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The association of cognitive reserve in chronic-phase functional and neuropsychological outcomes following traumatic brain injury

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Abstract

Objective—Examine the association of cognitive reserve (CR) factors (estimated premorbid IQ, years of education, and occupational attainment) and traumatic brain injury (TBI) severity with functional and neuropsychological outcomes 1 to 5 years following TBI.

Participants—Patients with mild (N=58), moderate (N=25), or severe (N=17) TBI.

Main Measures—CR factors (estimated premorbid IQ, years of education, and occupational attainment); neuropsychological test battery; Glasgow Outcome Scale-Extended; Short Form-36 Health Survey.

Analyses—Spearman-Brown correlations, linear regression models, and ANCOVAs, were used to analyze the relation between CR factors and outcome measures.

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Author Disclosure Statement

No competing financial interests exist.

Results—Analyses revealed significant relations between estimated premorbid IQ and neuropsychological outcomes ($p < 0.004$): California Verbal Learning Test (CVLT), Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV) working memory (WM), Booklet Category Test, Trail Making Test (TMT) B, and Grooved Pegboard Test (PEG). There was also a significant correlation between estimated premorbid IQ and WAIS-IV processing speed (PS). Years of education had significant relations with CVLT and WAIS-IV WM and PS scores. There were significant differences between TBI severity groups and performance on the TMT A, PEG, and Finger Tapping Test.

Conclusions—CR factors may be associated with outcomes following TBI. Additional alternatives to TBI severity are needed to help guide rehabilitative planning post-injury.

Keywords

cognitive reserve; pre-morbid function; traumatic brain injury; neuropsychological tests; TBI severity; intelligence

Introduction

Recent literature has shown that current traumatic brain injury (TBI) severity classifications may not be the best predictors of long term post-injury functional and neuropsychological outcomes.^{1–3} Some patients with mild head injuries experience post-concussive symptoms lasting months or even years after initial trauma, while some with moderate-to-severe TBI have displayed fuller recoveries.^{2–3} Though the predictive value of TBI severity is unclear due to conflicting reports, these findings raise an important question: if injury severity does not necessarily inform prognosis, what additional factors may help to predict recovery after TBI?

Efforts to better identify outcome predictors in neurodegenerative diseases have focused on the concept of cognitive reserve (CR). The “CR hypothesis” suggests that patients with higher levels of premorbid functioning fare better in the face of neurodegenerative disease and neurological insult as manifested by better preservation of function despite increasing pathology over the course of a given disease.⁴ The mechanism for this phenomenon is believed to be a higher capacity for adapting to, or compensating for, damage to structures within existing neural networks. A consensus across the literature suggests that CR consists of 4 factors: premorbid intelligence quotient (IQ), years of education, occupational attainment, and participation in cognitively stimulating activities.⁵ Numerous studies have shown support for the protective role of CR factors on neuropsychological and behavioral outcomes in Alzheimer’s disease,⁶ stroke,⁷ Parkinson’s disease,⁸ and multiple sclerosis,⁹ as well as in normal aging.¹⁰ In addition, several reports have demonstrated that patients with a TBI who have greater CR experience better post-injury recovery.^{11–13}

Evidence suggests that the risk of developing disorders such as Parkinson’s disease, Alzheimer’s disease, and seizures is elevated for individuals who have sustained a TBI.^{14–16} This relation between TBI and comorbid neurological disorders, as well as the beneficial role seemingly played by CR in mitigating deficits among neurological conditions, warrants further investigation into the impact of CR factors on post-TBI outcomes. Increasing support

has been shown for factors of CR influencing post-TBI functional and neuropsychological outcomes.^{3, 11–12} However, few studies have conducted a broad evaluation of outcomes in neuropsychological functioning, instead focusing primarily on learning, memory, and executive function.^{3, 17–18} Relatively few studies have examined the role of CR in preservation of day-to-day functional abilities or its impact on mental and physical health outcomes.¹³ Moreover, although the factors of CR have been well-defined, the vast majority of studies of CR in TBI continue to use a single measure (e.g., years of education) to represent the larger concept of CR, rather than examining the relative contributions of various components.^{3, 12}

The present study sought to address these gaps in the literature by investigating the relation between CR factors (estimated premorbid IQ, years of education, occupational attainment) and post-injury functional and neuropsychological outcomes following adult TBI. We hypothesized that greater estimated premorbid IQ, years of education, and occupational attainment would be positively correlated with functional and neuropsychological outcomes following injury. We were also interested in the degree to which TBI severity was related to functional and neuropsychological outcomes, and we hypothesized that TBI severity would not be significantly associated with recovery post-injury.

Materials and Methods

Participants

Participant data in the study were drawn from a larger data set from an ongoing 5-year longitudinal study of TBI that began in 2011 and continued through 2016. The objective of the longitudinal study was to collect magnetic resonance imaging (MRI), biomarker, and neuropsychological measures to better understand factors influencing diagnosis and prognosis of TBI.¹⁹ These individuals were classified as having sustained a non-penetrating mild, moderate, or severe TBI as defined by the Department of Veterans Affairs and Department of Defense TBI severity rating scale.²⁰ The scale stratifies patients according to the presence of structural acute computed tomography (CT) imaging findings, Glasgow Coma Scale (GCS) score, and duration of loss of consciousness, alteration of mental state, and post-traumatic amnesia.

Participants were selected for the current study if they had available data 1 year post-injury or later and had valid neuropsychological testing. For those seen at multiple time points, data from the most recent assessment was used. Extensive validity and effort testing was performed, and only subjects who passed all stand-alone and embedded validity measures were included.

There were 28 participants who were unemployed at the time of injury and were excluded from occupational attainment analyses; therefore, analyses examining occupational attainment were conducted on 72 participants.

Measures

Factors of CR—The Wechsler Advanced Clinical Solutions Test of Premorbid Function (ToPF) was used to generate an estimate of participant premorbid IQ. Years of education

was collected during a demographic interview and was used to measure educational attainment. A vocational history interview was also conducted by a licensed vocational therapist to determine occupational attainment. Occupational attainment was categorized using participants' pre-injury occupation according to the 2010 Standard Occupational Classification System by the Bureau of Labor Statistics, where 1 represents professional/managerial occupations, 2 represents skilled occupations, and 3 represents unskilled/manual labor occupations.²¹

Neuropsychological Outcome Measures—A comprehensive battery of neuropsychological tests was administered by a trained psychometrist. Information on specific assessments is shown in Table 1. The Beck Depression Inventory (BDI) was used as a measure for depression, with a score of greater than 16 indicating depression.²²

Functional Outcome Measures—The Glasgow Outcome Scale-Extended (GOS-E) was administered to participants to evaluate the level of recovery of function in activities of daily living (ADLs) following injury. The Short Form-36 Health Survey (SF-36), a self-report measure, was administered to gather information about participants' ratings of physical and mental health outcomes. Physical Component (SF-36 P) and Mental Component (SF-36 M) summary scores were generated based upon participant responses.

Imaging Pathology Identification—Structural brain images were obtained using a Siemens Biograph MR 3T scanner. Radiology reports from a board-certified neuroradiologist were analyzed to identify patients with evidence of frontal or temporal lobe damage, including encephalomalacia, contusions, and hemorrhage. As the frontotemporal injury findings were assessed using MRI reports, unlike the TBI severity classification that uses CT scans, there are patients with positive MRI findings in the mild group.

Statistical Analysis

Two-tailed Spearman-Brown correlations were calculated to examine relations between estimated premorbid IQ, years of education, occupational attainment, TBI severity, age, time since injury, depression, and cognitive and functional outcome measures. These correlations were calculated on the entire cohort, on a subset with MRI evidence of damage to frontotemporal brain regions, and on the rest of the cohort without frontotemporal injury MRI findings. The correlations were also calculated on the subset of the sample that sustained a severe TBI.

Relations between study outcomes and estimated premorbid IQ and occupational attainment for the entire cohort were assessed using linear regression models that included age, TBI severity, and years of education as covariates. Partial correlations were determined to examine the relation between BDI scores and outcome measures, with age, time since injury, and TBI severity as covariates.

ANCOVAs were used to examine the relation between occupational attainment and cognitive and functional outcomes as well as between TBI severity and these outcomes. Age, time since injury, and depression were used as covariates. TBI severity was used as an additional covariate in the occupational attainment analysis. The relation between TBI

severity and cognitive outcomes in the subset of participants with frontotemporal damage was also analyzed using ANCOVA, with age, time since injury, and depression as covariates. Finally, the outcomes of the group with frontotemporal damage and the rest of the cohort were compared using ANCOVAs with age, time since injury, ToPF scores, and depression as covariates.

To control for the overall Type I error rate, the Šidák correction was used to set the significance for all analyses at $p < .004$.

Results

The sample included 100 total participants (63 male). See Table 2 for participant demographics.

The results show significant positive Spearman correlations between both estimated premorbid IQ and years of education with performance on several neuropsychological assessments (Table 3a). Similarly, linear regression models revealed significant relations between both ToPF scores and years of education and scores on neuropsychological tests (Table 4). Furthermore, ANCOVAs revealed no differences in neuropsychological outcomes between occupational attainment levels in the entire cohort. No significant findings were identified between occupational attainment, time since injury, or injury severity variables and neuropsychological outcomes in either the Spearman correlations or the linear regression models. There were no significant relations observed between any of the CR factors and functional outcome measures.

ANCOVAs revealed that TBI severity was significantly associated with FTT-ND, PEG-ND, and TMT-A performance (Table 5). The severe group performed significantly worse than the mild group on the FTT-ND ($p < .001$), PEG-ND ($p < .001$), and TMT-A ($p < .001$). Furthermore, the severe group performed significantly worse than the moderate group on the FTT-ND task ($p = .001$). In a sub-analysis of the severe TBI group, Spearman correlations revealed no significant findings between CR factors and outcome measures.

There were significant inverse Spearman-Brown and partial correlations between BDI scores and performance on several neuropsychological measures and all of the functional outcomes (Table 6).

Of the 97 subjects who had usable MRI scans, 51 were positive for imaging findings related to TBI. Forty-one (80.4%) participants positive for imaging findings showed evidence of damage to frontotemporal brain regions. In this group, there were 9 persons with mild, 15 with moderate, and 17 with severe injuries.

In the frontotemporal injury group, there were significant positive correlations between occupational attainment and performance on WAIS-IV PS, in addition to significant correlations between both estimated premorbid IQ and years of education and several neuropsychological measures (Table 3b). ANCOVAs of TBI severity in the frontotemporal damage group showed that severity was significantly associated with TMT-A performance (Table 5), with the severe group performing significantly worse than the mild group ($p = .$

001). Analyses of the non-frontotemporal injury group revealed significant positive correlations between ToPF scores and performance on the CVLT and WAIS-IV WM (Table 3c). In the ANCOVAs comparing outcome measures between frontotemporal damage positive and negative groups, there was a significant group difference for WAIS-IV WM scores (Table 5), with the group with frontotemporal damage showing poorer performance on this measure.

Discussion

Prior studies have shown that individuals with greater CR show some degree of resilience to the impact of injury or neurodegenerative disease, as they can withstand greater levels of pathology before exhibiting outward signs of a given disorder.²³ Our findings support the relation between CR factors and neuropsychological outcomes in patients with TBI, as those with stronger CR fared better than those with lower CR prior to injury.

The findings suggest that the CR factor of estimated premorbid IQ is related to neuropsychological outcomes following TBI. This finding is not unexpected due to the large overlap between general intelligence factor (“g”) and many neuropsychological measures. It is likely that “g”, associated with crystallized intelligence which is relatively resistant to brain injury, is affecting the ToPF scores. In addition, it is likely that “g” associated with fluid aspects of intelligence is also helping individuals adapt and overcome deficits related to their head injury. Although IQ tests have been found to be more multifactorial than the concept of verbal or performance IQ, “g” is still shared by these factors and provides a good estimate for outcomes.²⁴ The educational attainment factor was correlated with neuropsychological outcomes, though to a lesser degree than premorbid IQ. This finding is also not unexpected due to the relation between IQ and education.

Occupational attainment did not correlate with neuropsychological or functional outcome scores after TBI. This may be attributable to the fact that the 2010 Standard Occupational Classification System by the US Bureau of Labor Statistics does not differentiate skill level. The system categorizes occupational level such that jobs within a particular field are given equal weight and classified within the same attainment level, instead of being stratified by the level of success attained and skill required in each specific career path. For future studies, a more in-depth classification system is needed that accounts for both job field and skill level in categories of occupational attainment.

In contrast to the neuropsychological findings, functional outcome measures were not related to aspects of CR. This may be due, in part, to the fact that our study participants had a higher average premorbid IQ than the general population (Table 2). As defined by David Wechsler, “Intelligence is the aggregate or global capacity of the individual to act purposefully, to think rationally and to deal effectively with his environment.”^{24(p3)} Individuals with higher estimated premorbid IQ may be more likely to be more adaptable or have better compensatory mechanisms which provide them an advantage in effectively interacting with their environment, despite the burden of neurological damage. The lack of findings between functional outcomes and CR factors may also be due to the fact that participation in cognitively stimulating activities prior to injury, which was not examined in

our study, could influence functional outcomes to a greater extent than the analyzed CR factors.

Our findings further contribute to the evidence indicating that TBI severity is not the only factor to consider in the prognosis for recovery from TBI. Although TBI severity was associated with a subset of study outcomes, this finding must be interpreted with caution due to the small number of participants who were classified as having sustained severe injuries, while mild and moderate injuries were better represented in our sample. CR factors appeared to have stronger relations with outcomes than did severity in our study.

Depression was highly correlated with neuropsychological and functional outcomes in our study, which replicates the findings of previous studies.^{25–27} Future CR research needs to consider the effects of depression and other psychopathologies, including personality disorders, when examining outcomes after TBI, especially as depression was the only factor in our study that was significantly correlated with functional outcomes.

Considering the pattern of frontotemporal damage that frequently characterizes TBI, these neuropsychological functions are often susceptible to impairment due to their reliance on the frontal and temporal lobe circuit. The damaged structures are parts of larger neural networks, making the exact impact of these injuries difficult to define. Our results support the conclusion that frontotemporal injury is associated with cognitive outcomes. Studies have suggested that individuals with high CR suffering from neurodegeneration may increasingly recruit frontotemporal executive resources to improve neuropsychological function and modulate symptoms of deterioration.^{28–29} Faced with direct frontotemporal damage, these resources may become jeopardized, and greater CR may become more important for providing the compensatory cognitive resources that help to overcome deficits due to injury.

Despite the thorough investigation of the association of factors of CR with post-injury outcomes, the present study is not without its limitations. The generalizability of our findings may be limited due to the fact that participants were primarily residents of the greater Washington, D.C. area with an above-average level of education who had persistent post-TBI symptoms and sought out our study. The above-average educational level in our sample may have resulted in less differentiation between levels of educational attainment. We did not have data available on subjects' participation in cognitive rehabilitation post-injury which may be a confounding factor related to outcomes. Access to treatment may depend on education and/or socioeconomic status. Although not a direct measure, we offer data on the health insurance status of participants as a proxy for the accessibility of rehabilitation. Data was available for 97 participants, and 88.2% reported that they had health insurance, which may have provided access to rehabilitation services (Table 2). Furthermore, the imaging analysis used in this study was an anatomical approach. To achieve a more thorough understanding of CR in TBI, neural networks and connectivity should be studied. While we incorporated a relatively encompassing view of CR, we did not measure premorbid participation in cognitively stimulating activities. This factor should be taken into account in future works in order to get a more global view of the impact of CR on

post-TBI outcomes. In addition, we were not able to measure premorbid emotional reserve, although the growing body of evidence shows that emotional reserve contributes to CR.²⁷

The use of a much larger sample of a more diverse population with a better method of assessing premorbid psychopathology may be the next step in the process of studying CR in TBI. While this is one of the largest cohorts to study CR in TBI to date, sample size issues remain. The ideal prospective study would collect several measurements prior to TBI including emotional reserve, IQ, etc. However, this would be difficult to achieve, except within cohorts of individuals likely to sustain a TBI such as military service members or athletes.

Conclusion

Together, these findings suggest that alternative factors contributing to neuropsychological outcomes, including factors of CR, may better characterize the trajectory of patient recovery following TBI. Clinicians may be able to use measures of premorbid functioning such as estimated premorbid IQ, in concert with TBI severity ratings to provide greater insight into prognosis and treatment planning for post-TBI neuropsychological outcomes. The factors of CR examined in this study can be determined following a TBI, and this would allow clinicians to consider these attributes when developing a rehabilitation plan. This information could be used to help determine patient recovery trajectories and design more appropriate rehabilitation plans, based on the level of functioning to which a patient can be expected to return. Studies using diffusion tensor imaging and functional MRI may benefit the study of CR in TBI, as these modalities could reveal the ability of networks to compensate for damage to certain brain regions, which may foster better functioning following TBI.

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Table 1

Neuropsychological assessment battery

Assessment	Sub-Test	Measure
Booklet Category Test (BCT)		Executive function, problem solving
California Verbal Learning Test (CVLT)	Trials 1–5 total free recall	Learning
Finger Tapping Test (FTT)	Dominant hand (D) Non-Dominant hand (ND)	Sensory motor Sensory motor
Grooved Pegboard Test (PEG)	Dominant hand (D) Non-Dominant hand (ND)	Sensory motor Sensory motor
Trails Making Test (TMT)	A B	Attention, processing speed Executive function, cognitive flexibility
Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV)	Arithmetic, Digit span Symbol search, Coding	Working memory (WM) Processing speed (PS)

Table 2

Patient demographic information (N = 100)

Mean age (SD)		46.6 (16.4)
Mean education in years (SD)		15.7 (2.5)
Mean pre-morbid IQ (SD)		107.0 (13.9)
Ethnicity	Caucasian	71
	Asian	4
	Latino	9
	Black/African-American	13
	Multiple	3
TBI severity	Mild	58
	Moderate	25
	Severe	17
Mean time since injury in years (SD)		2.5 (1.2)
Mechanism of injury (%)	Fall	30
	Impact with object	38
	Acceleration/deceleration	19
	Assault	5
	Blast	8
Individuals with BDI scores >16		21
Health insurance status	Yes	82
	No	11

Table 3

Results for Spearman correlations between CR factors and outcome measures

Outcome Measures:		GOS-E	SF-36 P	SF-36 M	BCT	CVLT	FTT-D	FTT-ND	PEG-D	PEG-ND	TMT-A	TMT-B	WAIS-IV WM	WAIS-IV PS
a. Entire cohort (N=100)	ToPF	$p=.053$ $r=.194$	$p=.166$ $r=.146$	$p=.055$ $r=.201$	$p<.001^*$ $r=.367$	$p<.001^*$ $r=.534$	$p=.473$ $r=.080$	$p=.321$ $r=.109$	$p=.001^*$ $r=.322$	$p=.034$ $r=.215$	$p=.063$ $r=.189$	$p=.001^*$ $r=.328$	$p<.001^*$ $r=.580$	$p<.001^*$ $r=.358$
	Edu	$p=.267$ $r=.112$	$p=.696$ $r=.041$	$p=.057$ $r=.199$	$p=.105$ $r=.170$	$p=.001^*$ $r=.333$	$p=.849$ $r=.021$	$p=.485$ $r=.077$	$p=.224$ $r=.125$	$p=.429$ $r=.081$	$p=.327$ $r=.100$	$p=.200$ $r=.131$	$p=.002^*$ $r=.320$	$p=.001^*$ $r=.348$
	Occ	$p=.176$ $r=.161$	$p=.635$ $r=.058$	$p=.416$ $r=.100$	$p=.244$ $r=.144$	$p=.024$ $r=.268$	$p=.235$ $r=.147$	$p=.553$ $r=.074$	$p=.023$ $r=.267$	$p=.180$ $r=.160$	$p=.213$ $r=.151$	$p=.082$ $r=.209$	$p=.006$ $r=.327$	$p=.014$ $r=.291$
b. Frontotemporal damage (n=41)	ToPF	$p=.300$ $r=.166$	$p=.642$ $r=.075$	$p=.346$ $r=.151$	$p=.002^*$ $r=.465$	$p<.001^*$ $r=.536$	$p=.169$ $r=.222$	$p=.035$ $r=.331$	$p<.004^*$ $r=.446$	$p=.464$ $r=.118$	$p=.181$ $r=.216$	$p=.008$ $r=.413$	$p<.001^*$ $r=.560$	$p=.001^*$ $r=.506$
	Edu	$p=.186$ $r=.211$	$p=.952$ $r=.010$	$p=.554$ $r=.095$	$p=.101$ $r=.260$	$p=.045$ $r=.314$	$p=.489$ $r=.113$	$p=.047$ $r=.312$	$p=.071$ $r=.289$	$p=.572$ $r=.091$	$p=.052$ $r=.310$	$p=.065$ $r=.295$	$p=.024$ $r=.362$	$p=.002^*$ $r=.480$
	Occ	$p=.474$ $r=.131$	$p=.969$ $r=.007$	$p=.520$ $r=.118$	$p=.062$ $r=.334$	$p=.123$ $r=.279$	$p=.519$ $r=.118$	$p=.831$ $r=.039$	$p=.173$ $r=.247$	$p=.835$ $r=.038$	$p=.027$ $r=.397$	$p=.033$ $r=.383$	$p=.051$ $r=.354$	$p=.003^*$ $r=.523$
c. Non- frontotemporal damage (n=59)	ToPF	$p=.076$ $r=.233$	$p=.183$ $r=.190$	$p=.101$ $r=.232$	$p=.046$ $r=.280$	$p<.001^*$ $r=.516$	$p=.752$ $r=.050$	$p=.742$ $r=.051$	$p=.093$ $r=.227$	$p=.022$ $r=.304$	$p=.245$ $r=.156$	$p=.025$ $r=.296$	$p<.001^*$ $r=.602$	$p=.069$ $r=.243$
	Edu	$p=.765$ $r=.040$	$p=.848$ $r=.028$	$p=.038$ $r=.291$	$p=.520$ $r=.092$	$p=.013$ $r=.329$	$p=.667$ $r=.068$	$p=.567$ $r=.089$	$p=.947$ $r=.009$	$p=.545$ $r=.082$	$p=.613$ $r=.068$	$p=.945$ $r=.009$	$p=.065$ $r=.251$	$p=.058$ $r=.253$
	Occ	$p=.318$ $r=.162$	$p=.860$ $r=.030$	$p=.639$ $r=.080$	$p=.357$ $r=.161$	$p=.165$ $r=.227$	$p=.244$ $r=.202$	$p=.218$ $r=.213$	$p=.054$ $r=.306$	$p=.067$ $r=.292$	$p=.730$ $r=.057$	$p=.881$ $r=.025$	$p=.150$ $r=.238$	$p=.599$ $r=.086$

a.) In the entire cohort, ToPF scores were significantly positively correlated with scores on the BCT, CVLT, PEG-D, TMT-B, WAIS-IV WM, and WAIS-IV PS. Years of education were significantly positively correlated with scores on the CVLT, WAIS-IV WM, and WAIS-IV PS. b.) Within the group positive for frontotemporal damage in MRI, ToPF scores were significantly positively correlated with BCT, CVLT, PEG-D, WAIS-IV WM, and WAIS-IV PS scores. Additionally, years of education and occupational skill were significantly correlated with performance on the WAIS-IV PS. c.) In the group that did not have evidence of frontotemporal damage, ToPF scores were significantly positively correlated with scores on the CVLT and WAIS-IV WM.

* indicates significant finding $p < .004$; Edu=years of education; Occ=occupational attainment

Table 4

Results for linear regression model analysis between CR factors and outcomes

Outcome Measures:	GOS-E	SF-36 P	SF-36 M	BCT	CVLT	FTT-D	FTT-ND	PEG-D	PEG-ND	TMT-A	TMT-B	WAIS-IV WM	WAIS-IV PS
ToPF	N/A **	$p=.162$ $R^2=.102$	$p=.065$ $R^2=.160$	$p<.001^*$ $R^2=.192$	$p<.001^*$ $R^2=.327$	$p=.185$ $R^2=.128$	$p=.486$ $R^2=.202$	$p<.001^*$ $R^2=.189$	$p=.023$ $R^2=.048$	$p=.241$ $R^2=.185$	$p=.003^*$ $R^2=.181$	$p<.001^*$ $R^2=.368$	$p=.036$ $R^2=.188$
Education	N/A **	$p=.850$ $R^2=.081$	$p=.317$ $R^2=.126$	$p=.054$ $R^2=.070$	$p<.001^*$ $R^2=.176$	$p=.732$ $R^2=.107$	$p=.474$ $R^2=.197$	$p=.180$ $R^2=.078$	$p=.466$ $R^2=.125$	$p=.075$ $R^2=.172$	$p=.114$ $R^2=.097$	$p=.001^*$ $R^2=.123$	$p<.001^*$ $R^2=.147$
Occupational Attainment	N/A **	$p=.781$ $R^2=.086$	$p=.577$ $R^2=.137$	$p=.179$ $R^2=.107$	$p=.351$ $R^2=.195$	$p=.009$ $R^2=.213$	$p=.263$ $R^2=.224$	$p=.553$ $R^2=.090$	$p=.817$ $R^2=.129$	$p=.979$ $R^2=.173$	$p=.605$ $R^2=.107$	$p=.547$ $R^2=.136$	$p=.480$ $R^2=.161$

Linear regression model analysis revealed significant relationships between ToPF scores and BCT, CVLT, PEG-D, TMT-B, and WAIS-IV WM. There were also significant relationships between years of education and CVLT, WAIS-IV WM, and WAIS-IV PS scores.

* indicates significant finding $p < .004$

** GOS-E relationships to the CR factors in the linear regression model are unavailable due to the ordinal nature of the GOS-E scores.

Table 5Results for significant findings ($p < .004$) in ANCOVAs

Cohort	Grouping variable	Significant outcome measures	p-value	F-value
Entire cohort (N=100)	TBI severity	FTT-ND	$p < .001$	8.811
		PEG-ND	$p = .002$	6.403
		TMT-A	$p < .001$	8.854
Positive frontotemporal MRI finding (n=41)	TBI severity	TMT-A	$p = .003$	6.872
Entire cohort (N=100)	Presence of frontotemporal damage	WAIS-IV WM	$p = .003$	9.084

Table 6

Significant results for Spearman-Brown and partial correlations between BDI scores and outcomes

	Spearman-Brown correlation		Partial correlation	
	p-value	r-value	p-value	r-value
GOS-E	<.001	-.609	<.001	-.560
SF-36 P	<.001	-.515	<.001	-.518
SF-36 M	<.001	-.813	<.001	-.853
BCT	.002	-.313	.001	-.375
PEG-D	.001	-.323	<.001	-.403
TMT-B	<.001	-.355		
WAIS-IV WM	.003	-.304		
WAIS-IV PS	<.001	-.414		