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The Influence of Cognitive Reserve on Recovery from Traumatic Brain Injury

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Abstract

Objective: we sought to determine the degree to which cognitive reserve, as assessed by the Test of Premorbid Functioning in combination with demographic variables, could act as a buffer against the effect of traumatic brain injury (TBI) on cognitive test performance.
Method: retrospective analysis of a cohort of 121 persons with TBI who completed the Wechsler Adult Intelligence Scale—Fourth Edition (WAIS–IV) within 1–12 months after injury.
Results: regression analyses indicated that cognitive reserve was a statistically significant predictor of all postinjury WAIS–IV factor index scores, after controlling for various premorbid and comorbid confounding variables. Only for Processing Speed did injury severity make an additional statistically significant contribution to the prediction model.
Conclusions: cognitive reserve has a protective effect with regard to the impact of TBI on cognitive test performance but this effect is imperfect and does not completely negate the effect of injury severity.

Keywords: Brain reserve; Protective factors; Injury severity; Processing speed; Risk factors; Sequelae

Traumatic brain injury (TBI) is common in adults, with an incidence of 824 per 100,000 persons in the USA (Centers for Disease Control, 2014). TBI occurs when there is an external force to the head that leads to at least temporary interruption of cerebral functioning. Particularly with more severe injuries, such as those associated with intracranial lesions on neuroimaging and/or prolonged time to follow verbal commands, significant cognitive deficits can result (for reviews, see: Roebuck-Spencer, Baños, Sherer & Novack, 2010; Stucky, Kirkwood & Donders, 2014). The main focus of the current investigation was on the degree to which such outcomes may be affected by cognitive reserve.

Cognitive reserve refers to the hypothesis that the relationship between brain pathology and its behavioral manifestation is affected at least in part by premorbid factors (Satz, 1993; Stern, 2002). These can range from cerebral integrity (e.g., the gray and white matter volume prior to injury) to cognitive enrichment (e.g., years of completed education at the time of injury). There have been several studies that have reported that lower cognitive reserve is associated with worse outcomes after TBI, such as more prolonged subjective symptoms after uncomplicated mild injuries (Oldenburg, Lundin, Edman, Nygren-deBoussard & Bartfai, 2016) or reduced likelihood of disability-free recovery after moderate-severe injuries (Schneider et al., 2014). However, those studies typically did not include or report on persons with premorbid complicating factors, such as a history of learning disability. Furthermore, such studies have typically not controlled for level of effort and/or emotional distress, which can both affect performance on cognitive tests after TBI.

Consideration of a history of learning disability is potentially important because cognitive reserve is often assessed with tests of word reading, which can be affected in adults with a history of special education service for reading difficulty (Semrud-Clikeman & Fine, 2008). There is also some evidence that histories of learning disability and mild TBI are independently related to lower baseline cognitive performance in college athletes (Collins et al., 1999).

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It is also well known that effort has a significant impact on cognitive test performance, including after TBI, particularly but not exclusively in the context of financial compensation-seeking (P. Green, Rohling, Lees-Haley & Allen, 2001; Lange, Pancholi, Bhagwat, Anderson-Barnes & French, 2012). Consequently, several professional organizations have recommended for the routine inclusion of performance validity measures during clinical neuropsychological evaluations (Bush et al., 2005; Heilbronner et al., 2009). Subsequent research has also demonstrated that effort and injury severity are both independent predictors of neuropsychological test performance after TBI (Donders & Strong, 2011).

There is more controversy in the literature about the degree to which psychological distress can affect cognitive test performance. For example, Khan-Bourne and Brown (2003) suggested that there was a significant impact of depression on outcomes in persons with TBI or stroke. On the other hand, Sherman, Strauss, Slick and Spellacy (2000) found evidence for only a very small effect of depression on neuropsychological test performance in persons with TBI and then only in persons with relatively mild cognitive deficits. Furthermore, Gass and Gutierrez (2017) did not find evidence for an impact of depression on any of the four factor index scores from the Wechsler Adult Intelligence Scale—Fourth Edition (WAIS–IV; Wechsler, 2008) although they did find that health preoccupation and distorted perceptions did have a negative effect on Verbal Comprehension. None of these studies considered the potential impact of degree of depression at the time of the evaluation in the context of protective factors like cognitive reserve or risk factors like financial compensation-seeking.

The main goal of this investigation was to determine the degree to which cognitive reserve served as a protective factor with regard to performance on a test of psychometric intelligence after TBI; specifically, when cognitive reserve was considered in concert with the potential influences of injury severity, time since injury, history of learning disability and other premorbid complicating factors, financial compensation-seeking, and level of emotional distress. The dependent variables of interest were obtained from the WAIS–IV because previous research has supported the criterion validity of this instrument, and particularly that of its Processing Speed index, in patients with TBI (Carlozzi, Kirsch, Kisala & Tulsky, 2015; Donders & Strong, 2015).

The specific hypotheses for this study were that: (a) cognitive reserve would be a statistically significant predictor of performance on all WAIS–IV factor score indices, even when controlling for history of learning disability, other premorbid psychosocial complicating factors, disputed financial compensation-seeking, time since injury and current level of emotional distress; and (b) injury severity would be a statistically significant predictor in the model of Processing Speed, even after controlling for cognitive reserve.

Method

Participants

Data were retrieved from patients who were evaluated at a regional Midwestern rehabilitation facility over 30 consecutive months between January 2015 and June 2017. As such, this was a cross-sectional study based on retrospective analysis of a clinical database. Selection criteria were as follows: (a) $\geq$20 years and $\leq$75 years old, (b) diagnosis of TBI, and (c) neuropsychological assessment with inclusion of the WAIS–IV completed within 1–12 months postinjury. The WAIS–IV had been routinely included in neuropsychological evaluations at the facility where this study was conducted, except if the examinees were not fluent in English or if they had other limitations (e.g., severe uncorrected visual impairment, orthopedic injury to the dominant hand) that would have precluded completion of some of the subtests in a valid manner. All assessments were conducted by Master's level psychometrists or postdoctoral residents, under the supervision of licensed psychologists who were board-certified in clinical neuropsychology by the American Board of Professional Psychology.

Only results from initial evaluations were considered in case patients were evaluated more than once. We included only persons who provided valid effort during their neuropsychological evaluation, as determined on the basis of passing two formal performance validity criteria, including the Test of Memory Malingering (Tombaugh, 1996) as well as the Reliable Digit Span index (Greiffenstein, Baker & Gola, 1994). Twenty-seven potential participants were excluded for failing to meet this performance validity criterion. Persons with severe premorbid developmental (e.g., autism; $n = 2$), neurological (e.g., dementia, $n = 7$), or psychiatric (e.g., schizophrenia $n = 6$) conditions were also excluded, based on review of medical records and personal histories by the licensed psychologists. Persons with other minor complicating premorbid histories, such as outpatient psychiatric treatment for adjustment disorder, ADHD or substance abuse, were not excluded. This was because of the potential influence of such histories to increase the risk for prolonged symptoms, especially in cases of uncomplicated mild TBI (Cassidy et al., 2014). We therefore planned to include those variables in the analyses. The final sample in the current study was completely independent of that used in a previous investigation in our laboratory that also used WAIS–IV data (Donders & Strong, 2015).

The final sample (n = 121) included 71 men and 50 women, with a mean of 13.35 years of education (SD = 2.33). The majority (n = 103, 85%) self-identified as Caucasian, with other racial backgrounds including African (n = 9), Latino/a (n = 8), and Asian (n = 1). They were on average 41.12 years of age (SD = 14.99) and received their neuropsychological evaluation at a mean of 182.52 days after injury (SD = 86.59). Fourteen participants (12%) had a history of special education services for learning disability. Forty-nine participants (41%) had one or more other prior complicating histories (ADHD [n = 21], adjustment disorder [n = 32], personal trauma [n = 19] and/or substance abuse [n = 25]). Thirty-two participants (27%) were involved in disputed financial compensation-seeking at the time of the neuropsychological evaluation.

The majority of injuries were sustained in motor vehicle accidents (n = 71, 59%). The remaining injury circumstances included falls (n = 21, 17%), recreational activities (n = 15, 12%), and various other events (n = 14, 12%). We defined injury severity on the basis of a combination of duration to follow commands (also known as coma) and acute neuroimaging findings, as documented in the available medical records that were reviewed by the licensed psychologists. Because of significant positive skew in the distribution of time to follow commands, we decided to dichotomize the injury severity variable. Persons with uncomplicated mild TBI (n = 75, 62%) had duration to follow commands <30 min and no intracranial findings on neuroimaging. All other participants (n = 46, 38%) were classified as having complicated mild to severe TBI. In this subgroup, 44 had positive neuroimaging scans and 19 had duration to follow commands that exceeded 24 hrs.

Procedure

Neuropsychological evaluations were completed on an outpatient basis when patients were medically stable and could recall meaningful information from day to day. All evaluations were carried out with informed consent. This research was conducted with approval from the Institutional Review Board at Mary Free Bed Rehabilitation Hospital, and in compliance with the Helsinki Declaration.

Measurements

The WAIS–IV is a measure of psychometric intelligence that yields standard scores (M = 100, SD = 15) in four domains: Verbal Comprehension, Perceptual Reasoning, Working Memory, and Processing Speed. Performance on the entire test can also be expressed in terms of a Full Scale IQ. However, for purposes of this investigation, we focused on the factor index scores, in light of previous research that had indicated that they differ considerably in their sensitivity to TBI severity.

There is ample precedent in the literature for using a test of reading in concert with demographic background as an index of cognitive reserve (O'Shea et al., 2015; Shapiro, Mahoney, Peyser, Zingman & Verghese, 2014). We measured cognitive reserve with the Test of Premorbid Functioning (TOPF; Holdnack Drozdick, Weiss & Iverson, 2013; NCS Pearson, 2009) in combination with demographic variables. The TOPF is based on a reading paradigm that requires the pronunciation of a list of written words that have irregular grapheme-to-phoneme conversion. The total number of words correctly read can be combined with demographic variables to yield premorbid estimates of any of the four factor index scores (M = 100, SD = 15). We used the prediction method based on TOPF raw score in combination with the following demographic variables: geographic region, gender, race/ethnicity, highest years of education, and highest occupation.

Level of depressive symptoms at the time of assessment with the WAIS–IV was measured with the Patient Health Questionnaire (PHQ–9; Spitzer, Kroenke & Williams, 1999). This is a widely used and psychometrically sound depression screening instrument that has been specifically validated for use after TBI (Dyer, Williams, Bombardier, Vannoy & Fann, 2016). The PHQ–9 includes nine questions that each requires a response on a four-level Likert scale as pertaining to experiences over the last 2 weeks. The total raw score can range from 0 to 27, with scores ≥10 typically being considered clinically significant.

Statistical Analyses

Standard scores from the WAIS–IV were used in all statistical analyses. Since the TOPF prediction included demographic variables already, we did not correct obtained WAIS–IV scores for demographic background. We evaluated the difference between the actual and the TOPF/demographically predicted factor index scores with t-tests for paired observations. In order to correct for spurious inflation of alpha due to multiple independent comparisons, we applied the Bonferroni correction to set alpha at .0125 (.05/4).

We then used linear regression to determine the relative influence of a number of variables on the WAIS–IV index scores. Separate analyses were conducted for, respectively, Verbal Comprehension, Perceptual Reasoning, Working Memory, and

Processing Speed. In each of these analyses, the independent variables were cognitive reserve (based on the TOPF in combination with demographic variables), presence/absence of prior learning disability, presence/absence of any other premorbid complicating history, injury severity, interval between injury and assessment, presence/absence of current disputed financial compensation-seeking, and level of current depressive symptoms as measured by the PHQ–9. Additional demographic variables (e.g., gender, ethnicity) were not added to the model because those were already included in the calculation of the cognitive reserve index. We used the adjusted R^2 index as a measure of the proportion of variance in the dependent variable that each model accounted for. Consistent with conventional standards (Murphy & Myors, 2004), we considered values <10% as small, values 10–25% as medium, and values >25% as large. The study size was considered sufficient because it allowed for >15 participants per variable in the regression models, a ratio that has been recommended by Stevens (2002, p. 143).

Results

In the complete sample, the mean Full Scale IQ was 96.57 (SD = 12.29; range 67–129) and the mean total score of depressive symptoms on the PHQ–9 was 9.41 (SD = 6.28; range 0–25). Table 1 presents the predicted and obtained WAIS–IV factor index scores in the complete sample. Only for the Processing Speed index did the difference between the predicted and obtained scores meet our criterion for statistical significance, with the obtained scores being on average 5.82 (SD = 12.43) standard scores points below the TOPF/demographically predicted ones, t (120) = –5.15, $p < .0001$, $d = 0.47$.

Tables 2–5 present the regression models for the various WAIS–IV index scores. There was no evidence for collinearity in any of the models, with all Variance Inflation Factors below 1.16, which is excellent by conventional standards (O'Brien, 2007).

The model for Verbal Comprehension was statistically significant, $F(1, 113) = 34.34$, $p < .0001$ and explained a large proportion of the variance, Adjusted $R^2 = .66$. Greater cognitive reserve, longer time since injury and lower level of depressive symptoms were all statistically significant predictors of higher obtained Verbal Comprehension scores.

The model for Perceptual Reasoning was also statistically significant, $F(1, 113) = 4.74$, $p < .0001$. It accounted for a moderate proportion of the variance, Adjusted $R^2 = 0.18$. Higher cognitive reserve and longer time since injury were both statistically significant correlates of better Perceptual Reasoning scores.

Table 1. WAIS–IV results persons with TBI

	Complete sample				Uncomplicated mild TBI				Complicated mild—severe TBI			
	(*n* = 121)				(*n* = 75)				(*n* = 46)			
	Predicted		Obtained		Predicted		Obtained		Predicted		Obtained	
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Verbal Comprehension	97.25	10.16	97.74	13.78	96.59	10.54	97.20	13.87	98.32	9.53	98.63	13.72
Perceptual Reasoning	98.74	7.33	100.70	14.36	97.95	7.63	101.07	14.60	100.02	6.71	100.11	14.09
Working Memory	97.39	8.43	95.50	13.37	96.60	8.73	95.08	13.72	98.67	7.85	96.17	12.90
Processing Speed*	99.02	6.21	93.20	13.35	99.44	6.67	95.33	11.95	98.33	5.38	89.72	14.85
Full Scale IQ	97.55	9.93	96.57	12.29	96.89	10.41	97.01	12.07	98.60	9.10	95.87	12.74

Note: Predicted scores derived on the basis of Test of Premorbid Functioning in combination with demographic variables. Obtained scores were derived from age-based norms.
*$p < .0001$ for comparison in complete sample.

Table 2. Regression model for Verbal Comprehension

Variable	*B*	SE B	ß	*t*	*p*<
Cognitive reserve index[a]	1.07	0.08	0.79	14.01	.0001
History of special education[b]	−1.36	2.40	−0.03	−0.57	.58
Other premorbid complicated history[b]	−0.04	1.51	−0.01	−0.02	.98
Injury severity[b]	−1.29	1.57	−0.05	−0.82	.42
Time since injury[a]	0.03	0.01	0.17	3.13	.003
Disputed financial compensation-seeking[b]	−1.02	1.69	−0.04	−0.60	.55
Level of depressive symptoms[a]	−0.32	0.12	−0.14	−2.55	0.02

[a]Continuous variable.
[b]Dichotomized variable.

Table 3. Regression model for Perceptual Reasoning

Variable	*B*	SE B	ß	*t*	*p*<
Cognitive reserve index[a]	0.86	0.17	0.44	5.06	.0001
History of special education[b]	−0.69	3.85	−0.02	−0.18	.86
Other premorbid complicated history[b]	−1.87	2.45	−0.06	−0.76	.45
Injury severity[b]	−2.66	2.56	−0.09	−1.04	.30
Time since injury[a]	0.03	0.01	0.18	2.13	.04
Disputed financial compensation-seeking[b]	−1.21	2.73	−0.04	−0.44	.66
Level of depressive symptoms[a]	−0.12	0.20	−0.06	−0.60	.55

[a]Continuous variable.
[b]Dichotomized variable.

Table 4. Regression model for Working Memory

Variable	*B*	SE B	ß	*t*	*p*<
Cognitive reserve index[a]	0.88	0.13	0.56	7.00	.0001
History of special education[b]	−3.86	3.29	−0.09	−1.17	.24
Other premorbid complicated history[b]	−1.24	2.10	−0.05	−0.59	.56
Injury severity[b]	−0.88	2.19	−0.03	−0.40	.69
Time since injury[a]	−0.01	0.01	−0.04	−0.52	.60
Disputed financial compensation-seeking[b]	−3.57	2.34	−0.12	−1.53	.13
Level of depressive symptoms[a]	−0.03	0.17	−0.01	−0.16	.87

[a]Continuous variable.
[b]Dichotomized variable.

Table 5. Regression model for Processing Speed

Variable	*B*	SE B	ß	*t*	*p*<
Cognitive reserve index[a]	0.78	0.20	0.36	3.99	.0001
History of special education[b]	−0.96	3.75	−0.02	−0.26	.80
Other premorbid complicated history[b]	−1.35	2.33	−0.05	0.58	.57
Injury severity[b]	−5.62	2.44	−0.21	−2.30	.03
Time since injury[a]	−0.01	0.01	−0.02	−0.27	.79
Disputed financial compensation-seeking[b]	−2.01	2.63	−0.07	−0.77	.45
Level of depressive symptoms[a]	−0.19	0.19	−0.09	−0.99	.33

[a]Continuous variable.
[b]Dichotomized variable.

The model for Working Memory was likewise statistically significant, $F(1, 113) = 8.63$, $p < .0001$ and explained a large proportion of the variance, Adjusted $R^2 = 0.31$. Cognitive reserve was the only statistically significant independent variable in this model.

Finally, the model for Processing Speed was statistically significant, $F(1, 113) = 3.78$, $p < .001$. This model explained a moderate proportion of the variance, Adjusted $R^2 = 0.14$. Whereas greater cognitive reserve was associated with better Processing Speed scores, greater injury severity was associated with worse results on this index.

Discussion

The main purpose of this investigation was to determine the extent to which cognitive reserve could be a protective factor against the effects of TBI on performance on the WAIS–IV. Hypothesis (1) was confirmed: Cognitive reserve, as measured by the TOPF in combination with demographic variables, was consistently a statistically significant variable in the regression models for all four WAIS–IV factor indices. In each case, greater cognitive reserve was strongly associated with better obtained factor index scores. Hypothesis (2) was also confirmed: Even after accounting for cognitive reserve and all other variables, injury severity was still a statistically significant predictor in the model for Processing Speed, and only in that model. Participants with intracranial lesions on neuroimaging and/or prolonged duration to follow commands did worse on Processing Speed than those with uncomplicated mild injuries.

The finding that cognitive reserve emerged as a statistically significant predictor in all of the four WAIS–IV regression models is consistent with previous research suggesting a protective effect of this variable in persons with TBI (Mathias & Wheaton, 2015; Oldenburg et al., 2016; Schneider et al., 2014). The fact that cognitive reserve was relatively much more influential than injury severity on cognitive test performance is also consistent with recent research (Leary et al., 2018; Steward et al., 2018). The novel contribution of the current investigation is that we were able to demonstrate this protective effect of cognitive reserve in a sample that was carefully selected to exclude those who were not providing valid effort during the cognitive testing, while at the same time also controlling for any effects of premorbid and concurrent complicating factors.

Consistent with our original prediction, injury severity contributed only to the model for Processing speed. This is consistent with prior research in our laboratory with an independent sample that demonstrated the unique sensitivity of this WAIS–IV index to TBI (Donders & Strong, 2015). In this context, it is important to appreciate that this influence of injury severity was still apparent, even after accounting for the effect of cognitive reserve. This finding suggests that cognitive reserve is a protective factor with regard to the influence of TBI, only up to a certain point. Greater injury severity will still affect performance on those domains, such as efficiency of information processing, that are less overlearned or crystallized and therefore more sensitive to acquired cerebral dysfunction.

The effect of injury severity was not conflated with time since injury, because the latter variable did not contribute to the model for Processing Speed. Longer time since injury was associated, however, with slightly better performance on both Verbal Comprehension and Perceptual Reasoning. It is possible that TBI may have a transient effect on these domains but that its impact is more substantial and more prolonged on measures of speed and efficiency of information processing.

A prior history of special education services for learning disability did not make a statistically significant contribution to any of the regression models. This suggests that even in persons with such a history, the degree and impact of cognitive reserve can still be measured in a valid manner with the TOPF in combination with demographic variables. Furthermore, the fact that the influence of both cognitive reserve as well as injury severity could still be measured on the Processing Speed index, in a sample with 12% who had a history of learning disability and 38% who had complicated mild to severe injuries, should put to rest potential concerns about under-estimation of premorbid levels of functioning of persons with TBI on the basis of word-recognition tasks (Mathias, Bigler, Bowden & Rosenfeld, 2007). Our findings are consistent with conclusions of previous researchers who have endorsed the use of such tasks in persons with TBI (Green et al., 2008).

Disputed financial compensation-seeking at the time of the neuropsychological assessment also did not contribute in a statistically significant manner to the prediction of any of the obtained WAIS–IV index scores. This is most likely because we excluded from this investigation any potential participants who failed performance validity tests. Previous research in our laboratory with a completely independent sample demonstrated that after accounting for the influence of performance validity, presence or absence of financial compensation-seeking no longer accounted for variance in neuropsychological test performance (Donders & Strong, 2011). Our current findings suggest that the routine use of performance validity tests during neuropsychological evaluations of persons with TBI, as recommended by several national professional organizations (Bush et al., 2005; Heilbronner et al., 2009), can help to facilitate the external validity of research with this population.

Level of depressive symptoms as measured by the PHQ–9 at the time of neuropsychological assessment contributed in a statistically significant manner only to the model for Verbal Comprehension. Previous research on the effect of depression on sequelae of TBI has yielded inconsistent results (Gass & Gutierrez, 2017; Khan-Bourne & Brown, 2003). Our findings are relatively most consistent with those of Sherman and colleagues (2000), who suggested that this effect is small and not widespread.

Potential limitations of this investigation must also be acknowledged. We used a referred convenience sample and limited our time frame to 1–12 months postinjury. Different results could potentially be found in a sample of consecutive emergency room visits (which would most likely include more persons with uncomplicated mild injuries) and/or with inclusion of persons who were several years postinjury. In this context, it is important to appreciate that many of the persons with uncomplicated mild TBI in the current study were referred because they remained subjectively symptomatic for more than 3 months, which is not the norm for such injuries (Karr, Areshenkoff & Garcia-Barrera, 2014; Kashluba, Paniak & Casey, 2008). Another limitation is that we did not include other measures of distress in our study, such as symptoms of anxiety, which are known to be common after TBI (Scholten et al., 2016). We were also not able to include in our definition of cognitive reserve other variables that have been considered in the literature, such as premorbid brain volume (Kesler, Adams, Blasey & Bigler, 2003), leisure activity (Levi, Rassovsky, Agranov, Sela-Kaufman & Vakil, 2013) or personality characteristics (Sela-Kaufman, Rassovsky, Agranov, Levi & Vakil, 2013).

With those reservations in mind, we conclude that cognitive reserve is a protective factor with regard to the cognitive sequelae of TBI but does not offer a complete buffer. The effect of injury severity can still be ascertained, after accounting for cognitive reserve and while controlling for premorbid and comorbid confounding factors, on measures that have previously been validated as being sensitive to TBI severity. The current findings support the use of the TOPF in conjunction with demographic variables as a measure of cognitive reserve in persons with TBI but future studies should incorporate additional premorbid characteristics. Another specific goal for future research is to elucidate the relative weight of specific individual demographic variables (e.g., geographic region, ethnicity) with regard to the concept of cognitive reserve. This would require a multi-center effort and more diverse sample.

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Conflict of interest

The authors report no conflict of interest.

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