Title

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Journal

Journal of Neurotrauma, 39(1-2)

ISSN

0897-7151

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Publication Date

2022

DOI

10.1089/neu.2020.7516

Peer reviewed

Journal of Neurotrauma
39:238–242 (January 2022)

DOI: 10.1089/neu.2020.7516

Journal of Neurotrauma

SHORT COMMUNICATION

Elevated Neuropsychological Intraindividual Variability Predicts Poorer Health-Related Quality of Life in Veterans with a History of Mild Traumatic Brain Injury

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Abstract

We examined the association between cognitive functioning and health-related quality of life (HR-QOL) in military veterans with a history of mild traumatic brain injury (mTBI) using two methods to assess cognition: mean performance on cognitive composite scores and across-test intraindividual variability (IIV). The sample included 73 veterans (84.9% male; age, mean = 32.47 years) who completed neuropsychological testing and self-report questionnaires ~7 years post-injury. Three cognitive composite scores representing mean performance were computed, including memory, attention/processing speed (A/PS), and executive functioning (EF). Three IIV indices were also calculated reflecting degree of dispersion across the same cognitive domains: memory-IIV, A/PS-IIV, and EF-IIV. The Posttraumatic Stress Disorder (PTSD) Checklist-Military Version (PCL-M) was used to assess current PTSD symptoms, and the World Health Organization Quality of Life Short Version Physical Health domain was used to assess HR-QOL. Hierarchical linear regressions adjusting for PTSD symptoms demonstrated that IIV indices, but not mean cognitive composite scores, significantly predicted HR-QOL. Specifically, memory-IIV, A/PS-IIV, and EF-IIV, when taken together, made an independent and significant contribution to the prediction of HR-QOL. Examination of the standardized coefficients showed that the A/PS-IIV index was uniquely associated with HR-QOL, such that higher A/PS-IIV scores significantly predicted poorer HR-QOL. Our results are the first to show that, in veterans with remote mTBI histories, greater fluctuations in cognitive performance significantly contribute to poorer HR-QOL, even after accounting for PTSD symptom severity. Moreover, findings suggest that, compared to traditional mean cognitive performance scores, measures of IIV may represent more sensitive indicators of clinical outcome and better align with subjective experiences of distress.

Keywords: concussion; cognitive dispersion; head injury; health outcomes; IIV; military

Introduction

It has been well documented that military veterans with a history of mild traumatic brain injury (mTBI) demonstrate reduced health-related quality of life (HR-QOL) post-injury.[1–3] Many definitions of HR-QOL have been proposed in the literature, and, although there is no universal definition of this construct, the World Health Organization (WHO) has long emphasized that HR-QOL refers to one's *subjective* evaluation or *perception* of well-being.[4] Specifically, the WHO defines HR-QOL as ''individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.''[4]

In the context of military mTBI, a number of factors have been shown to be associated with poorer HR-QOL—particularly mental health comorbidities such as post-traumatic stress disorder.[5,6] However, few studies have evaluated associations between cognitive functioning and HR-QOL in this population. Even within the

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broader TBI literature, the relationship between cognitive performance and HR-QOL is not well understood. Whereas some studies have found an association between cognitive dysfunction and poorer HR-QOL,[7,8] other studies have shown no such relationship, especially after adjusting for comorbid mental health symptoms.[9] Better clarifying this relationship is essential, given that this information could be leveraged when assessing veterans with mTBI histories and tailoring treatments to optimize clinical outcomes in the aftermath of remote mTBI.

The purpose of the present study was to examine the association between cognitive functioning and HR-QOL using two methods to assess cognition: 1) mean performance on cognitive composite scores and 2) across-test intraindividual variability (IIV), or cognitive dispersion. Although cognitive functioning is traditionally evaluated using measures of central tendency—specifically, mean scores—it is possible that a strict focus on mean performance may obscure important nuances associated with one's cognitive profile, especially in mTBI populations where objective cognitive deficits are typically more subtle and mild, at least in younger populations. As such, past research has advocated for the use of IIV measures, suggesting that this approach may better capture unique aspects of cognitive functioning that may be associated with recovery and clinical outcomes.[10,11] We therefore hypothesized that, within our well-characterized sample of military veterans with a history of mTBI, measures of IIV would have stronger associations with HR-QOL than measures of mean cognitive performance.

Methods

Participants and procedures

Participants ($N = 73$) were veterans with a history of mTBI who were recruited from the VA San Diego Healthcare System (VASDHS). Study procedures involved completion of a semistructured interview assessing TBI history, neuropsychological testing, and self-report questionnaires (see below under *Measures* for details). Inclusion criteria included having a history of at least one mTBI as defined by Department of Veterans Affairs/Department of Defense (VA/DoD) criteria[12] and completing all relevant study procedures. Exclusion criteria included having a history of moderate or severe TBI, a serious neurological/medical condition (e.g., dementia, stroke) or psychiatric condition (e.g., schizophrenia, bipolar disorder), and current or recent (within the past month) substance abuse or dependence. Additional exclusion criteria included performance validity test failure (described below under *Measures*). Institutional review board approval was obtained from the VASDHS, and all participants provided informed consent before participating in research activities.

Measures

A modified version of the VA Semi-Structured Clinical Interview for TBI[13] was used to gather details pertaining to lifetime TBI history. Specifically, the interview is designed to collect information pertaining to date(s) of injury, mechanism(s) of injury, and the presence/duration of loss of consciousness (LOC), alteration of consciousness (AOC), and post-traumatic amnesia (PTA) for any injury event reported. Those with a confirmed history of at least one mTBI based on VA/DoD guidelines[12] were eligible for participation.

A comprehensive neuropsychological assessment was administered to all veterans to assess the broad domains of memory, attention and processing speed, and executive functioning. The test battery included the following measures: California Verbal Learning Test-Second Edition (CVLT-II); Logical Memory and Visual Reproduction from the Wechsler Memory Scale-Fourth Edition (WMS-IV); Rey Complex Figure Test (RCFT); Block Design from the Wechsler Abbreviated Scale of Intelligence-Second Edition (WASI-II); Coding and Symbol Search from the Wechsler Adult Intelligence Scale-Fourth Edition (WAIS-IV); Design Fluency, Trail Making, and Verbal Fluency from the Delis-Kaplan Executive Function System (D-KEFS); and the Wisconsin Card Sorting Test-64 Card Version (WCST-64). In addition to the above core tests, the Reading subtest from the Wide Range Achievement Test 4 (WRAT4) was administered to assess pre-morbid functioning, and measures of performance validity included the Test of Memory Malingering (TOMM) and the CVLT-II Forced Choice Recognition subtest. Performance validity test failure was defined as inadequate performance (based on manual-specific guidelines) on either TOMM Trial 2, TOMM Retention, *or* CVLT-II Forced Choice Recognition; participants demonstrating inadequate performance on *one or more* of these measures were excluded.

In total, 25 variables were selected from the neuropsychological assessment and were converted from raw to norm-referenced standard scores using procedures described previously.[14] Three cognitive composite scores, including memory (eight items: CVLT-II Trials 1–5 Total Recall, Short Delay Free Recall, and Long Delay Free Recall; WMS-IV Logical Memory I and II; WMS-IV Visual Reproduction I and II; and RCFT Delay), attention/processing speed (A/PS; seven items: D-KEFS Trail Making Visual Scanning, Number Sequencing, Letter Sequencing, and Motor Speed; WASI-II Block Design; and WAIS-IV Coding and Symbol Search), and executive functioning (EF; 10 items: D-KEFS Design Fluency Filled, Empty, and Switching; D-KEFS Trail Making Number-Letter Switching; D-KEFS Verbal Fluency Letter, Category, Switching, and Switching Accuracy; and WCST-64 Perseverate Responses and Total Errors), were computed to represent mean cognitive performance.

Additionally, three IIV indices were calculated reflecting degree of dispersion across the same cognitive domains (memory-IIV, A/PS-IIV, and EF-IIV). Each IIV index was computed by taking the standard deviation of the standard scores associated with each cognitive domain.

The 17-item PTSD Checklist-Military Version (PCL-M)[14] was used to assess current PTSD symptoms. Veterans were asked to evaluate the degree to which they have been bothered by each symptom over the past month, using a rating scale ranging from ''1'' (not at all) to ''5'' (extremely). A PCL-M total score is generated by summing together the 17 items; higher scores on this measure reflect more severe PTSD symptoms.

The 26-item World Health Organization Quality of Life Short Version (WHOQOL-BREF)[4] was used to assess HR-QOL; for the purpose of this study, the Physical Health domain from the WHOQOL-BREF was evaluated. The Physical Health domain includes items assessing activities of daily living, reliance on medical treatments, sleep, pain, mobility, capacity for work, and energy. The Physical Health domain score ranges from 0 to 100; higher scores reflect better functioning.

Statistical analysis

To examine the association between cognitive functioning and HR-QOL, hierarchical linear regressions were conducted. PTSD symptoms (PCL-M total score) were entered in the first block, and cognitive scores were entered in the second block. Mean cognitive performance indices and IIV indices were evaluated in separate regressions. Although there were significant associations among the mean cognitive composite scores (rs = 0.345 to 0.529; ps = <0.001 to 0.003), tolerance and variance inflation factor (VIF) statistics indicated that multi-collinearity was not an issue (tolerance = 0.64–0.78; VIF = 1.28–1.57). As for the IIV indices, there were no significant associations among these variables (rs = −0.020 to 0.181; ps = 0.126 to 0.867). All analyses were conducted using SPSS software (Version 27; SPSS, Inc., Chicago, IL).

Availability of data

The data that support the findings of this study are available from the corresponding author, L.D.W., upon reasonable request.

Results

Veterans participating in this study had predominantly served in the Iraq and Afghanistan conflicts (98.6%), and the majority of participants had a history of combat exposure (74.0%). On average, veterans completed neuropsychological testing 7 years after their most recent mTBI. Participant characteristics, including sociodemographic variables, psychiatric measures, cognitive performance measures, and HR-QOL, are presented in Table 1.

Table 1. Participant Characteristics (N = 73)

Variable	*Mean (SD)/N (%)*
Sociodemographic characteristics	
Age, years	32.47 (6.69)
Education, years	14.16 (1.72)
WRAT-4 Reading (SS)	101.78 (10.73)
Sex	—
Male	62 (84.9%)
Female	11 (15.1%)
Ethnicity	—
White	37 (50.7%)
Hispanic	22 (30.1%)
Black	7 (9.6%)
Asian/Pacific Islander	6 (8.2%)
Native American	1 (1.4%)
Military branch of service	—
Air Force	5 (6.8%)
Army	20 (27.4%)
Marines	26 (35.6%)
Navy	22 (30.1%)
Injury characteristics	—
AOC present	32 (43.8%)
LOC present	41 (56.2%)
PTA present	38 (52.1%)
Time since most recent injury, months	66.27 (33.30)
Lifetime no. of mTBIs	2.56 (1.37)
Psychiatric measures	
PCL-M Total Score	43.23 (16.48)
Mean cognitive performance	
Memory Composite (SS)	99.36 (10.48)
Attention/Processing Speed Composite (SS)	99.65 (9.99)
Executive Functioning Composite (SS)	99.00 (8.21)
IIV cognitive performance	
Memory-IIV	10.08 (3.91)
Attention/Processing Speed-IIV	10.91 (4.61)
Executive Functioning-IIV	11.91 (4.10)
HR-QOL	
WHOQOL-BREF Physical Health Domain Score	48.95 (12.27)

SD, standard deviation; WRAT-4, Wide Range Achievement Test 4; SS, standard score (mean [M] = 100, standard deviation [SD] = 15); AOC, alteration of consciousness; LOC, loss of consciousness; PTA, post-traumatic amnesia; mTBIs, mild traumatic brain injuries; PCL-M, Posttraumatic Stress Disorder (PTSD) Checklist-Military Version; IIV, intraindividual variability; HR-QOL, health-related quality of life; WHOQOL-BREF, World Health Organization Quality of Life Short Version.

Hierarchical linear regression revealed that PTSD symptoms significantly contributed to the prediction of HR-QOL (F = 9.84; p = 0.002) and accounted for roughly 12% of the variance in HR-QOL. Although the overall model remained significant when the three mean cognitive composite scores were added in the second block (F = 3.42; p = 0.013), the change in R^2 (5%) was not significant (ΔF = 1.25; p = 0.299). In contrast, with PTSD symptoms entered in the first block and the three IIV indices entered in the second block, the overall model was significantly associated with HR-QOL (F = 5.02; p = 0.001) and the change in R^2 was significant (ΔF = 3.12; p = 0.031), with the IIV indices explaining an *additional* 11% of the variance in HR-QOL. Examination of the standardized coefficients showed that the A/PS-IIV index was uniquely associated HR-QOL, such that higher A/PS-IIV scores significantly predicted poorer HR-QOL (B = −0.29; p = 0.007). These results are presented in Table 2.

Table 2. Results of Hierarchical Linear Regression Analyses Examining Associations between Mean Cognitive Performance and Cognitive Intraindividual Variability on Health-Related Quality of Life after Mild Traumatic Brain Injury

	R	R^2	B	t	p *value*
Block 1: PTSD	0.35	0.12			
PCL-M Total Score			–0.35	–3.14	0.002
Block 2: Mean Cognitive Performance	0.41	0.17			
PCL-M Total Score			–0.32	–2.80	0.007
Memory Composite			–0.11	–0.90	0.373
Attention/Processing Speed Composite			0.22	1.67	0.100
Executive Functioning Composite			–0.14	–1.04	0.301
Block 1: PTSD	0.35	0.12			
PCL-M Total Score			–0.35	–3.14	0.002
Block 2: IIV Cognitive Performance	0.48	0.23			
PCL-M Total Score			–0.36	–3.37	0.001
Memory-IIV			–0.03	–0.29	0.774
Attention/Processing Speed-IIV			–0.29	–2.76	0.007
Executive Functioning-IIV			–0.13	–1.24	0.221

PTSD, post-traumatic stress disorder; PCL-M, PTSD Checklist-Military Version; IIV, intraindividual variability.

Discussion

In the present study, we showed that, in veterans with remote mTBI histories, higher cognitive IIV—or greater inconsistences in cognitive performance—was significantly associated with poorer HR-QOL, even after accounting for PTSD symptom severity. In contrast, mean cognitive performance was not associated with HR-QOL. These findings suggest that 1) it is important to leverage metrics beyond those of central tendency to examine cognitive functioning and 2) measures of IIV may be a more robust and sensitive marker of meaningful clinical outcomes than traditional mean cognitive performance in this population.

Surprisingly, few studies have examined the association between cognitive functioning and HR-QOL after mTBI, and, among the published studies available for review, findings have been mixed.[7–9] Our results suggest that although mean cognitive performance does not appear to be associated with veterans' HR-QOL after mTBI, IIV indices *are* related to this key functional outcome. Specifically, greater variability across measures of attention/processing speed was associated with poorer HR-QOL across the sample. Stated differently, greater dispersion of scores associated with attention and processing speed was predictive of poorer physical health (e.g., sleep, pain, activities of daily living, capacity for work, etc.) in veterans with a history of mTBI.

These findings are particularly interesting in light of earlier research showing that *subjective* symptoms do not align well with *objective* markers of cognitive functioning.[15,16] Traditionally, performance on a neuropsychological assessment has been evaluated using measures of central tendency—that is, comparing an individual's test scores to group means and standard deviations derived from a normative sample to determine that individual's cognitive strengths and weaknesses.[17] Although this approach has tremendous utility for many clinical populations, it is possible that an exclusive focus on mean cognitive performance may overlook some nuances associated with one's cognitive profile.[18] As a result, there has been a recent trend in the neuropsychological literature to develop and utilize other innovative methods to assess cognitive dysfunction—expressly, measures of IIV or cognitive dispersion.[17]

Although still a relatively new area of exploration within TBI, there is accumulating evidence to suggest that, relative to mean performance, IIV indices may better predict poor recovery from brain injury. Our results further support this literature by establishing an important association between elevated IIV and poorer HR-QOL. Moreover, our findings suggest that although there may not be a strong association between mean cognitive functioning and subjective distress after mTBI, measures of IIV may serve as more sensitive indicators of HR-QOL and better align with one's subjective experience of distress.

Although our findings have important clinical relevance, there are limitations associated with the study that should be considered. First, our sample size was relatively small and findings will need to be replicated using larger samples. Second, as with previous research evaluating IIV, it is possible that different results may have been obtained had we used other neuropsychological tests or included other variables in our IIV indices. More research is needed in order to verify the reliability and validity of IIV metrics. Third, given that our sample specifically evaluated military service members with a remote history of mTBI, caution should be taken when generalizing the results of this study to non-military populations, acutely injured samples, and those with more severe injuries.

Relatedly, it should be acknowledged that the observed relationship between IIV and HR-QOL may not be specific to mTBI. In other words, it is possible that other clinical samples may demonstrate greater cognitive IIV and that the association between elevated IIV and poorer HR-QOL may occur irrespective of mTBI status. Although past research has demonstrated that IIV is elevated in mTBI samples relative to non-TBI samples,[11,12] more research is needed to clarify the extent to which elevated IIV is a function of mTBI. Future research is also needed to determine what other factors (e.g., comorbid mental health conditions, other health and lifestyle factors, etc.) contribute to elevated IIV and whether this increased variability is uniquely related to mTBI or mTBI-related characteristics (e.g., presence or duration of LOC or PTA, lifetime number of mTBIs, extent of combat exposure, etc.). Finally, the data used in this study were cross-sectional and future studies are needed to better determine and elucidate cause-effect relationships.

Conclusion

These study findings add to a growing body of literature highlighting that, compared to traditional mean cognitive performance scores, measures of IIV represent more robust and sensitive indicators of clinical outcomes after mTBI. Taken together, our results suggest that evaluating IIV indices may help identify veterans at risk for poor HR-QOL after mTBI, and they may help clinicians tailor treatments to optimize clinical outcomes in this vulnerable population. In particular, in addition to utilizing measures of central tendency and comparing an individual's performance to normative data, it may be worthwhile for clinicians to also compute cognitive dispersion scores to determine the extent to which patients are displaying elevated cognitive IIV. Based on the results of this study, such elevations may be a clinically meaningful risk factor for poor long-term outcomes.

Acknowledgments

The authors sincerely thank the veterans who volunteered to participate in this study.

Authors' Contributions

V.C.M.: Conceptualization, Methodology, Formal Analysis, Writing–Original Draft. M.S.S.: Conceptualization, Writing–Review & Editing. S.F.S.: Investigation, Writing–Review & Editing. A.L.C.: Writing–Review & Editing. M.W.B.: Writing–Review & Editing. D.M.S.: Investigation, Writing–Review & Editing. L.D.W.: Conceptualization, Methodology, Investigation, Writing–Review & Editing.

Funding Information

This work was supported by Veterans Affairs research grants awarded to Drs. Delano-Wood (CDA-2-034-07F; I01 CX000842-01) and Schiehser (CDA-2-065-10S), as well as a Department of Defense Investigator-Initiated Research Grant awarded to Dr. Delano-Wood (W81XWH-10-2-0169). This work was further supported by a grant awarded by the National Institute of Neurological Disorders and Stroke of the National Institutes of Health (F31NS09870) to Dr. Clark and a grant awarded by the National Institutes of Health (F31NS0987) to Dr. Bondi. Drs. Merritt and Sorg both received salary support during this work from Career Development Awards from the VA Clinical Science Research & Development Service (Merritt: IK2 CX001952; Sorg: CX001508-02).

Author Disclosure Statement

No competing financial interests exist.

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