post-injury, with a 93% follow-up rate.

Measures

Demographics. Demographic variables examined were age at injury, education, and gender. Education was assessed as number of years completed at the time of the injury and as a grouped variable (did not graduate from high school, high school graduate or in high school at the time of the injury, and college graduate).

Other potential confounders. Participants were asked about pre-injury alcohol treatment, and neurologic and psychiatric conditions. Information also was collected on past or current litigation related to the injury and in three studies on planned litigation.

TBI severity. Traumatic brain injury severity was evaluated with the post-resuscitation GCS in the ED.[1] The GCS score measures depth of coma. In addition, all CT scans were reviewed and evaluated to determine if there were abnormal findings. Abnormal findings included any evidence of abnormality impacting the brain, including contusion, hematoma (e.g., subdural, epidural, intracerebral), hemorrhage (e.g., subarachnoid, intraventricular), edema, focal swelling, depressed skull fracture, or midline shift. CT findings of linear skull fracture, basilar skull fracture, or pneumocephalus only were considered normal. At least 60% of the participants with CT abnormalities were seen within 24 h of injury. Fifty-one subjects did not receive a CT scan because medical personnel judged it unnecessary. These subjects were placed in the CT normal group.

Neuropsychological measures. Subjects were administered a comprehensive battery of measures at 1 and 12 months post-injury. The battery included the Trail Making Test Part A and B, Seashore Rhythm Test, and Digit Symbol Subtest of the Wechsler Adult Intelligence Scale to evaluate attention, inhibitory control, flexibility of thinking, and processing speed. The Selective Reminding Test sum of recall (SRCL) assessed episodic memory and learning involving verbal information. Motor performance was evaluated with the Finger Tapping Test for Dominant and Non-dominant hands. Verbal intellectual skills were assessed by the Verbal Intelligence Quotient and visual spatial manipulatory skills by the Performance Intelligence Quotient of the Wechsler Adult Intelligence Scale. A more complete description of these measures can be found in Reitan and Wolfson [25] and other publications.[17,26,27]

Functional status measure. Subjects were administered the Glasgow Outcome Scale (GOS),[28] a global measure of outcome that classifies individuals on a 5-point scale; death, persistent vegetative state, severe disability, moderate disability, and good recovery. The GOS is available for only 364 TBI subjects and 120 trauma comparison subjects at 1 month post-injury because the Behavioral Outcome Study did not collect this information at that time.

Post-traumatic symptom checklist. The Symptom Checklist is a list of 12 symptoms that commonly occur following TBI.[29,30] Subjects endorse a symptom if it is new or worse, compared with pre-injury. Symptoms evaluated included problems with cognition (memory, concentration), physical symptoms (headaches, fatigue, dizziness, blurred vision, sensitivity to light, sensitivity to noise, trouble with sleep), and emotional symptoms (irritability, temper, and anxiety).

Statistical analysis

Demographics, neuropsychological functioning, and functional status measures were examined at 1 month and at 1 year post-injury across four groups of subjects. The groups consisted of trauma

controls and traumatic brain injured subjects with an initial GCS score of 13- 15 without CT abnormalities (uncomplicated mild), and two groups of traumatic brain injured subjects with CT abnormalities—one with initial GCS of 15 and abnormal CT and one with GCS 13–14 and abnormal CT. Demographics and potential confounders were analyzed using chi-squared tests or one-way analysis of variance. Outcome data were analyzed using linear models adjusting for demographics differing among groups with Dunnett's test to compare individual TBI groups with trauma controls. To limit the effect of skewness, Trail Making Test Part B scores greater than 175 sec were recoded to 175 sec. GOS was grouped into two categories, good recovery versus moderate/severe disability.

Comparisons between TBI groups were not examined because the focus was on whether there were deficits, compared with subjects without head injury. Subjects who were too impaired neurologically to be tested on neuropsychological variables were assigned a score equal to 1 worse than the worst observed (1 month: $n=4$ in the GCS 15 CT abnormal group and $n=13$ in the GCS 13–14 CT abnormal group; 1 year: $n=1$ in the GCS 15 CT abnormal group and $n=4$ in the GCS 13–14 CT abnormal group). A significance level of $p<0.001$ is used for the overall tests due to the large number of comparisons, although nominal significance levels at $p<0.01$ and $p<0.05$ also are presented. When the overall test was at least nominally significant, a significance level of 0.01 is used for Dunnett's test.

Results

Table 1 summarizes the demographic, potential confounder, and severity information among the groups. Subjects were on average young males with a high school education. Age was significantly different among the groups ($p<0.001$), with the trauma comparison group significantly younger than the group with GCS 13–14 and abnormal CT ($p<0.001$). There were no other significant differences among the groups on demographic information. The groups were well-matched on prior alcohol treatment and psychiatric disorders. Those in the CT abnormal subgroups had fewer pre-injury neurologic disorders since many of the cases with CT abnormalities came from the seizure prophylaxis studies that excluded patients with most pre-injury neurologic disorders. Litigation was reported by less than a quarter of the participants, but was more common among those with mild TBI with CT abnormalities.

All 1 month and 1 year, outcome variables were analyzed adjusted for age (four groups, <21, 21–40, 41–60, and >60). At 1 month post-injury, all neuropsychological variables differed significantly among the groups ($p\leq0.001$) except Tapping Dominant and Tapping Non-dominant hand, which showed just nominal significance ($p<0.05$; Table 2). Compared with the trauma comparison group, the GCS 13–15 CT normal group showed no significant differences on any neuropsychological measure or GOS. The GCS 15 CT abnormal group performed significantly worse on only SRCL and GOS. The GCS 13–14, CT abnormal group performed significantly worse than the trauma comparison group on each of the neuropsychological measures and GOS.

At 1 month post-injury, mean percent of symptoms endorsed as new or worse differed significantly ($p<0.001$), with each TBI group reporting significantly more symptoms than the trauma comparison group. Further, percentages endorsing three or more symptoms were significantly higher in each of the TBI subgroup than in controls. Compared with the trauma comparison group, each of the TBI subgroups endorsed more cognitive and physical symptoms. There was no difference in endorsement of emotional symptoms.

At 1 year post-injury, the only neuropsychological measure that differed even nominally significantly among the groups ($p<0.01$) was SRCL, the episodic memory measure (Table 3). There were no significant differences between the groups on the GOS. Mean

Table 1. Demographics and Severity Information

	TCs	*CT normal GCS 13–15*	*CT abnormal*		p
			GCS 15	*GCS 13–14*	
n	120	130	133	158	
Mean age (SD)	31 (13.7)	28 (9.8)	35 (14.3)	38 (19)**	<0.001
Male *n* (%)	86 (72)	92 (71)	108 (81)	116 (73)	0.198^
Mean years of education (SD)	12.1 (2.5)	12.4 (2.5)	12.2 (2.2)	12.6 (2.6)	0.371
Education group *n* (%)					0.653^
<High school	31 (26)	27 (21)	38 (29)	33 (22)	
High school–some college (12–15 years)	76 (63)	82 (63)	78 (59)	100 (65)	
College or more (≥16 years)	13 (11)	21 (16)	17 (13)	20 (13)	
Severity *n* (%)					
GCS 13		9 (7)		60 (38)	
GCS 14		25 (19)		98 (62)	
GCS 15		96 (74)	133 (100)		
Potential confounders *n* (%)					
Alcohol treatment	32 (27)	34 (26)	33 (25)	34 (22)	0.839
Psychiatric	12 (10)	14 (11)	6 (4)	10 (7)	0.196
CNS disorder or prior TBI	34 (28)	27 (21)	10 (8)**	11 (7)**	<0.001
Involved with litigation or planning to be involved n (%)				**	<0.001
No	96 (80)	74 (57)	69 (52)	67 (42)	
Yes	15 (12)	19 (15)	26 (20)	40 (25)	
Missing	9 (8)	37 (28)	38 (29)	51 (32)	

Superscripts are Dunnett's *post hoc* tests. *$p<0.01$, **$p<0.001$.

^chi-square test

CT, computed tomography; TCs, trauma comparison subjects; GCS, Glasgow Coma Scale; SD, standard deviation; CNS, central nervous system; TBI, traumatic brain injury.

Table 2. 1 Month Outcome

	TCs	CT normal GCS 13–15	CT abnormal GCS 15	CT abnormal GCS 13–14	p
Neuropsychological measures mean (SD)					
n	120	130	120	144	
VIQ	102 (14)	103 (14)	100 (18)	94 (23)*	0.001
PIQ	104 (12)	105 (14)	101 (14)	94 (18)**	<0.001
Digit Symbol	10 (3)	10 (3)	8 (3)	7 (4)**	<0.001
SRCL	86 (10)	83 (11)	77 (17)**	69 (23)**	<0.001
Trails A	28 (15)	28 (13)	33 (19)	42 (28)**	0.001
Trails B†	73 (36)	69 (29)	84 (42)	100 (48)**	<0.001
Rhythm	26 (3)	26 (3)	25 (5)	22 (7)**	<0.001
Tapping D	52 (7)	51 (7)	50 (10)	46 (13)*	0.017
Tapping ND	48 (7)	48 (6)	45 (11)	42 (16)	0.029
Glasgow Outcome Scale *n* (%)			**	**	<0.001
Moderate/severe	17 (14)	24 (24)	64 (52)	97 (69)	
Good	103 (86)	78 (76)	58 (48)	43 (31)	
Mean % of symptoms endorsed new or worse (SD)					
n	119	128	119	130	
Physical (7)	0.25 (0.22)	0.39 (0.26)**	0.46 (0.27)**	0.44 (0.28)**	<0.001
Cognitive (2)	0.18 (0.32)	0.39 (0.42)**	0.48 (0.45)**	0.51 (0.43)**	<0.001
Emotional (3)	0.30 (0.32)	0.32 (0.35)	0.27 (0.30)	0.28 (0.34)	0.775
Total (12)	0.25 (0.21)	0.37 (0.24)**	0.41 (0.25)**	0.41 (0.26)**	<0.001
≥3 symptoms *n* (%)	63 (53)	89 (70)*	90 (76)**	96 (74)**	0.001

The *p* values are adjusted for age. Superscripts are Dunnett's *post hoc* tests. *$p < 0.01$, **$p < 0.001$.

†Trail Making Test Part B scores >175 sec were recoded to 175 sec.

CT, computed tomography; TCs, trauma comparison subjects; GCS, Glasgow Coma Scale; SD, standard deviation; VIQ, Verbal Intelligence Quotient; PIQ, Performance Intelligence Quotient; SRCL, Selective Reminding Test Sum of Recall; Trails A and Trails B, Trail Making Test Part A and B; Rhythm, Seashore Rhythm Test; Tapping D and Tapping ND, Finger Tapping Test for Dominant and Non-Dominant hands.

Table 3. 1 Year Outcomes

	TCs	CT normal GCS 13–15	CT abnormal GCS 15	CT abnormal GCS 13–14	p
Neuropsychological measures mean (SD)					
n	109	114	96	114	
VIQ	104 (14)	105 (14)	105 (14)	104 (17)	0.572
PIQ	109 (13)	110 (14)	110 (13)	108 (14)	0.645
Digit Symbol	10 (3)	11 (3)	10 (3)	9 (4)	0.142
SRCL	87 (11)	86 (11)	82 (12)	80 (16)*	0.003
Trails A	28 (16)	24 (9)	26 (14)	33 (22)	0.108
Trails B†	71 (40)	67 (32)	68 (34)	79 (43)	0.590
Rhythm	26 (4)	26 (3)	26 (4)	24 (6)	0.285
Tapping D	52 (7)	51 (6)	51 (8)	49 (11)	0.206
Tapping ND	48 (7)	48 (6)	47 (10)	46 (11)	0.382
Glasgow Outcome Scale *n* (%)					0.125
Moderate/severe	9 (8)	8 (7)	15 (15)	21 (18)	
Good	103 (92)	113 (93)	84 (85)	97 (82)	
Mean % of symptoms endorsed new or worse (SD)					
n	111	121	100	115	
Physical (7)	0.15 (0.22)	0.24 (0.27)	0.28 (0.26)*	0.23 (0.25)	0.003
Cognitive (2)	0.17 (0.33)	0.32 (0.42)*	0.42 (0.44)**	0.41 (0.40)**	<0.001
Emotional (3)	0.16 (0.28)	0.26 (0.36)	0.30 (0.36)*	0.30 (0.38)*	0.003
Total (12)	0.15 (0.21)	0.26 (0.28)*	0.30 (0.27)**	0.28 (0.26)**	<0.001
≥3 symptoms *n* (%)	27 (24)	55 (46)**	54 (54)**	53 (47)**	<0.001

The *p* values are adjusted for age. Superscripts are Dunnett's *post hoc* tests. *$p < 0.01$, **$p < 0.001$;

*Trail Making Test Part B scores >175 seconds were recoded to 175 seconds

CT, computed tomography; TCs, trauma comparison subjects; GCS, Glasgow Coma Scale; SD, standard deviation; VIQ, Verbal Intelligence Quotient; PIQ, Performance Intelligence Quotient; SRCL, Selective Reminding Test Sum of Recall; Trails A and Trails B, Trail Making Test Part A and B; Rhythm, Seashore Rhythm Test; Tapping D and Tapping ND, Finger Tapping Test for Dominant and Non-Dominant hands.

percent of total symptoms endorsed as new or worse in each of the TBI subgroups continued to be significantly higher than the control group, as well as percentage endorsing three or more symptoms. Endorsement of cognitive symptoms also differed significantly while physical and emotional symptom differences were nominally significant ($p = 0.003$).

Questions are often raised about whether potential gains from litigation drive the results for self-reported TBI outcomes, such as symptoms. Three of the four studies included asked about involvement with past or current litigation and whether the participants were planning to sue about their injury. Table 4 presents symptom findings from participants with no past, current, or planned litigation. Results for trauma controls and the two milder subgroups of TBI are almost identical to the overall results. Non-litigants with GCS 13–14 and CT abnormalities report slightly fewer symptoms than the overall group and with the smaller sample size, fewer differences were significant for this subgroup. Note that litigation involvement was highest for this group, with 40/158 (25%) involved in litigation, compared with 15/120 (12%), 19/130 (15%), and 26/133 (20%) for the trauma control, GCS 13–15 CT normal, and GCS 15 CT abnormal groups, respectively.

Discussion

The results indicate that mild TBI is associated with a broad range of difficulties However, the severity and the pervasiveness of these difficulties vary as a function of initial GCS (15 vs. 13–14), presence of CT abnormalities, time since injury (1 vs. 12 months post-injury), and the type of outcome in question. The subgrouping of mild TBI used here provides more granularity with meaningful relationship to outcome. Consistent with prior literature, compared with controls, those with GCS 13- 15 and no CT abnormalities do not show cognitive deficits or overall functional limitations on the GOS at 1 month post-injury.[6,8,9] The complicated mild TBI group with GCS 15 and CT abnormalities shows selective difficulties in episodic memory and functional limitations on the GOS. Diffuse difficulties on the majority of the cognitive measures and the GOS are seen in those with complicated mild TBI with GCS 13- 14 at 1 month after injury. Interestingly, all three mild TBI groups show more post-traumatic symptoms as reflected in the mean percent of symptoms endorsed and percent with three or more symptoms, compared with controls. While about 50% of the controls report three or more symptoms, the rates in the TBI subgroups are about 75%. At 1 year, the two milder TBI groups show no cognitive deficits or functional limitations. The group with GCS 13- 14 and CT abnormalities show a trend toward episodic memory difficulties only. No differences are apparent in functional limitations as measured by the GOS at 1 year but post-traumatic symptoms continue to be reported by all three subgroups of mild TBI.

The percent with three or more symptoms at 1 year has decreased from about 75% to about 50% in the TBI subgroups and from about 50% to about 25% for the controls. At 1 month after injury, all three subgroups reported more physical and cognitive problems but not emotional symptoms, compared with controls. At 1 year, emotional complaints emerged in addition to physical and cognitive difficulties. This was due to decreased report of emotional symptoms from 1 month to 12 months in the trauma controls but not in those with TBI. It is important to note that symptom endorsement is considerably higher in the TBI subgroups than in the trauma control subjects at both 1 and 12 months after injury, in spite of comparability of the groups with respect to variables associated with symptom reporting, such as pre-existing alcohol and psychiatric conditions, and the small demographic differences which were accounted for in the analysis.[30]

The results clearly indicate that the difficulties of those with complicated mild TBI, in particular those with CT abnormalities and GCS 13–14, are broad and substantial soon after injury. While by 1 year they show considerable improvement, it is difficult to know the timing of this recovery. These results might shed some light regarding the complexity of determining TBI effects in this severity range and suggest some reasons for the inconsistent findings in the literature. Soon after injury, the pervasiveness and the magnitude of the difficulties in those with CT abnormalities are sufficiently large to be demonstrated with a moderate sample size.

Table 4. New or Worse Symptoms for Those Not Involved with Litigation and/or Planning To Be Involved in Litigation[†]

		CT normal	*CT abnormal*		
1 Month	*TC*	*GCS 13–15*	*GCS 15*	*GCS 13–14*	
n	*96*	*74*	*61*	*56*	p
Mean % of symptoms endorsed new or worse (SD)					
Physical (7)	0.23 (0.22)	0.37 (0.25)**	0.43 (0.27)**	0.36 (0.24)*	<0.001
Cognitive (2)	0.17 (0.31)	0.40 (0.42)**	0.46 (0.43)**	0.54 (0.42)**	<0.001
Emotional (3)	0.30 (0.32)	0.28 (0.34)	0.25 (0.30)	0.22 (0.30)	0.625
Total (12)	0.24 (0.21)	0.35 (0.23)*	0.39 (0.24)**	0.35 (0.24)*	<0.001
≥3 symptoms *n* (%)	48 (50)	53 (72)*	44 (72)*	35 (64)	0.011
1 Year					
n	95	74	68	64	
Mean % of symptoms endorsed new or worse (SD)					
Physical (7)	0.14 (0.21)	0.22 (0.26)	0.28 (0.28)**	0.18 (0.21)	0.003
Cognitive (2)	0.18 (0.34)	0.34 (0.44)	0.41 (0.45)**	0.35 (0.37)	0.001
Emotional (3)	0.15 (0.29)	0.22 (0.31)	0.28 (0.36)	0.19 (0.31)	0.051
Total (12)	0.15 (0.21)	0.24 (0.26)	0.30 (0.28)**	0.21 (0.23)	0.001
≥3 symptoms *n* (%)	23 (24)	32 (43)*	35 (52)**	24 (38)	0.003

[†]Based on three studies since one study did not ask subjects if they were planning to be involved in litigation.
The *p* values age-adjusted. Superscripts are Dunnett's *post hoc* tests. *$p < 0.01$, **$p < 0.001$.
CT, computed tomography; TCs, trauma comparison subjects; GCS, Glasgow Coma Scale; SD, standard deviation.

With recovery over a year period, the residual cognitive difficulties are small enough that variations in study methods can lead to effects that may mimic or mask injury effects.[31] Consistent with the findings from sports concussions,[8] where pre-season testing allows within-subject as well as between-group comparisons, no neuropsychological deficits were found in those without CT abnormalities even at 1 month. This is also consistent with the findings of Rabinowitz and colleagues[6] for comparison with orthopedic controls. When looking at a mixed group of mild TBI, the fraction with GCS 15, the fraction with CT abnormalities, and the type of CT abnormalities are likely to influence the extent of neuropsychological difficulties, as does the time after injury, the type of comparison group used, and the specific domains of function examined. To sort out the effects, large studies, perhaps with several different groups without TBI as comparators, are needed, as is careful attention to possible selection biases.

An interesting, but puzzling, finding is the apparent recovery in those with mild TBI on formal cognitive and functional measures but not on post-traumatic symptoms. The uniformity of the complaints across the injury severity groups is puzzling, as well. The reason for this is not readily clear. One potential explanation is that symptom reporting represents within-individual change (i.e., comparing present difficulties with those of pre-injury) and thus likely more sensitive to injury-related changes or reaction to the changes. In contrast, performance-based cognitive measures, as sensitive as they are to injury severity, are generally analyzed in terms of between-group differences and thus likely to be less sensitive. However, studies based on within-individual changes in concussed athletes tested on performance measures prior to the season also find no cognitive effects after the first few weeks.[8]

Our results pertaining to the magnitude of symptom reporting both in the subacute and chronic time periods are consistent with other more recent reports.[32,33] Kraus and colleagues[32] used a dual cohort to compare post-traumatic symptoms in mild TBI patients versus non-TBI subjects seen in five collaborating EDs. Outcomes examined in addition to post-traumatic symptoms included health services received and social disruptions in everyday life (e.g., employment, driving) at 3 and 6 months. Symptom reports on the Rivermead Post-Concussion Symptoms Questionnaire[34] were greater in those with mild TBI at both 3 and 6 months than in the non-TBI group. Health services used and indicators of social disruptions also were more frequent in those with mild TBI. In a longitudinal, population based study in New Zealand, nearly 50% of the sample reported four or more post-traumatic symptoms as measured by the Rivermead at 1 year post- mild TBI.[33] Findings of a TBI effect on reported symptoms are not universal however. For example, Meares and colleagues[35,36] found comparable rates of symptom endorsement in cases with mild TBI without CT abnormalities and trauma controls at 5 days and 3 months post-injury.

Lack of sensitivity of post-traumatic symptom reporting to injury severity and characteristics is potentially due to the insensitivity of our biomarkers (i.e., GCS within the 13- 15 range and any brain CT abnormality). Recent advances in high-resolution neuroimaging techniques, including methods such as diffusion tensor imaging, voxel-based morphometry, functional MRI, and magnetic resonance spectroscopy, may allow better and more detailed views of microscopic changes in the brain following mild TBI. One of the primary aims of the Transforming Research and Clinical Knowledge in TBI study is to improve classification methods, determine the clinical relevance of imaging findings, and identify biomarkers.[37] These methods may substantially decrease heterogeneity of outcome from mild TBI in the future but to date their use has been limited. More research is needed to understand their contributions and clinical relevance,[38] especially with respect to symptoms.

Undoubtedly, outcome following TBI is related not only to the effects of the injury and its severity but to the characteristics of the persons injured. The World Health Organization (WHO) Task Force in 2004 and 2014 concluded that post-traumatic symptoms are not specific or diagnostic of mild TBI and that poorer recovery is likely to be associated with pre-morbid mental and physical health and more injury-related stress.[14,15] The work of Meares and colleagues[36] supports the WHO taskforce conclusions. In the current study the trauma controls and the TBI group were comparable with respect to pre-existing alcohol and psychiatric conditions and the small demographic differences were accounted for in the analysis. While pre-existing neurologic conditions were more common in the trauma controls and those without CT abnormalities, pre-existing neurologic conditions are not related to symptom endorsement.[30] Potential gain from litigation also is often mentioned as a possible reason for report of symptoms long after the TBI. However, as seen in Table 4, those not involved in litigation also are reporting more symptoms at both 1 month and 1 year, compared with controls. Regardless of the exact source of post- traumatic symptoms, patients with all levels of mild TBI continue to experience and report higher levels of post-traumatic symptoms through at least 1 year after injury.

The results of this study and those available in the literature have important clinical implications. First, although symptoms are not specific to mild TBI, differences in level of symptom reporting can be found between mild TBI and trauma controls even 1 year post-injury and it is possible to identify those at high risk for symptoms long after the injury.[30] Early identification of patients at risk (targeting modifiable risk factors as recommended by WHO review) and providing them with education and appropriate interventions could prevent long-term sequelae. In a randomized study we conducted in people with mild TBI recruited from the ED, five sessions of a treatment focusing on symptoms and their interference in everyday activities, delivered by phone, was effective in reducing symptoms and their interference in everyday activities.[39]

In conclusion, the present results raise a cautionary note regarding the commonly held belief that mild TBI is rarely associated with post-traumatic symptoms or problems after about 3 months post-injury. While factors other than the effects of TBI can contribute to symptom reporting (e.g., secondary gains, pre-existing emotional problems, demographics, stress reactions to the injury or injury event), the present results indicate that even at 1 year post-injury, mild TBI is associated with three or more symptoms in about 25% of cases beyond the rate seen in those with similar characteristics with non-head injuries. This finding suggests that the commonly held belief that three or more symptoms associated with mild TBI after about three months post-injury are rare needs to be re-evaluated.

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