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The Effects of Mild Traumatic Brain Injury, Post-Traumatic Stress Disorder, and Combined Mild Traumatic Brain Injury/Post-Traumatic Stress Disorder on Returning Veterans

Hannah L. Combs,[1] David T. R. Berry,[1] Theresa Pape,[2,3] Judith Babcock-Parziale,[4] Bridget Smith,[2,3] Randal Schleenbaker,[5,6] Anne Shandera-Ochsner,[1,7] Jordan P. Harp,[1] and Walter M. High, Jr.[5,6]

Abstract

United States veterans of the Iraqi (Operation Iraqi Freedom [OIF]) and Afghanistan (Operation Enduring Freedom [OEF]) conflicts have frequently returned from deployment after sustaining mild traumatic brain injury (mTBI) and enduring stressful events resulting in post-traumatic stress disorder (PTSD). A large number of returning service members have been diagnosed with both a history of mTBI and current PTSD. Substantial literature exists on the neuropsychological factors associated with mTBI and PTSD occurring separately; far less research has explored the combined effects of PTSD and mTBI. The current study employed neuropsychological and psychological measures in a sample of 251 OIF/OEF veterans to determine whether participants with a history of mTBI and current PTSD (mTBI + PTSD) have poorer cognitive and psychological outcomes than participants with mTBI only (mTBI-o), PTSD only (PTSD-o), or veteran controls (VC), when groups are comparable on intelligence quotient, education, and age. The mTBI + PTSD group performed more poorly than VC, mTBI-o, and PTSD-o groups on several neuropsychological measures. Effect size comparisons suggest small deleterious effects for mTBI-o on measures of processing speed and visual attention and small effects for PTSD-o on measures of verbal memory, with moderate effects for mTBI + PTSD on the same variables. Additionally, the mTBI + PTSD group was significantly more psychologically distressed than the PTSD-o group, and PTSD-o group was more distressed than VC and mTBI-o groups. These findings suggest that veterans with mTBI + PTSD perform significantly lower on neuropsychological and psychiatric measures than veterans with mTBI-o or PTSD-o. The results also raise the possibility of mild but persisting cognitive changes following mTBI sustained during deployment.

Key words: assessment; mild TBI; PTSD; veterans

Introduction

In military settings, mild traumatic brain injury (mTBI) has gained widespread attention and has been labeled as the ''signature injury'' of the Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) conflicts. Recent studies estimate that approximately 12% to 16% of veterans sustained an mTBI during deployment.[1,2] The vast majority of these mTBIs were associated with blast exposures from improvised explosive devices, which are common in contemporary combat zones.[3] In civilian contexts, cognitive difficulties, including impairments in attention, memory efficiency, and processing speed, immediately following mTBI are common.[4] However, most studies with appropriate comparison groups that objectively measure cognitive effects, have shown that the cognitive effects of mTBI resolve within days to at most three months post-injury.[5–8]

Nevertheless, small subsets of civilians with mTBI report the subjective experience of chronic cognitive deficits despite a positive long-term prognosis.[9,10] Several explanations for persistent subjective cognitive complaints after mTBI have been offered. In a comprehensive review, Binder and colleagues[11] suggested that either most individuals with mTBI experience a very small (~5%) but statistically significant decline in attention, compared with pre-injury ability levels, or approximately 4% to 6% of those with mTBI experience lasting deficits in attention. The subjective experience of cognitive decline also has been explained using psychological mechanisms such as distress, problematic coping, iatrogenic effects, or the effects of substance abuse.[12,13] However,

[1]Department of Psychology, [5]Department of Physical Medicine and Rehabilitation, University of Kentucky, Lexington, Kentucky.
[2]Edward Hines Jr. Hospital, Hines, Illinois.
[3]Northwestern University Feinberg School of Medicine, Chicago, Illinois.
[4]Southern Arizona Department of Veterans Affairs Health Care System, Tucson, Arizona.
[6]Lexington Veterans Affairs Medical Center, Lexington, Kentucky.
[7]Department of Psychiatry and Psychology, Mayo Clinic, Jacksonville, Florida.

some researchers argue that these alternative factors cannot account for all individuals reporting chronic cognitive impairment.[14–16]

Post-traumatic stress disorder

Post-traumatic stress disorder (PTSD), a severe anxiety disorder that may develop after exposure to a traumatic experience, also is common in veterans. Rates of PTSD in returning service personnel are roughly comparable to rates of mTBI, ranging from 13–17%.[17] Evidence indicates that the development of PTSD in veterans is highly specific to combat experience and being injured rather than the result of simply being deployed to a war zone.[18,19]

Although PTSD is often viewed primarily as dysfunctional regulation of fear conditioning, PTSD also has a significant impact on neuropsychological functioning.[20] Research has shown that PTSD is highly associated with impairments in memory, attention, and executive functioning on objective cognitive measures.[20–22] Further, impairments in memory and attention also are common to the clinical presentation of PTSD as referenced in the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (Text Revision)* diagnostic criteria.[23]

A recent meta-analysis found a small to moderate association between PTSD symptoms and immediate and delayed verbal memory impairments.[22] Johnsen and Asbjørnsen[24] concluded that these memory impairments were seen in both military and civilian samples, although the strongest effects were seen amongst veterans. Samuelson and colleagues[25] found significant verbal memory impairments in veterans with PTSD, even after controlling for depression and substance abuse. Samuelson and colleagues controlled for intelligence quotient (IQ) score (a potential risk factor for developing PTSD) and education differences and found that a PTSD group still performed significantly worse than controls on the California Verbal Learning Test, suggesting that memory impairments cannot be accounted for solely by pre-morbid IQ differences.[26] It should be noted that the study by Samuelson and colleagues investigated neuropsychological functioning in children, and these findings may not replicate with adults.

Mild traumatic brain injury and post-traumatic stress disorder

Military personnel who serve in combat areas are at greater risk for both mTBI and PTSD than military personnel without such service. Recent data indicate an increasing number of veterans returning from deployment with both mTBI and PTSD. Vanderploeg and colleagues[10] indicated that approximately one-third of OIF veterans with mTBI also have PTSD (or depression); similar high comorbidity rates were found by Hoge and colleagues.[1] Given the frequent co-occurrence of these disorders in returning veterans, clinical and research interest is high, however, research has only recently begun to systematically study PTSD and mTBI as comorbid conditions.

Studying the effect of combined mTBI and PTSD (mTBI+PTSD) on neuropsychological functioning has proven challenging. Findings are conflicting, especially as to whether or not the co-occurrence of mTBI+PTSD leads to deficits over and above their individual effects. Brenner and colleagues[27] examined the performance of veterans on neurocognitive tasks and compared a group with PTSD only (PTSD-o) and a group with mTBI+PTSD. The test battery included measures of processing speed, inhibition, abstract concept formation, set shifting and maintenance, immediate memory, delayed recall, visual search, tracking, sustained attention, and working memory. The authors found no statistically significant differences between the groups on any of these tests. Gordon and colleagues reported similar null results.[28]

However, there has been some evidence indicating neuropsychological deficits unique to patients with mTBI+PTSD. One study demonstrated lower processing speed scores (as measured by Stroop Word Reading task) in veterans with mTBI+PTSD, compared with those with PTSD-o.[27] This finding supported an earlier study by Nelson and colleagues[29] who looked at OIF/OEF veterans with history of mild to moderate TBI-o and found that the mTBI+PTSD group scored worse than the mild-moderate TBI-o group on measures of speed of information processing and response inhibition. Barrett and colleagues[30] also found evidence for veterans with mTBI+PTSD performing worse on set-shifting (an executive function task) using PTSD-o and PTSD+comorbid psychiatric diagnosis comparison groups. Brenner and colleagues[31] examined a sample of Iraq veterans, those with mTBI+PTSD and those with only mTBI. The authors found no statistically significant differences between the two groups on cognitive variables; however, they reported that large effect sizes seen on tests of attention, inhibition, and executive functioning may suggest poorer performance in the combined mTBI+PTSD group. In this sample, there was no estimate of pre-morbid IQ and the mTBI+PTSD group were significantly less educated than the mTBI-o group.[31] These studies suggest that the co-occurrence of mTBI and PTSD may be associated with greater cognitive difficulties; however, there are several methodological issues to be considered.

Effect sizes for the mTBI+PTSD groups in the studies by Brenner and colleagues and Nelson and colleagues suggest potentially important differences in neuropsychological performance between veterans with mTBI+PTSD and veterans with mTBI-o, but both studies lacked a PTSD-o comparison group.[29,31] Without a PTSD-o comparison group, it is extremely difficult to confidently distinguish the effects of PTSD from mTBI or to evaluate the possible interactive effects. Campbell and colleagues[32] were the first to include a critical PTSD-o control group. The authors found mixed results, possibly due to limited statistical power from a small sample. The mTBI+PTSD group performed significantly worse than PTSD-o on a verbal processing speed task (Stroop Color Reading) and both the PTSD-o and mTBI+PTSD groups had significantly poorer performances than mild-moderate TBI-o group on a test of inhibition (Stroop Color-Word).

Given the potential for compensation for disability resulting from either mTBI or PTSD in veterans, another noteworthy limitation to the current literature on the combined effects of mTBI+PTSD is that most neuropsychological studies have not employed measures of psychiatric symptom validity. Where validity measures have been used, only measures of neurocognitive symptom validity have been employed. This limitation, combined with the reliance on brief self-report questionnaires for diagnosing PTSD, may raise possible questions about the validity of the PTSD diagnoses.

Shandera-Ochsner and colleagues[33] were among the first to explore both neurocognitive and psychiatric impairments following mTBI+PTSD, PTSD-o, and mTBI-o, compared with a combat control group. Their study of 81 OIF/OEF veterans suggested that PTSD has the greatest effect on neuropsychological functioning post-deployment. There were no significant differences between the mTBI+PTSD and the PTSD-o groups on any neuropsychological measure and the mTBI-o group performed comparably to the combat control group on all neuropsychological measures. However, the mTBI+PTSD group was significantly more psychologically distressed than the mTBI-o or the PTSD-o group, and the

mTBI-o group was more distressed than the combat controls. This study suggested that PTSD contributes more to neurocognitive impairments when compared with the contribution of mTBI. However, conclusions that can be drawn from that study are limited because the groups were not equivalent on estimated pre-morbid IQ, education level, and combat exposure. A further limitation of the study was the small sample size. Examination of the effect sizes suggested a possible small to moderate effect for mTBI but the study was only powered to detect a large effect-size.

The present study employs neuropsychological and psychological assessment measures in a much larger sample to determine whether veterans with mTBI + PTSD have poorer cognitive and psychological outcomes, compared with veterans with mTBI-o, PTSD-o, and veteran controls (VC). The larger sample also allowed for control of potentially confounding variables such as age, education, and estimated pre-injury IQ (as estimated by the Wechsler Test of Adult Reading). Based on previous work, it was expected that the mTBI + PTSD and PTSD-o groups would perform more poorly on the neuropsychological measures, compared with the mTBI-o and VC groups and that there would be no differences between the mTBI + PTSD and PTSD-o groups. It also was expected there would be no differences between the mTBI-o and VC groups on neuropsychological measures. It was further hypothesized that the mTBI + PTSD group would endorse more psychiatric distress than all other groups on diagnostic measures. As described below, groups were comparable on estimated pre-injury IQ, education, and combat exposure to address the methodological concerns identified in the previous study.

Methods

Participants

The present study was funded by the Health Services Research and Development (HSR&D) service of the Department of Veterans Affairs (VA). The main study's purpose was to examine the sensitivity and specificity of screening measures and comprehensive evaluations for persisting symptoms following mTBI sustained during OIF/OEF deployments. As part of that study, extensive neuropsychological and psychological evaluations were conducted on 438 OIF/OEF veterans identified at Veterans Affairs Medical Centers (VAMCs) in Lexington, KY, Tucson, AZ, and Hines, IL. Participants were recruited through three strategies: 1) Veterans were referred to research staff by polytrauma clinic staff; 2) A random sampling of veterans was mailed an introductory letter along with an opt-out postcard. If a veteran did not return the postcard then they were contacted by phone; and 3) Study flyers were disseminated at large events frequented by OIF/OEF veterans. It should be noted that the present sample potentially included all veteran participants from the three centers involved, whereas the previous report by Shandera-Ocshner and colleagues was based on a subset of participants from the Lexington VAMC alone ($n = 81$).[33] Approval for the study was obtained from the VA Centralized Institutional Review Board (IRB) and the Lexington, Tucson, and Hines VA Medical Center Research and Development Committees. Informed consent and Health Insurance Portability and Accountability Act authorization were obtained from all study participants. Veterans were required to complete full-day clinical or research test batteries and were paid $160 for their participation.

Measures

All tests were administered on a single day with a minimum of two breaks. The order of tests was fixed for all participants and the evaluation took approximately 4–6 h. Since projections indicate that approximately 40% of mTBI claims and 20–30% of PTSD claims contain probable invalid symptom reporting,[34,35] several tests of psychiatric symptom validity or inadequate effort were incorporated in the test battery. As noted earlier, much of the current research has not studied the issue of effort in this particular context. All participants were administered the Letter Memory Test (LMT), which is a 45-item, forced-choice recognition task that uses letters as stimuli and manipulates apparent difficulty level through variation of the number of letters to be remembered and the number of choices from which the target stimulus must be selected.[36] Inman and colleagues found that the LMT discriminated poorly motivated from well-motivated groups at a moderately high level of accuracy and had high internal consistency reliability.[36] A recent meta-analysis showed LMT efficacy in differentiating feigned and honest responders to be comparable to the Word Memory Test (WMT), the Digit Memory Test (DMT), and the Test of Memory Malingering (TOMM).[37] Using the optimal cut-rate of 93%, the LMT has moderate sensitivity (70.2%) and high specificity (93%) to detect feigning.[37]

The participants also were administered the Miller Forensic Assessment of Symptoms Test (M-FAST), a 25-item structured interview designed to screen for invalid psychiatric symptoms.[38] All participants also completed the Minnesota Multiphasic Personality Inventory-2 Restructured Form (MMPI-2-RF).[39] The MMPI-2-RF is a 338-item self-report measure of personality and psychopathology, a revised version of the MMPI-2. The MMPI-2-RF contains embedded validity scales designed to detect random responding, faking-bad, defensiveness, and other problematic response sets. Mason and colleagues examined the sensitivity of the MMPI-2-RF validity scales at detecting feigned PTSD symptoms.[40] The authors found that using a cut-off of 100T on the revised F scale provided optimal sensitivity and specificity for detecting feigned PTSD.

To assess for PTSD, participants were administered the Clinician Administered PTSD Scale (CAPS). Regarded as the gold standard diagnostic assessment tool for PTSD, the CAPS is a structured interview used clinically to determine whether a person meets DSM-IV criteria for PTSD.[41] The measure has 30 items and takes approximately 45 min to 1 h to administer. Determination of mTBI was made utilizing a Structured Interview for TBI Diagnosis in OEF/OIF Veterans, based on an interview validated by Donnelly and colleagues at the BuffaloVA.[42] A veteran was considered to have sustained a deployment mTBI if the criteria provided by the American Congress of Rehabilitation Medicine were met by his or her responses to the TBI interview questions regarding loss of consciousness and alteration of consciousness with likelihood of mTBI rated as ''almost certainly'' or ''very likely.''[43] The form was modified by researchers at the Lexington, Tucson, and Hines VAs for use in the multi-site study.

All participants also were administered the Beck Depression Inventory (BDI-II) and the Beck Anxiety Inventory (BAI). The BDI-II is a 21-item self-report measure that assesses the presence and severity of symptoms of depression.[44] The BDI-II has excellent reliability, an internal consistency alpha of 0.92, and one week test–retest correlation of 0.93. The BAI is a 21-item self-report measure that assesses the presence and severity of anxiety symptoms.[45] The BAI has high internal consistency (alpha = 0.92) in outpatients and good test-retest reliability after one week ($r = 0.75$).

All participants were administered the Wechsler Test of Adult Reading (WTAR),[46] which uses irregular word reading ability and demographic information to estimate pre-morbid Full Scale IQ (FSIQ). The California Verbal Learning Test (CVLT-II) was administered to measure verbal memory ability. The CVLT-II involves oral presentation of a 16-item word list over five learning trials, an interference trial, short-delay recall (free and cued portions), 20-min ''long-delay'' recall, and recognition trials.[47] The Conners' Continuous Performance Task (CPT-II) was administered as a measure of attention, response speed, variability, errors in failing to inhibit a response, and errors in failing to respond. The CPT-II is a computerized test that requires the participant to make a response to all stimuli (letters) that appear on the screen

except for the letter ''x.''[48] The rate at which the stimuli appear varies throughout the test.

Participants also were administered the ''classic'' neuropsychological tests of executive functioning (Trail-Making Test, Verbal Fluency, Figural Fluency, Stroop) subtests of the Delis-Kaplan Executive Function System (D-KEFS). The D-KEFS provides a standardized method of examination of executive function sub-systems and a consistent normative group on which to base interpretations.[49] Reliability and validity data for the D-KEFS subtests used in the current study indicate good psychometric properties overall. Test–retest reliability (average interval length of 25 d) correlations fall in the moderate to high range for the Trail Making Tests, Verbal Fluency, and Color-Word with some evidence of practice effects.

The Wechsler Adult Intelligence Scale (WAIS-IV) is known as the ''gold standard'' intelligence test in the assessment of adults.[50] All participants were administered two of the 10 core subtests—Coding and Symbol Search—allowing for the calculation of the Processing Speed Index (PSI).

Selection of study sample

Subjects from the primary study database were potentially included in the present study sample if they met the recommended cutting scores for the aforementioned effort tests. Of the 438 veterans seen for clinical and/or research purposes at the Lexington, Tucson, and Hines VAMCs during the 15-month duration of the study, 75 were excluded from data analyses because they violated the recommended cutoff scores on one or more of the effort tests or validity scales: 33 scored less than 93% on LMT, 40 scored above 6 on M-FAST, four scored above 80T on Variable Response Inconsistency, six scored above 80T on True Response Inconsistency, 10 scored above 80T on L Scale, and 48 scored above 100T on F Scale (the recommended cut-off score suggested for invalid PTSD responding).[39] Out of the 75 veterans excluded, 43 failed one effort measure, 21 failed two effort measures, and 11 failed three effort measures. Additionally, 34 were excluded due to post-deployment mTBI and 26 were excluded due to history of childhood attention-deficit/hyperactivity disorder/attention deficit disorder.

Other psychiatric and substance abuse diagnoses were not excluded in the present study due to the high prevalence of these diagnoses in OIF/OEF veterans (over 85% of veterans with mTBI and over 40% of those without mTBI) described by Carlson and colleagues.[51] Also, estimates from the literature suggest more than two-thirds of individuals with PTSD have at least one other comorbid Axis I diagnosis.[52, 53]

Diagnostic assignment

For veterans remaining after the above noted exclusionary criteria, diagnostic assignment was based on the veteran's responses to a Structured TBI Diagnostic Interview and the CAPS.[42,41] For purposes of this study, a veteran was considered to have a deployment-related mTBI (mTBI-o) if the American Congress of Rehabilitation Medicine criteria for mTBI were met as determined by his or her responses to the TBI interview questions.[51] A veteran was considered to have PTSD based on the lenient scoring rule (F1/I2) provided in the CAPS manual (PTSD-o). Veterans who met both criteria were assigned to the mTBI + PTSD group and veterans who did not meet criteria for either mTBI or PTSD were assigned to the veteran control group (VC).

Procedures to create comparable groups

As previously noted, an important goal of the present study was to compare veteran groups, which were comparable on potentially confounding variables. Therefore, the first author carried out procedures to create such groups, blind to the neuropsychological test performance.

The following process was employed in order to make the groups more similar: First, group descriptives were compared to identify significant differences on demographic variables (age, estimated IQ, and education). Initially, the most consistent difference between groups involved the VC group having significantly higher age, education levels, and predicted FSIQ than the mTBI + PTSD group. Therefore, we eliminated outliers on age, education, and higher predicted FSIQ from the VC for whom there were no comparable veterans with either mTBI or PTSD. To do this, seven VC individuals age 51 or older were excluded from data analyses.

Next, 19 individuals with higher levels of education and higher predicted FSIQ were removed from VC. Because the mTBI + PTSD group had many veterans with lower education achievement and low estimated pre-deployment IQs, 10 veterans were eliminated from the low end of this distribution in this group. Only one veteran was excluded from the PTSD-o group due to an outlying low estimated IQ score. No veterans were excluded from the mTBI-o group. Therefore, of the 288 veterans remaining after the validity screens mentioned above, 37 subjects were excluded in order to make the four groups comparable on age, estimated IQ, and education level.

Results

Examination of the data characteristics showed departure from normal distribution (absolute values of skewness and kurtosis ratios to their standard errors exceeded 2.0) for approximately one-third of the dependent variables. SPSS was the software program used to run all analyses (Version 21.0, IBM Corp., Armonk, NY). Data analyses using non-parametric tests were compared with those using parametric tests. Out of 27 neuropsychological variables, only two tests provided discrepant results when comparing non-parametric with parametric findings (CPT-II Perseverations & Omissions). Therefore, those two test measures were eliminated from further analysis. For ease of understanding, we report findings from all of the parametric analyses.[54] Group differences were evaluated using one-way analysis of variance (ANOVA) tests and follow-up contrasts with *t*-tests. In order to control for possible type I error, outcome variables were considered significant at $p < 0.01$. Effect sizes are presented in Cohen's *d*.[55]

The final sample included 116 OIF/OEF veterans (VC) with no history of deployment-related TBI or PTSD, 53 OIF/OEF veterans with histories of deployment mTBI (mTBI-o), 32 OIF/OEF veterans with current PTSD (PTSD-o), and 50 OIF/OEF veterans with a history of deployment mTBI and current PTSD (mTBI + PTSD). Table 1 presents demographics and other characteristics of the final study groups. The groups did not differ significantly in terms of age, education, predicted FSIQ, gender, ethnicity, months post-mTBI, and number of pre-deployment civilian mTBIs.

Neuropsychological results

Table 2 presents neuropsychological results. Initial analyses indicated overall group differences ($p < 0.01$) on several variables: D-KEFS Visual Scanning, D-KEFS Number Sequencing, D-KEFS Category Fluency, CVLT-II Trials 1–5, CVLT-II Long Delay Free Recall, CVLT-II Long Delay Cued Recall, and WAIS-IV Digit Symbol. D-KEFS Number-Letter Switching, CVLT-II Short Delay Free Recall, and WAIS-IV Processing Speed Index approached significance.

Figure 1, a graphical representation of the between-group comparisons on the significant outcome variables, indicates that the mTBI-o and mTBI + PTSD groups performed significantly worse than VC on D-KEFS Visual Scanning, Number Sequencing, and WAIS-IV Digit Symbol. The mTBI + PTSD group also produced significantly lower scores than VC on D-KEFS Category Fluency,

Table 1. Demographic Characteristics of Participants in Final Analyses

Variable		*VC* n = *116*	*mTBI-o* n = *53*	*PTSD-o* n = *32*	*mTBI + PTSD* n = *50*	*F or X^2* n = *251*	p
Male	%	86.2	88.7	87.5	98.0	5.206	.157
Age	M(SD)	31.64 (8.21)	29.96 (7.70)	31.53 (7.24)	30.04 (7.73)	.844	.471
Education	M(SD)	14.12 (1.69)	14.19 (1.75)	14.25 (1.95)	13.62 (1.32)	1.438	.232
Race							
Caucasian	%	77.6%	69.8%	71.9%	82.0%	1.570	.197
Afr. Amer.	%	6.9%	13.2%	21.9%	4.0%		
Other	%	15.5%	17.0%	6.2%	14.0%		
Ethnicity							
Hispanic	%	19.1%	19.2%	12.5%	14.3%	1.958	.121
Non-Hispanic	%	79.1%	71.2%	71.9%	75.5%		
WTAR FSIQ	M(SD)	102.76 (8.11)	102.66 (6.97)	100.06(9.20)	103.34 (8.43)	1.191	.314
# Deployment mTBI	M(SD)	-	2.94 (13.46)	-	3.18 (13.85)	.006	.936
# Months Post mTBI	M(SD)	-	44.68 (35.12)	-	40.43 (26.08)	1.505	.223
Previous Hx of mTBI	%	26.1%	35.5%	35.5%	30.6%	3.443	.328

VC, veteran controls; mTBI-o, deployment mild traumatic brain injury only; PTSD-o, current post-traumatic stress disorder only; mTBI + PTSD, deployment mild traumatic brain injury and current post-traumatic stress disorder; M, mean; SD, standard deviation; WTAR FSIQ, Wechsler Test of Adult Reading estimated Wechsler Adult Intelligence Scale-III Full Scale Intelligence Quotient; mTBI, mild traumatic brain injury; Hx, history.

CVLT-II Total Trials, and CVLT-II Long Delay Free Recall. The PTSD-o group was significantly worse than VC on CVLT-II Total Trials and D-KEFS Category Fluency. There were no significant differences between mTBI-o and PTSD-o on any neuropsychological variable. The mTBI + PTSD group produced significantly lower scores than mTBI-o on CVLT-II Total Trials and CVLT-II Long Delay Free Recall. Lastly, the mTBI + PTSD group performed significantly worse than PTSD-o on D-KEFS Visual Scanning. Effect size contrasts are presented in Table 3.

Psychiatric results

Figure 2, a graphical representation of the between-group comparisons on the psychiatric variables, indicates that overall significant group differences were found for all measures. Of course, given diagnostic criteria, significant differences on the CAPS between the two PTSD and remaining groups were to be expected. Follow-up contrasts revealed that the mTBI + PTSD group produced significantly higher scores on BDI and CAPS than PTSD-o but there was no significant difference on BAI. The mTBI + PTSD group also was significantly worse than mTBI-o and VC groups on all psychiatric measures. The mTBI-o and PTSD-o groups had significantly poorer scores than the VC group on all psychiatric measures. Lastly, PTSD-o had significantly higher scores on the CAPS, as well as the BDI-II and BAI, than the mTBI-o group. As expected, presence of PTSD appears to have a greater impact on psychiatric measures than mTBI and the combination of the two conditions appears to be associated with greater emotional distress and symptom complaints.

Examination of effect size contrasts illustrates the impact of PTSD diagnosis on psychiatric measures. The presence of mTBI + PTSD and PTSD-o were associated with very large effect sizes on all psychiatric measures ($d = 1.18$ to $d = 1.96$). In addition, the mTBI-o had a large effect size on all psychiatric measures, compared with the VC group.

Discussion

A recent comprehensive systematic review of the burgeoning literature on mTBI in veterans and military personnel noted minimal to small effect sizes for mTBI on neuropsychological measures.[56] The picture in that review was consistent with findings from the more methodologically rigorous, prospective, longitudinal studies conducted in civilian populations. Most objective cognitive test results indicated no significant differences in veterans and military personnel with mTBI and control participants. Some differences do occur shortly after injury but most often resolve within hours to months. In that context, the present study has produced unexpected findings using different methodology that 1) addresses the confounding effects of PTSD; 2) screens for both invalid cognitive and psychiatric responding; and 3) balances participants on education and prior ability level.

The present study used a comprehensive test battery to examine the neuropsychological and psychological performance associated with deployment-related mTBI (mTBI-o), current PTSD (PTSD-o), and the combination of deployment-related mTBI and current PTSD (mTBI + PTSD) in returning veterans from the OIF/OEF conflicts more than three years following their deployment. Veterans with mTBI-o, PTSD-o, and mTBI + PTSD and a veteran comparison group were comparable on age, education, and IQ to mitigate their effects on test performance. The study included a wide-ranging battery of neurocognitive, psychiatric, and validity measures. The mTBI-o group performed more poorly than the VC group on many neuropsychological measures. This was in contrast to previous findings with a smaller sample, restricted to the Lexington VAMC, that was not matched for age, education, and estimated pre-injury IQ.[33] Compared with VC, the mTBI-o group performed worse on measures of visual scanning and visual attention (D-KEFS Visual Scanning), as well as measures of processing speed (WAIS-IV Digit Symbol Coding). These differences reflect a small to moderate effect for mTBI-o ($d = 0.31$ to $d = 0.45$).

Additionally, the mTBI + PTSD group performed significantly worse on several neuropsychological measures than the VC group. The mTBI + PTSD group was significantly different from VC on measures assessing visual scanning (D-KEFS Visual Scanning), visual attention (D-KEFS Number Sequencing), semantic fluency (D-KEFS Category Fluency), immediate/short delay and long delay recall (CVLT-II), as well as processing speed (WAIS-IV Digit Symbol Coding; small to moderate effects, $d = 0.38$ to $d = 0.65$). There were no significant differences between mTBI + PTSD and

Table 2. Group Comparisons of Neuropsychological Variables

	Descriptives				*Omnibus Test*	
Outcome Variable	*VC* n = *116* *M* *SD*	*mTBI-o* n = *53* *M* *SD*	*PTSD-o* n = *32* *M* *SD*	*mTBI + PTSD* n = *50* *M* *SD*	*F* N = *251*	p
D-KEFS (Scaled Score)						
Visual Scanning	10.83	9.92	10.31	8.86	6.454**	0.000
	2.172	2.401	2.645	3.844		
D-KEFS (Scaled Score)						
Number Seq.	10.87	10.00	10.25	9.44	4.133**	0.007
	2.217	2.660	2.806	2.880		
D-KEFS (Scaled Score)						
Letter Seq.	10.90	10.25	10.16	10.00	2.191	0.090
	2.010	2.303	2.713	3.051		
D-KEFS (Scaled Score)						
N-L Switching	10.31	9.51	10.28	9.18	2.952*	0.033
	2.095	2.991	2.020	3.274		
D-KEFS (Scaled Score)						
Motor Speed	11.50	11.09	11.13	11.22	0.941	0.422
	1.489	2.169	1.680	1.607		
D-KEFS (Scaled Score)						
Letter Fluency	10.41	9.49	9.38	10.16	1.484	0.219
	3.424	2.998	3.035	3.093		
D-KEFS (Scaled Score)						
Categ. Fluency	11.97	11.51	11.00	10.02	4.443**	0.005
	3.301	3.533	2.794	2.959		
D-KEFS (Scaled Score)						
Categ. Switch	11.03	10.55	10.13	9.74	1.826	0.143
	3.383	3.343	3.035	3.999		
D-KEFS (Scaled Score)						
Color Naming	9.24	9.56	8.09	9.28	1.525	0.209
	3.427	2.725	3.166	2.997		
D-KEFS (Scaled Score)						
Word Reading	9.74	10.37	8.72	9.26	1.899	0.130
	3.549	2.151	3.324	3.752		
D-KEFS (Scaled Score)						
Inhibition	9.70	9.73	8.88	9.76	0.561	0.641
	3.487	3.088	3.696	3.543		
CPT (T Score)						
Commissions	49.05	50.66	49.90	49.50	0.369	0.776
	9.750	9.698	6.694	9.779		
CPT (T Score)						
Hit Rate	47.52	45.67	46.30	48.13	0.670	0.571
	10.109	8.698	7.131	12.471		
CPT (T Score)						
Standard Error	47.65	49.29	52.16	51.49	2.394	0.069
	10.210	9.120	9.988	13.334		
CVLT-II (Raw Score)						
Trials 1–5	54.17	53.21	49.97	48.40	5.308**	0.001
	8.935	7.682	10.721	10.753		
CVLT-II (Z Score)						
Short Delay	.22	.18	−.06	−.29	3.316*	0.021
	.967	.986	.948	1.187		
CVLT-II (Z Score)						
Long Delay Free	.07	.11	−.23	−.58	5.554**	0.001
	.972	.939	1.047	1.259		
CVLT-II (Z Score)						
Long Delay Cued	.06	.09	−.28	−.53	5.060**	0.002
	1.040	.741	1.016	1.162		
WCST (T Score)						
Total Correct	50.34	51.13	47.00	51.18	2.555	0.056
	7.601	5.735	10.791	5.858		

(*continued*)

Table 2. (Continued)

	Descriptives				Omnibus Test	
Outcome Variable	*VC* n = *116* *M* *SD*	*mTBI-o* n = *53* *M* *SD*	*PTSD-o* n = *32* *M* *SD*	*mTBI + PTSD* n = *50* *M* *SD*	*F* N = *251*	p
WCST (T Score)						
Total Errors	50.10	50.49	45.75	50.44	2.677*	0.048
	8.599	7.462	11.007	7.349		
WCST (T Score)						
Perseverative Errors	49.19	48.28	44.44	47.94	2.553	0.056
	7.240	7.767	8.424	5.666		
WCST (T Score)						
Non-persev. Errors	48.02	49.66	44.75	48.54	2.392	0.069
	8.565	7.555	10.271	7.098		
WAIS-IV (Scaled Score)						
Digit Symbol	10.50	9.49	10.19	9.24	4.551**	0.004
	2.149	1.938	2.494	2.847		
WAIS-IV (Scaled Score)						
Symbol Search	10.90	10.06	9.88	10.18	2.544	0.057
	2.305	2.134	2.673	2.876		
WAIS-IV (Standard Score)						
PSI	103.34	98.60	100.03	98.46	3.422*	0.018
	10.334	9.580	11.803	14.116		

*$p < 0.05$; **$p < 0.01$.

VC, veteran controls; M, mean; SD, standard deviation; mTBI-o, deployment mild traumatic brain injury only; PTSD-o, current post-traumatic stress disorder only; mTBI + PTSD, deployment mild traumatic brain injury and current post-traumatic stress disorder; D-KEFS, Delis Kaplan Executive Function System; CPT, Continuous Performance Test; CVLT-II, California Verbal Learning Test, 2nd edition; WCST, Wisconsin Card Sorting Test; WAIS-IV, Weschler Adult Intelligence Scale, 4th edition; PSI, Processing Speed Index.

mTBI-o on any measures of visual scanning or processing speed, however the combined mTBI + PTSD group performed worse than mTBI-o on measures of semantic fluency and verbal memory. These differences involved moderate effects between mTBI + PTSD and mTBI-o ($d = 0.44$ to $d = 0.65$).

Another important finding was the relative lack of differences when comparing PTSD-o to VC. Although there was a significant difference between PTSD-o and VC on immediate verbal recall (CVLT-II Total Trials), based on previous research it was expected that the PTSD-o group would perform worse than VC on a measure

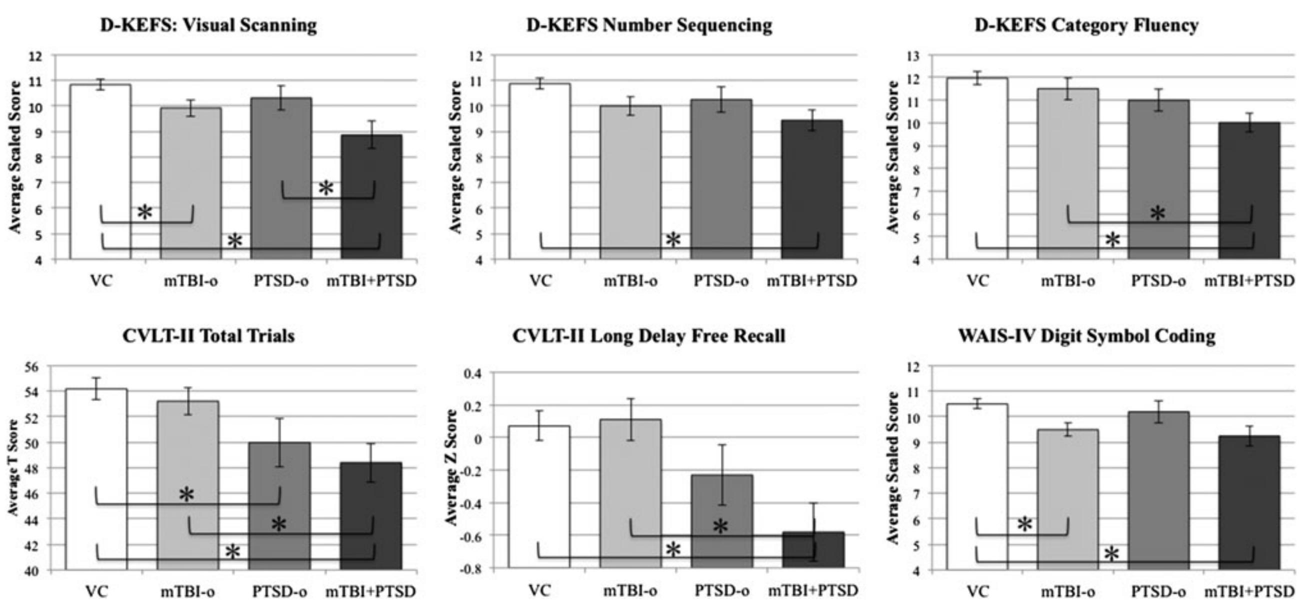

FIG. 1. Bar graph depicting the average group scores on significant neuropsychological measures. VC, veteran controls; mTBI-o, deployment mild traumatic brain injury only; PTSD-o, current posttraumatic stress disorder only; mTBI + PTSD, deployment mild traumatic brain injury and current posttraumatic stress disorder; D-KEFS, Delis-Kaplan Executive Function System; CVLT, California Verbal Learning Test, 2nd Edition; WAIS-IV, Wechsler Adult Intelligence Scale, 4th Edition; PSI, Processing Speed Index. Standard errors are represented in the figures by error bars. *$p < .01$

TABLE 3. EFFECT SIZES (D) FOR GROUP COMPARISONS AMONG SIGNIFICANT OUTCOME VARIABLES

	VC vs. mTBI-o	*VC vs. PTSD-o*	*VC vs. mTBI+PTSD*	*mTBI-o vs. PTSD-o*	*mTBI-o vs. mTBI+PTSD*	*mTBI-o vs. mTBI+PTSD*
D-KEFS Visual Scanning	0.375	0.187	0.654	0.153	0.338	0.453
D-KEFS Number Sequencing	0.344	0.218	0.543	0.090	0.204	0.281
D-KEFS Category Fluency	0.128	0.252	0.563	0.152	0.460	0.334
CVLT-II Total Trials	0.105	0.373	0.560	0.355	0.522	0.144
CVLT-II Long Delay Free	0.039	0.258	0.566	0.348	0.633	0.289
WAIS-IV Digit Symbol	0.452	0.116	0.489	0.316	0.104	0.345

General guidelines for interpreting Cohen's *d* (Cohen, 1992) are as follows: ±0.20 is a small effect, ±0.50 is a medium effect, and ±0.80 is a large effect.

VC, veteran controls; mTBI-o, deployment mild traumatic brain injury only; PTSD-o, current posttraumatic stress disorder only; mTBI+PTSD, deployment mild traumatic brain injury and current posttraumatic stress disorder; D-KEFS, Delis-Kaplan Executive Function System; CVLT-II, California Verbal Learning Test, 2nd Edition; WAIS-IV, Weschler Adult Intelligence Scale, 4th Edition.

of verbal memory and executive functioning. However, it is important to note that the PTSD-o group had the smallest sample size out of all groups and there may not have been sufficient power to detect the differences between the other groups and PTSD-o.

Examinations of the effect sizes are consistent with small effects for verbal memory measures, less than the moderate to large effects seen in previous research. It was expected that the PTSD-o group would perform more poorly than the mTBI-o group on many of the neuropsychological variables; however, there were no significant differences between the two groups on any variable. Consideration of the effect sizes suggests the mTBI-o group tended to perform worse than PTSD-o on measures of flexibility of thinking (D-KEFS Number Letter Switching) and visual-motor coordination (WAIS-IV Digit Symbol Coding), whereas the PTSD-o group tended to perform worse than mTBI-o on measures of verbal memory (CVLT-II).

It also was hypothesized that there would be no differences between the mTBI+PTSD group and the PTSD-o group on any neuropsychological variable. However, significant differences

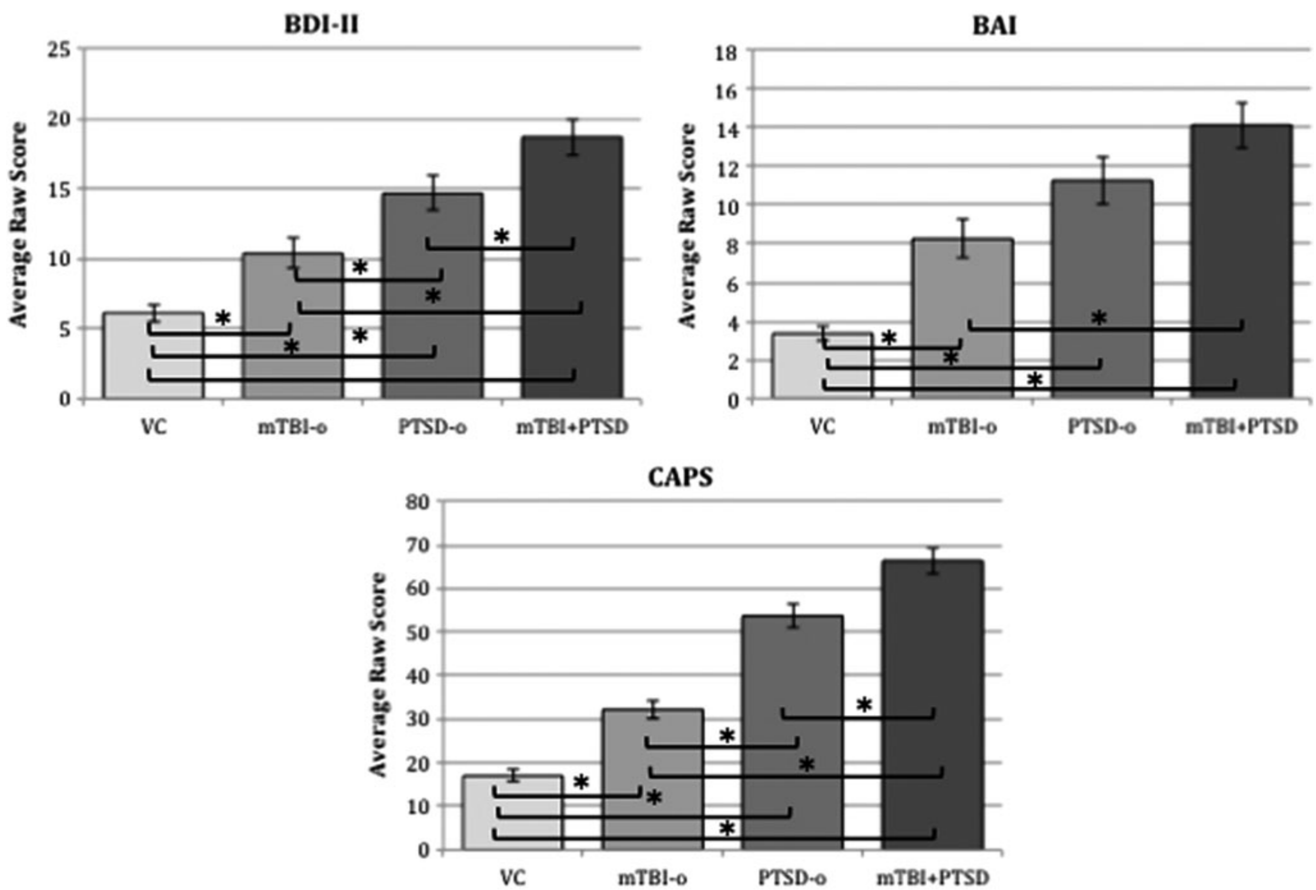

FIG. 2. Bar graph depicting the average group scores on psychiatric measures. VC, veteran controls; mTBI-o, deployment mild traumatic brain injury only; PTSD-o, current post-traumatic stress disorder only; mTBI+PTSD, deployment mild traumatic brain injury and current post-traumatic stress disorder; BDI-II, Beck Depression Inventory, Second Edition; BAI, Beck Anxiety Inventory; CAPS, Clinician Administered PTSD Scale. Standard errors are represented in the figures by error bars. $^*p < 0.05$

were found here on measures of visual scanning (D-KEFS Visual Scanning), with the combined group producing lower scores. After examining the effect size comparisons, there was a small effect for the difference between mTBI + PTSD and PTSD-o group on measures of number sequencing (D-KEFS Number Sequencing), delayed verbal memory (CVLT-II), and visual-motor coordination/mental speed (WAIS-IV Digit Symbol Coding).

Lastly, it was hypothesized that the mTBI + PTSD group would report more psychopathology than the other three groups. Although the mTBI + PTSD group reported greater symptoms of depression and PTSD symptoms than all other groups, as well as greater anxiety and insomnia than the VC and mTBI-o groups, there were no significant differences between mTBI + PTSD and PTSD-o on measures of anxiety or insomnia. Nevertheless, the trend of severity for every psychiatric measure was mTBI + PTSD > PTSD-o, PTSD-o > mTBI-o, and mTBI-o > VC.

Implications

In contrast to the civilian mTBI literature, these results provide some evidence for mild, statistically significant decrements in long-term processing speed and visual scanning associated with deployment-related mTBI-o. These decrements may be perceptible to the individual but the magnitude of the changes on cognitive performance is not likely to be disabling. Given what is known about the demographic and psychiatric characteristics of this sample, several possible explanations for the disparity between these results and typical findings in the civilian mTBI literature are offered.

First, the veterans in the mTBI-o group all reported having experienced a deployment-related concussion. Deployment concussions often occur in the context of months of chronic stress. Civilian mTBI findings are based on concussions and other injuries that occur outside of combat situations, where the environment is presumably lower in chronic stress. Another important difference between civilian and military mTBIs is the injury mechanism (e.g., blast injury). It is possible that the differences found in this study can be attributed to the stressful environment or the mechanism in which the mTBI occurred. Further, it is important to note that the veterans who reported deployment-related mTBI had, on average, three mTBI. The impact of multiple concussions may account for some of the differences between the present findings and the civilian literature.

Another explanation is the possible influence of ''diagnosis threat.'' In a study by Suhr and Gunstad,[57] individuals with mTBI who were alerted to the possible cognitive consequences of a head injury (i.e., ''diagnosis threat'') performed worse on cognitive measures than participants with mTBI who were not alerted. Since veterans in our study were thoroughly questioned about the details of their mTBI, it is conceivable they may have been inadvertently primed to perform more poorly than the veterans without mTBI.

Given the evidence for processing speed and scanning decrements (e.g., D-KEFS Visual Scanning, D-KEFS Number Sequencing, and WAIS-IV Coding) for the mTBI-o group in the current sample, it is important to note that veterans in the mTBI-o group had significantly higher psychiatric distress than the veteran comparison group. It is possible that the differences in the visual scanning deficits and processing speed are due, in part, to the higher levels of psychiatric distress in the mTBI-o group. However, the PTSD-o group also reported higher levels of psychiatric distress than the VC group and the mTBI-o group but there were no accompanying differences in visual scanning and processing speed, suggesting it is unlikely that psychiatric distress completely accounts for the novel finding of differences between mTBI-o and VC in this present study.

A final explanation for the discrepant findings for the effect of mTBI may be the methodical differences in procedures relative to previous studies. These differences include: 1) the rigorous screening for poor effort and invalid psychiatric responding; 2) the careful balancing of participants on confounding variables of age, education, and pre-injury ability; and 3) the cautious portioning of variance due to affective disturbance in the experimental design. It is possible that these methodological differences have reduced the error variance, making the small chronic effects of mTBI more discernible. However, it is important to note that the mean scaled scores for all groups on the significant neuropsychology variables fell within the average range, and thus these scores probably do not translate into significant clinical impairments.

The results from the present study also suggest that mTBI + PTSD produces greater decrements in cognitive functioning than PTSD alone. The small effect sizes present in both the PTSD-o and mTBI-o groups translate to moderate effect sizes when the two conditions are comorbid. Further, the cognitive impairments related to mTBI + PTSD group do not appear to be completely attributable to greater levels of distress, as there were no significant differences on any psychiatric measures between mTBI + PTSD and PTSD-o.

The present study also found small effect sizes for verbal memory (e.g., CVLT-II Total Trials and Long Delay Recall) between PTSD-o and VC—much smaller than what was expected based on previous literature. As this was the first study to compare the four groups (VC, mTBI-o, PTSD-o, and mTBI + PTSD) when they were comparable on age, intelligence, and level of education, this would suggest that a portion of the larger effect sizes seen in other studies may be due to the inherent demographic differences and not exclusively the effect of the PTSD diagnosis. Previous studies also have not excluded subjects with questionably valid psychiatric responses on the MMPI-2-RF.

Limitations

While this study provides a potentially useful contribution to the current body of literature on neuropsychological functioning in OEF/OIF veterans with PTSD and deployment mTBI, limitations must be acknowledged. Though care was used to arrange demographically and diagnostically clean groups, matching based on psychiatric distress was not possible. Because of the fluctuating level of distress and PTSD within this sample, the cross-sectional design is a weakness. A second limitation of the present study is the use of parametric analyses. Although ANOVA is typically robust to violations of normality, this is less so when sample sizes are uneven, as is the case in the present study.

A third limitation to the present study is that it was not possible to assess differences in number of deployments, duration of deployments, or combat exposure between the four groups. It would be expected that mTBI + PTSD would have the greatest amount of combat exposure and longer deployments; however, future studies will need to include measures of these variables in order to determine what, if any, influence this variable has on the impairments of interest.

A fourth major limitation to the present study is the subjective nature of the structured face-to-face interview process for determining whether participants had sustained an mTBI. Though this process has several strengths, including consistency of diagnosis, it also can allow for false-positives, especially when attempting to

determine the presence of an mTBI without medical records. This limitation must be kept in mind while reviewing the results of the current study, as with all studies on combat mTBI.

Conclusions

In summary, if cross-validated, the results of the current study suggest that the impact of mTBI (alone and when combined with PTSD) on veterans' cognitive functioning, although apparently small, may be more than temporary, especially on measures of visual scanning and processing speed. Clinically, as more and more veterans are returning from the current OEF/OIF conflicts reporting both PTSD and mTBI symptoms, it is important to recognize that the subjective impairments veterans report may in fact translate into small objective cognitive decrements.

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Author Disclosure Statement

No competing financial interests exist.

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Address correspondence to:
Walter M. High, Jr., PhD
Lexington VAMC
1101 Veterans Drive
Lexington, KY 40502-2236

E-mail: walter.high@va.gov