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Duration of Post-Traumatic Amnesia Predicts Neuropsychological and Global Outcome in Complicated Mild Traumatic Brain Injury

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Abstract

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Conflicts of Interest: None

Objectives—Examine the effects of post-traumatic amnesia (PTA) duration on neuropsychological and global recovery from 1 to 6 months after complicated mild traumatic brain injury (cmTBI).

Participants—330 persons with cmTBI defined as Glasgow Coma Scale score of 13–15 in Emergency Department, with well-defined abnormalities on neuroimaging.

Methods—Enrollment within 24 hours of injury with follow-up at 1, 3, and 6 months.

Measures—Glasgow Outcome Scale-Extended, California Verbal Learning Test II, Controlled Oral Word Association Test. Duration of PTA was retrospectively measured with structured interview at 30 days post injury.

Results—Despite all having a Glasgow Coma Score of 13–15, a quarter of the sample had a PTA duration of greater than 7 days; half had PTA of 1–7 days. Both cognitive performance and GOS-E outcomes were strongly associated with time since injury and PTA duration, with those with PTA> 1 week showing residual moderate disability at 6-month assessment.

Conclusions—Findings reinforce importance of careful measurement of duration of PTA to refine outcome prediction and allocation of resources to those with cmTBI. Future research would benefit from standardization in CT criteria and use of severity indices beyond GCS to characterize cmTBI.

Keywords

traumatic brain injury; cognitive function; outcome measures; post-traumatic amnesia

INTRODUCTION

Based on estimates from the Centers for Disease Control and Prevention, there are more than one million emergency department (ED) visits for head injury each year in the US, with approximately 300,000 resulting hospitalizations.[1] The vast majority are so-called mild traumatic brain injuries (mTBI), which are at least tenfold more prevalent than more severe injuries.[2] While the likelihood of favorable recovery from mTBI within a few months is high,[3–5] a proportion of patients experience long-standing cognitive, emotional, and/ or somatic symptoms that interfere with work, school, and/or family responsibilities.[6] Thus, it is likely that the societal burden resulting from mTBI is at least equivalent to that resulting from severe TBI, given the considerably higher prevalence of the former.[2, 6]

One common definition of mTBI, put forth by the American Congress of Rehabilitation Medicine (ACRM) in 1993, specifies a Glasgow Coma Scale (GCS) score of 13–15 in the ED and loss of consciousness (LOC) ≤ 30 minutes.[7] While some loss or alteration of consciousness is necessary to signal a TBI by this definition, post-traumatic amnesia (PTA) must not exceed 24 hours for the TBI to be considered mild. However, it has become apparent that there are clinically important variations within the group of injuries that result in GCS 13–15, which may help to explain the diverse outcomes experienced by this group of patients. In 1990, Williams et al. used the term “complicated mild” TBI (cmTBI) to refer to cases where GCS is 13–15 but there are CT abnormalities such as contusions or other trauma-related brain lesions.[8] Although the cmTBI patients in this sample did not differ

from mTBI patients on LOC or PTA duration, their 6-month outcomes were worse. This led the authors to suggest that an intracranial lesion should place such patients into the "moderate" severity category, or at least into a different category from those with uncomplicated mTBI. More recent work has suggested that as many as 30–50% of patients with TBI presenting to the ED with GCS 13–15 may have trauma-related intracranial pathology visible on CT.[6, 9, 10]

The research comparing outcomes of mTBI to those of cmTBI has been equivocal; it is difficult to synthesize findings due to the generally small samples and the differences among studies in how cmTBI was defined, the measures used (neuropsychological tests, symptom checklists, global outcome measures, etc.), and the intervals at which outcomes were measured, ranging from 1 week to 1 year. Several prospective[9–11] and retrospective[4] studies have reported no or very small differences between cmTBI and mTBI in neuropsychological test performance, return to work rates, or global outcomes. Others have found worse outcomes for cmTBI on global outcome measures[12] or neuropsychological tests.[13] Two reports from the ongoing TRACK-TBI project have reported worse global outcomes for cmTBI compared to mTBI at 3 months, but differences had attenuated by 6 months.[6, 14]

While all previous reports on cmTBI outcomes have used GCS 13–15 and positive CT findings as defining characteristics, there is variation in the literature as to the inclusion of other TBI severity indices, notably LOC (also known as Time to Follow Commands or TFC) and PTA duration. A few studies have used the ACRM criteria for both mTBI and cmTBI cases, meaning that LOC and PTA are brief for both groups and the only difference is the presence of visible brain pathology.[10, 14] Most others have focused on GCS and CT findings to define the groups, and have not reported the other indices. LOC is difficult to measure accurately in these patients since by definition, they are conscious in the ED, and LOC duration would need to be determined by accounts of field rescue staff or other witnesses, all of whom may be unavailable. However, PTA duration has been shown to vary widely in patients who present to the ED with GCS 13–15, in many cases lasting well beyond the 24 hours stipulated in the ACRM definition of mTBI.[15] PTA duration is considered the most sensitive index of the degree of diffuse axonal injury (DAI)[16] and can be measured prospectively, using serial testing, or retrospectively using structured interviewing to estimate the length of the gap in recall following the TBI. But a recent report pointed out that PTA is not routinely assessed in the ED, and that many patients who are "fully oriented" (GCS = 15) are found still to be in PTA when tested with more sensitive measures of anterograde memory.[17] Thus, it is possible that some of the variable results in the cmTBI literature could be explained by differing amounts of DAI within the range insufficient to cause deep or prolonged unconsciousness, which could nonetheless combine with focal injuries to adversely affect outcomes.

A more comprehensive understanding of the determinants of cmTBI outcome is important because of its prevalence among so-called mild brain injuries, because of the current difficulty in predicting outcome for patients with this clinical presentation, and because some people with cmTBI may require more extensive rehabilitation services than are typically offered to them. In the current study, we performed a secondary analysis on a large sample of persons with cmTBI who had been enrolled in the 8-center COBRIT

neuroprotection trial.[18, 19] Advantages of this dataset included capture of both neuropsychological and global outcomes at 3 time points within the first 6 months after injury; rigorous characterization of neuroimaging results used to diagnose cmTBI; and standardized assessment of PTA duration. We examined the trajectory of recovery in 2 important cognitive domains as well as global outcome, hypothesizing that longer PTA would be associated with worse outcomes after controlling for other variables known to affect TBI outcome.

METHOD

Participants

Participants were a sub-group of those identified as having cmTBI in the COBRIT study, an 8-center, placebo-controlled Phase III trial examining the neuroprotective effects of citicoline administered within 24 hours of injury.[18, 19] COBRIT inclusion criteria were: non-penetrating TBI of at least complicated mild severity (defined below); aged 18 (19 in Alabama) to 70; sufficiently fluent in English to complete neuropsychological testing; and able to provide consent by self or proxy within 24 hours of injury. Patients were excluded from COBRIT if they were unlikely to survive to follow-up due either to the TBI or associated injuries, pregnant, incarcerated, or had a history of significant psychiatric illness (e.g., schizophrenia, suicide attempt in the past year) or neurological disorder (e.g., previous TBI with hospitalization, stroke, dementia).

For the current study, we selected patients from the inert-placebo arm of COBRIT who had experienced cmTBI. Citicoline-treated participants were excluded because although the parent trial showed no neuroprotective benefit of citicoline, there was some indication that cmTBI patients did worse in the active drug condition.[19] Thus, inclusion criteria for the present study were: assignment to the placebo arm of the trial; GCS of 13–15 in the ED; and evidence of one or more CT scan abnormalities at the time of study randomization, which took place within 24 hours of injury. A scan abnormality was defined as any of the following: ≥10 mm total diameter of all intraparenchymal hemorrhages; acute extra-axial hematoma thickness ≥5 mm; subarachnoid hemorrhage visible on at least two contiguous 5-mm slices or at least three contiguous 3-mm slices; intraventricular hemorrhage present on two slices; or midline shift ≥5 mm. These criteria were established by a study team that included neurosurgeons, neurologists, and physiatrists, with input from neuroradiologists, so as to avoid enrolling patients with equivocal TBI into the COBRIT study[19] and to minimize inter-observer variation across sites.[20] All CT scans were read by neuroradiologists at the participating sites who had received training in the COBRIT study protocol. The scans were subsequently reviewed by a panel of neurosurgeons and neurologists associated with the study to ensure adherence to inclusion guidelines.

Measures

Outcome was assessed at 30 (+/− 7), 90 (+/− 10), and 180 (+/− 10) days post injury with a battery that included the following measures.

Extended Glasgow Outcome Scale(GOS-E):[21]—The GOS-E consists of eight levels of functional recovery, ranging from Dead (0) to Good Recovery (8). Items comprising the scale focus on the capacity to care for oneself and function in the community, as well as effects of persistent TBI symptoms interfering with function. The GOS-E is commonly employed to measure functional recovery following TBI including cmTBI[6, 12, 14] and has demonstrated good test-retest reliability (r = .92).[22]

California Verbal Learning Test-II:[23]—The CVLT-II requires the individual to learn a list of 16 words over 5 trials. For this study, we used the T score for the sum of the 5 learning trials. The CVLT-II and its predecessor (CVLT) have proven to be sensitive measures of memory disorder after TBI,[24, 25] and the revised form has good test-retest reliability (r = .82). [23] To minimize practice effects, the standard form of the CVLT-II was administered at the 30- and 180-day intervals and the alternate version at the 90-day interval.

Controlled Oral Word Association Test (COWAT):[26]—In this test of verbal generativity, subjects are allowed 60 seconds to say as many words as possible that begin with a specific letter of the alphabet. Verbal fluency is commonly impaired following TBI, probably reflecting executive dysfunction more than linguistic impairment.[27, 28] In this study, the total number of words produced was analyzed after correction for age and education. The PRW version of the COWAT was administered at the 30-day interval and the CFL form at 90 and 180 days. These forms have been shown to be equivalent,[29] and the COWAT overall has adequate test-retest reliability (r = .74).[30]

Post-Traumatic Amnesia—PTA duration was measured retrospectively using a 5–10-minute structured interview in which a trained data collector assisted the participant in estimating the number of days or, if <1 day, the number of hours, between the TBI and resumption of continuous recall of events. The interview took place at the first follow-up assessment at which the participant achieved a score of greater than 75 on the Galveston Orientation and Amnesia Test (GOAT).[31] In nearly all cases of cmTBI, this was 30 days post injury. This interview has been used in prior studies of TBI.[32, 33] It has demonstrated construct validity in that PTA intervals based on the interview were shown to be monotonically related to psychiatric outcomes, with longer PTA predicting worse outcomes in the same cohort as studied in this investigation.[34] In another study, PTA durations ascertained using the interview correlated well with PTA prospectively measured using serial orientation testing, even in patients interviewed months or years after TBI (n = 35; r = 0.68, p<.001).[35] For this study we collapsed PTA durations into 3 levels: <24 hours (i.e., comparable to ACRM criterion for mTBI);[7] 1–7 days; and >7 days.

Procedures

The institutional review boards (IRB) of all participating sites approved the protocol and either the patients or their legally authorized representatives (LAR) provided written informed consent according to the local IRB rules for proxy consent. If an LAR consented originally, the participant directly consented for continued involvement upon recovery of decision-making capacity. Data collection was performed according to a manualized procedure. All data were double-scored at each site, and monthly teleconferences were held

among data collectors and investigators at each site to address questions of test administration, scoring, or coding. A Data Coordinating Center at Columbia University oversaw the trial, cleansed the data, and performed preliminary analyses. Upon completion of the COBRIT trial, de-identified data were provided to all participating sites.

Data Analysis

Chi-square tests were used to examine the associations of PTA with demographic variables and mechanism of injury. For the analyses of neuropsychological and global outcomes by PTA group, all outcome measures in the battery were treated as continuous variables. Predictors were all categorical. Descriptive analyses consisted of frequencies, means, and plots. Separate linear mixed effects models were used to evaluate each of the longitudinal outcomes. Preliminary model fitting evaluated demographic variables and mechanism of injury as predictors of each individual outcome. Potential confounding variables were selected based on best fit as assessed by Akaike's information criteria.[36] Next, PTA group was added to each of the models. Contrasts within the linear mixed effects analysis compared the PTA groups and the change between consecutive assessments. Participants were excluded from the analysis if they were missing all 3 assessments, racial/ethnic group, education, or PTA duration. As is common in studies of TBI, participants who could not perform the tests due to cognitive difficulties associated with the TBI were assigned 1 raw score unit worse than the lowest observed score on the CVLT-II and COWAT.[37, 38] Ten participants could not perform either neuropsychological measure at 30 days, and one could not perform COWAT. One participant could not perform either measure at 90 days due to cognitive difficulties. One participant died before the 180-day evaluation. His data were included until death, and then assigned a value 1 lower than that assigned to those too cognitively impaired to take the CVLT-II and COWAT. This was done because unlike the GOS-E, the neuropsychological measures do not have a score indicating death, and we preferred to maintain this participant's data on all measures via use of arbitrarily low scores.

RESULTS

The COBRIT study included 401 participants with cmTBI who were randomly assigned to the placebo group. Of these, 53 individuals had no outcome assessments; 6 were missing race/ ethnicity or education data; and 12 had unknown PTA, leaving a sample of 330. Analyses were separately conducted for GOS-E (n=330), COWAT (n=328) and CVLT-II (n=317).

Demographics and mechanism of injury for the PTA groups are summarized in Table 1. It is apparent that there was a wide range of PTA duration in this sample, despite all participants having an ED GCS of 13–15. Only 25% of the sample had PTA < 1 day, while 47% had PTA of 1–7 days and 28% reported > 7 days. Not surprisingly, participants involved in motor vehicle collisions were significantly more likely to have longer PTA durations than those injured by falls or assault. PTA duration was not significantly associated with age, sex, race/ ethnicity, or education.

Figure 1 displays the 3 outcome measures for each PTA group at each outcome assessment. It may be seen that the shortest PTA group has the highest, and the longest PTA group the

lowest, mean score at each time point on all 3 measures. For the GOS-E, at 1 month after injury, participants with PTA > 7 days were functioning, on average, in the moderate to severe disability range, while those experiencing briefer PTA duration were mostly in the moderate disability category. The shorter PTA groups improved to the good recovery range by 6 months post-injury, while the longest duration PTA group had only reached the upper moderate disability range on average. Clinically, upper moderate disability means that there are restrictions in the capacity to work at the premorbid level, and/ or limitations in social/ leisure activity participation, and/ or frequent disruption in family or friendship relationships attributable to the injury.

The pattern was similar overall for the neuropsychological measures. For the CVLT-II, total learning performance for the > 7 days PTA group fell within the borderline impaired range at 30 days on average, and scores increased to the average range by 6 months post-injury. Those with shorter duration PTA fell within the average range even at 1 month, but still increased over the next two administrations; the PTA <1 day group reached the high average range at 6 months after injury. Finally, on the COWAT, the long duration PTA group exhibited low average performance at 1 month that increased to average performance in subsequent administrations. The shorter PTA groups demonstrated average performance on the COWAT at all intervals.

Post-hoc rank order correlations among the 3 outcome measures were calculated in an attempt to shed light on the apparent discrepancy between cognitive and functional recovery, particularly in the group with the longest PTA duration. At the 180-day evaluation, CVLT-II and COWAT scores were moderately intercorrelated (rho = .42, p<.001). GOS-E scores were more weakly correlated with either cognitive measure (rho = .22 for CVLT-II, .15 for COWAT), although both were significant at p<.01 given the large sample size.

The initial mixed models indicated that age and race were potential predictors for GOS-E; age, sex, and education were potential confounders for COWAT; and age, race, and education were potential confounders for CVLT-II. Addition of PTA as a predictor significantly improved all three models. Table 2 gives the coefficients for the three models. Each outcome was strongly related to both time of observation and PTA group (each p <0.002). Contrasts are shown in Table 3. Compared to 30 days, scores improved significantly by 90 days and again from 90 to 180 days for each measure. Those with PTA >7 days had significantly worse outcome than either those with PTA <1 day or PTA 1–7 days on each measure (each p <0.001). Those with PTA <1 day had significantly better outcome than those with 1–7 days of PTA on GOS-E and CVLT-II, but the differences were less robust.

DISCUSSION

In a large, prospectively followed cohort of persons with cmTBI, all with GCS 13–15 in the ED and strictly defined CT scan abnormality, we observed a wide range of PTA duration that was strongly related to neuropsychological and global outcome within the first 6 months of injury. Only a quarter of the sample had resolution of PTA within 24 hours, the duration typically associated with mild TBI.[7] Nearly half experienced PTA of 1–7 days, with the

remaining 28% reporting more than a week of PTA. That longer PTA duration was associated with worse performance on tests of memory and verbal fluency, in addition to worse global outcome, suggests that PTA is an important measure in cases of cmTBI, just as in uncomplicated mild TBI.[15] From a research perspective, including PTA along with GCS and neuroimaging may help to reduce the discrepancies among study findings as well as helping us to understand the relative contributions of diffuse and focal brain injury to ultimate outcome. Clinically, ascertaining PTA in addition to GCS and CT findings should assist both in predicting recovery and in recommending rehabilitation services in cases of cmTBI. A brief retrospective interview such as the one described here could be administered shortly after the resolution of PTA or at a clinic follow-up and is substantially less labor-intensive than prospective tracking of anterograde learning ability, particularly in a busy ED or acute hospital setting. While PTA duration is potentially useful as a predictor in all cases of TBI, it is especially important to ascertain when the mechanism of injury is motor vehicle collision, as our data confirm that prolonged PTA (and presumably, more DAI) is more likely with this cause of TBI.

It is important to note that for all PTA duration groups, we observed continued improvement on all measures between all pairs of time points used in this investigation (1, 3, and 6 months). This attests to the sensitivity of the measures selected as well as the need for continued follow-up of cmTBI patients. Specifically, it would be useful for future research, as well as clinical services, to follow persons with cmTBI for longer than 6 months to capture the full recovery trajectory. This is particularly important for those with longer PTA, as the average participant with duration >1 week still reported limitations in social and/ or vocational functioning at 6 months after injury.

Regarding this last point, one limitation of this study is that we lack detailed information that might help to explain the residual disability of the group with the longest PTA. Although correlations between GOS-E and cognitive scores at 6 months were statistically significant, they were small in magnitude. In TBI it is not unusual to find normal psychometric test performance in the face of greater difficulty in less structured, real-world situations.[39] Other unmeasured factors could also be contributing to the GOS-E outcomes; these could include persistent post-concussive symptoms such as headache or insomnia, post-traumatic stress, irritability, or other emotional dysfunction; or cognitive dysfunction that could have been picked up by the use of more demanding measures, e.g., of information-processing speed.

Our findings may be difficult to compare to previous reports on cmTBI due to differences in the definition of the samples, especially with regard to the CT abnormalities. Our sample may have been skewed toward more serious cases of cmTBI due to the stringent CT scan criteria we employed. For example, a minor subarachnoid hemorrhage would have excluded a patient from the COBRIT study but perhaps not from other investigations of this population. However, many studies of cmTBI do not specify the CT abnormalities that qualify a patient for inclusion. In future, we recommend clear and precise definitions of CT criteria for cmTBI to improve the cross-walk between studies. To the extent that studies may be compared, our findings generally comport with previous work showing scores in the normal range at 3–6 months after cmTBI with respect to CVLT-II total learning[40] and

COWAT performance.[8] However, as documented in this study, those with PTA >7 days achieve these results more slowly and even at 6 months are not performing as well as those with shorter PTA.

Other than those noted above, several limitations of this study must be acknowledged. The study was limited to persons with cmTBI and lacked any sort of control or comparison group. A comparison group of patients with uncomplicated mTBI, as in the work of Yuh and colleagues,[14] would have allowed us to estimate the effects of focal cerebral injury; however, unless the ACRM definition had been disregarded and PTA duration allowed to vary, this comparison would have offered little information as to the effects of diffuse injury that may prolong alteration of consciousness. An uninjured control group may have helped to assess the effects of serial testing on the cognitive measures; however, practice effects were minimized by use of equivalent alternate forms. Finally, participants in the current study were enrolled in the placebo arm of a treatment study, and there may have been an expectation of improvement that affected performance.

In conclusion, these findings highlight the importance of assessing PTA duration to refine outcome predictions and rehabilitation treatment recommendations for people who experience cmTBI. Those with PTA > 1 week, in particular, may be at risk for residual disability as long as 6 months following injury. Specifying both PTA duration and CT criteria for cases of cmTBI will help to improve both comparisons across studies of this population and future clinical service provision.

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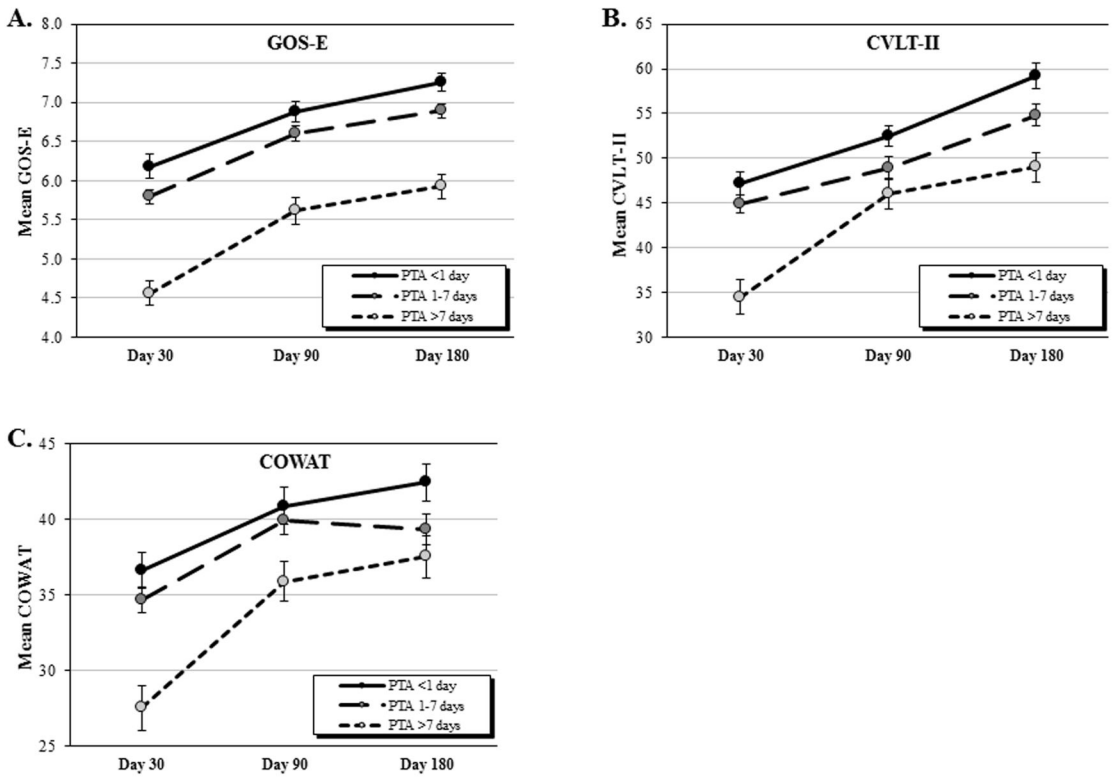

Figure 1.

Outcome measures for each PTA group. (A) Performance on the GOS-E based on time and PTA duration. (B) Performance on the learning trials of the CVLT-II based on time and PTA duration using T score. (C) Performance on the COWAT based on time and PTA duration with raw score adjusted for age and education. Observed values include death. Error bars are ±1 SE of the mean. GOS-E indicates Glasgow Outcome Scale-Extended; CVLT-II, California Verbal Learning Test II; COWAT, Controlled Oral Word Association Test.

Table 1

Demographics and mechanism of injury by PTA group

	PTA <1 day n = 84	PTA 1-7 days n = 155	PTA >7 days n = 91
Age			
18–30	21 (25%)	44 (28%)	20 (22%)
>30–45	14 (17%)	40 (26%)	26 (29%)
>45–60	29 (35%)	49 (32%)	31 (34%)
>60	20 (24%)	22 (14%)	14 (15%)
Sex			
Female	17 (20%)	47 (30%)	29 (32%)
Male	67 (80%)	108 (70%)	62 (68%)
Race/Ethnicity			
White	64 (76%)	126 (81%)	76 (84%)
Black/African American	13 (15%)	22 (14%)	12 (13%)
Hispanic	7 (8%)	7 (5%)	3 (3%)
Education			
Some elementary school or high school	11 (13%)	20 (13%)	13 (14%)
High school graduate, GED, technical, vocational, or trade school	27 (32%)	64 (41%)	36 (40%)
Some college	23 (27%)	42 (27%)	20 (22%)
College graduate, some graduate school, or completed graduate school	23 (27%)	29 (19%)	21 (23%)
Missing/Unknown	0 (0%)	0 (0%)	1 (1%)
Mechanism of Injury *			
Motor vehicle collision	26 (31%)	73 (47%)	60 (66%)
Fall from moving object	14 (17%)	20 (13%)	3 (3%)
Fall from stationary object	24 (29%)	39 (25%)	20 (22%)
Assault (Intentional Injury)	15 (18%)	16 (10%)	6 (7%)
Other	5 (6%)	7 (5%)	2 (2%)

Abbreviations: PTA, post-traumatic amnesia

* Significantly associated with PTA at $p < .001$

Table 2

Final longitudinal model for GOS-E, COWAT, and CVLT-II at 30, 90, and 180 days after injury

GOS-E	Estimate	Lower 95% CI	Upper 95% CI	p-value[a]
Time				**<0.001**
180 days (vs. 30 days)	1.20	1.06	1.34	<0.001
90 days (vs. 30 days)	0.86	0.73	1.00	<0.001
PTA				**<0.001**
<1 day (vs. >7 days)	1.42	1.12	1.71	<0.001
1–7 days (vs. >7 days)	1.05	0.79	1.31	<0.001
Age				**0.001**
>60 (vs. 18–30)	−0.57	−0.91	−0.23	0.001
46–60 (vs. 18–30)	−0.46	−0.76	−0.17	0.002
31–45 (vs. 18–30)	−0.10	−0.41	0.21	0.522
Race				**0.010**
Black (vs. White)	−0.48	−0.80	−0.17	0.003
Hispanic (vs. White)	0.03	−0.47	0.53	0.913

COWAT	Estimate	Lower 95% CI	Upper 95% CI	p-value
Time				**<0.001**
180 days (vs. 30 days)	6.58	5.51	7.66	<0.001
90 days (vs. 30 days)	5.54	4.65	6.43	<0.001
PTA				**<0.001**
<1 day (vs. >7 days)	6.34	3.40	9.28	<0.001
1–7 days (vs. >7 days)	4.05	1.52	6.59	0.002
Education				**<0.001**
College (vs. no HS)	9.59	5.85	13.33	<0.001
Some college (vs. no HS)	8.31	4.72	11.90	<0.001
HS/Other (vs. no HS)	3.20	−0.18	6.58	0.063
Sex (Female vs. Male)	2.50	0.08	4.91	**0.043**
Age				**0.016**
>60 (vs. 18–30)	−5.57	−8.96	−2.17	0.001
46–60 (vs. 18–30)	−2.41	−5.20	0.39	0.091
31–45 (vs. 18–30)	−2.08	−5.11	0.95	0.178

CVLT-II	Estimate	Lower 95% CI	Upper 95% CI	p-value
Time				**<0.001**
180 days (vs. 30 days)	11.11	9.75	12.47	<0.001
90 days (vs. 30 days)	6.04	4.73	7.35	<0.001
PTA				**<0.001**
<1 day (vs. >7 days)	7.55	4.35	10.75	<0.001

CVLT-II	Estimate	Lower 95% CI	Upper 95% CI	p-value
1–7 days (vs. >7 days)	4.54	1.76	7.32	0.001
Race				**<0.001**
Black (vs. White)	−6.32	−9.68	−2.97	<0.001
Hispanic (vs. White)	−6.50	−11.87	−1.12	0.018
Education				**<0.001**
College (vs. no HS)	10.26	6.17	14.34	<0.001
Some college (vs. no HS)	8.23	4.27	12.20	<0.001
HS/Other (vs. no HS)	2.77	−0.98	6.39	0.150
Age				**0.053**
>60 (vs. 18–30)	−3.56	−7.27	0.16	0.060
46–60 (vs. 18–30)	−1.73	−4.75	1.28	0.260
31–45 (vs. 18–30)	−4.37	−7.69	−1.05	0.010

Abbreviations: GOS-E, Glasgow Outcome Scale-Extended; CI, confidence interval; PTA, post-traumatic amnesia; HS, high school; COWAT, Controlled Oral Word Association Test; CVLT-II, California Verbal Learning Test II.

[a]The p-value on the line with the variable name reflects the entire multicategory variable, whereas the p-value on the line with a category reflects the comparison of that category with the reference category (indicated after ‘vs.’).

Table 3

Comparison of PTA groups and assessment times

GOS-E				
Contrasts	**Difference**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
<1 day vs1–7 days	0.37	0.10	0.64	**0.007**
<1 day vs >7 days	1.42	1.12	1.71	**<0.001**
1–7 days vs >7 days	1.05	0.79	1.31	**<0.001**
30 vs 90 days	0.86	0.73	1.00	**<0.001**
90 vs 180 days	0.33	0.20	0.47	**<0.001**

COWAT				
Contrasts	**Difference**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
<1 day vs 1–7 days	2.28	−0.35	4.91	**0.089**
<1 day vs >7 days	6.34	3.40	9.28	**<0.001**
1–7 days vs >7 days	4.05	1.52	6.59	**0.002**
30 vs 90 days	5.54	4.65	6.43	**<0.001**
90 vs 180 days	1.04	0.04	2.05	**0.043**

CVLT-II				
Contrasts	**Difference**	**Lower 95% CI**	**Upper 95% CI**	**p-value**
<1 day vs 1–7 days	3.01	0.15	5.87	**0.039**
<1 day vs >7 days	7.75	4.35	10.75	**<0.001**
1–7 days vs >7 days	4.54	1.76	7.32	**0.001**
30 vs 90 days	6.04	4.73	7.35	**<0.001**
90 vs 180 days	5.07	3.71	6.42	**<0.001**

Abbreviations: GOS-E, Glasgow Outcome Scale-Extended; CI, confidence interval; PTA, post-traumatic amnesia; COWAT, Controlled Oral Word Association Test; CVLT-II, California Verbal Learning Test II.