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Blast Concussion and Posttraumatic Stress as Predictors of Post-Combat Neuropsychological Functioning in OEF/OIF/OND Veterans

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Abstract

Objectives: Many combat Veterans exhibit cognitive limitations of uncertain origin. In this study, we examined factors that predict cognitive functioning by considering effects of blast-related concussion (BRC), non-blast-related concussion (NBRC), and posttraumatic stress disorder (PTSD) symptoms. Analyses specifically tested whether: (a) BRC and NBRC were distinct in their prediction of cognitive performance; (b) a dose-response relationship existed between recurrent concussion (BRC and NBRC) and cognitive impairment; and (c) PTSD symptoms mediated the relationship between BRC and cognitive performance.

Method: Two-hundred eighty Veterans with combat zone deployment histories completed semistructured clinical interviews to define BRC and NBRC histories, current and past mental health disorders, and dimensional ratings of PTSD symptomatology. Participants were also administered a number of neuropsychological measures to appraise cognitive functioning.

Results: A structural equation model (SEM) suggested that BRC and NBRC were not distinct in their prediction of cognitive performance, and there was no evidence that recurrent concussion (blast or non-blast) was directly associated with cognitive performance. BRC was significantly associated with PTSD symptoms ($r = .24$), PTSD symptoms were significantly associated with cognitive performance in the SEM ($r = -.27$), and PTSD symptoms significantly mediated the link between BRC and cognitive performance ($p = .03$).

Conclusions: These results suggest that concussion history fails to directly contribute to cognitive performance, regardless of mechanism (blast or non-blast) and recurrence. BRC is nonetheless unique in its contribution to PTSD and PTSD-related cognitive deficits. Results support interventions specific to PTSD management in the interest of promoting neuropsychological functioning among war Veterans.

Keywords

Blast concussion; Operation Iraqi Freedom; Operation Enduring Freedom; neuropsychological outcomes; posttraumatic stress disorder

Military personnel who participated in combat activities during previous wars in Iraq and Afghanistan frequently experienced combat-related mild traumatic brain injury (mTBI, also known as concussion). Prevalence of concussion in U.S. military personnel during Operation Iraqi Freedom (OIF) and Operations Enduring Freedom (OEF; later called Operation New Dawn, OND) has been estimated from 8% to 23% depending upon the cohort and assessment tools implemented (Hoge et al., 2008; Polusny et al., 2011; Schneiderman et al., 2008). The disconcertingly high prevalence of concussion in individuals deployed as part of OEF/OIF can largely be attributed to the high frequency of explosive blasts that military personnel encountered (MacGregor et al., 2011). Although several years have elapsed since the formal cessation of OEF/OIF, blast-related concussion (BRC) as a source of chronic cognitive limitations remains an important consideration in the clinical care of OEF/OIF Veterans. Clinical neuropsychologists who work within the Veteran's Health Administration (VHA) play an integral role in assessing the likelihood that previous blast events contributed to BRC and explain cognitive deficits and psychological symptoms, such as the severity of posttraumatic stress disorder (PTSD) symptoms that may be evident in individuals seeking care. Given the complex interplay of pre-existing conditions, and the array of potential effects of combat, clinicians often experience an understandable challenge in determining the most likely sources of cognitive impairments in OIF/OEF Veterans.

Most studies that have examined neuropsychological outcomes following concussion have included civilian samples, such as athletes who sustain non-blast-related concussion (NBRC) following blunt force head trauma. For example, in one of the largest known prospective concussion studies that has been conducted in athletes to date (McCrea et al., 2013), the authors found that most participants demonstrated spontaneous neuropsychological recovery within the first week post-injury. While a minority (approximately 25%) of those who experienced loss of consciousness (LOC) and/or posttraumatic amnesia (PTA) exhibited a more persistent pattern of symptoms, objective neuropsychological performances were not significantly different between non-injured controls and concussion groups at three months. Multiple meta-analytic investigations (e.g., Belanger & Vanderploeg, 2005; Frencham et al., 2005; Iverson, 2005; Schretlen & Shapiro, 2003) have also shown that neuropsychological residua of a single, uncomplicated, NBRC nearly always resolve within the first few months post-injury. Fewer studies have examined neuropsychological outcomes associated with BRC.

There are at least three reasons why neuropsychological outcomes following BRC might be less favorable than NBRC. First, explosive blast represents a unique injury mechanism, one that might contribute to concussion on the basis of primary (i.e., the blast wave itself), secondary (i.e., arising from objects directed to the head), and/or tertiary (i.e., thrown against the ground or other stationary object) effects (DePalma et al., 2005; Mayorga et al., 1997; Taber et al., 2006). While certain animal models suggest that primary blast exposure itself

may lead to memory and other impairments (e.g., Cernak et al., 2001), there is continued debate as to whether neuropsychological outcomes are necessarily distinct from NBRC in humans. Most researchers have failed to identify a mechanism-of-injury effect (blast *versus* non-blast) with respect to either self-reported symptoms (Lippa et al., 2010; Luethcke et al., 2011) or cognitive performance (Belanger et al., 2009; Lange et al., 2012; Luethcke et al., 2011). In contrast, others have found that those with a history of BRC demonstrated at least subtle signs of impairment (e.g., Kontos et al., 2013) that would presumably extend from distinct neurotrauma reported in some neuroimaging studies (cf., Newsome et al., 2016; Scheibel et al., 2012; Sullivan et al., 2018).

Second, whereas most studies have examined neuropsychological outcomes following a single, NBRC injury only, OEF/OIF Veterans often report a history of *multiple* BRCs and NBRCs sustained before, during, and/or after deployment. Whether neuropsychological outcomes among OEF/OIF Veterans might vary as a function of injury *recurrence* is uncertain. In one meta-analytic review, Belanger et al. (2010) compared neuropsychological performance among athletes with multiple concussions (i.e., two or more) with those who sustained a single concussion. It was not evident that a history of recurrent concussion resulted in any greater impairment in overall cognition compared with those who had a history of a single concussion ($d = .06$). Only small effect sizes of unclear clinical significance were observed in executive ($d = .24$) and delayed memory ($d = .16$) functioning. Given that the Belanger et al. (2010) study only included athletes, it is unclear that findings would generalize to Veteran samples with a recurrent history of BRC.

Some research suggests that military and Veteran samples with histories of recurrent BRC may show subtle chronic changes that would not be anticipated relative to a single concussion alone. For instance, Kontos et al. (2013) found limited evidence of a relationship between recurrent concussion and neuropsychological performance; while participants with three or more blast concussions demonstrated slower overall reaction times relative to those with no history of concussion, neurocognitive performances across other cognitive domains (e.g., verbal and visual memory) were not meaningfully different among those with recurrent concussion, a single concussion, or no concussion history.

Finally, long-term neuropsychological outcomes following BRC may be less favorable relative to NBRC as exposure to explosive blast may confer an increased risk of chronic psychological adjustment difficulties, such as PTSD symptoms, which may contribute to memory and other forms of impairment (Scott et al., 2015). Whereas adverse psychological and emotional symptoms following NBRC are negligible (cf., Panayiotou et al., 2010), several research groups have observed a significant association between BRC and PTSD symptom severity in combat Veteran samples (Belanger et al., 2009; Disner et al., 2017; Kontos et al., 2013; Macdonald et al., 2017; Troyanskaya et al., 2015; Verfaellie et al., 2014). Kontos et al. (2013) found evidence of a “dose-response gradient” between BRC and clinical symptoms of PTSD. Other researchers found PTSD symptoms and other emotional difficulties arising from BRC to be a greater determinant of neuropsychological functioning than BRC (e.g., Donnelly et al., 2018; Nelson et al., 2012; Storzbach et al., 2015). Still other research suggests that participants with comorbid BRC and PTSD symptoms demonstrated relatively worse cognitive performance than those with either PTSD or BRC alone (Combs

et al., 2015) or relative to deployment controls (Combs et al., 2015; Pagulayan et al., 2018), raising the possibility of an interactive effect on cognitive performance.

In a previous study (Nelson et al., 2012), we found that OEF/OIF Veterans who met criteria for PTSD and other primary psychiatric disorders demonstrated significantly worse neuropsychological performances than those who did not meet criteria of psychiatric diagnosis, regardless of concussion history. We did not, however, examine the role of PTSD symptom severity and its relationship with neurocognitive performances. In the current study, we extend what is known of the role of PTSD symptomatology with respect to the effects of concussion on the cognitive functioning of individuals who have been deployed to combat zones. Specifically, the current study addressed three questions:

- (1) Does *blast*-related concussion (BRC) emerge as a stronger predictor of neuropsychological impairment than *non-blast*-related concussion (NBRC)?
- (2) Is there evidence of a dose-response relationship between *recurrent* concussion (blast-related and non-blast-related) and neuropsychological impairment?
- (3) Does PTSD symptom severity mediate the relationship between BRC and neuropsychological performance?

Answers to these questions will clarify the likely sources of persisting cognitive deficits, and inform clinical decision-making among OEF/OIF Veterans.

Method

Participants and Procedures

Two-hundred-eighty OEF/OIF combat Veterans were recruited as a component of research studies that addressed BRC and various outcomes from 2006 to 2016. All participants were recruited through prior research and clinics at the Minneapolis VA Health Care System (VAHCS) in compliance with local institutional review board approval. The sample included Veteran patients who screened positive on the VA Traumatic Brain Injury Clinical Reminder (Donnelly et al., 2011) while seeking care through the Minneapolis VAHCS, National Guard soldiers, and in consultation with treating providers on the basis of their patients' status as OEF/OIF combat Veterans. All participants identified English as their primary language and were excluded if they met any of the following conditions: (a) traumatic brain injury greater than mild in severity (defined by LOC > 30 minutes and/or PTA > 24 hours); (b) history of any other neurologic condition diagnosed prior to deployment; (c) current psychotic disorder; (d) history of substance dependence/abuse disorder (other than alcohol, caffeine, or nicotine); (e) history of unstable medical condition that might contribute to central nervous system dysfunction (e.g., diabetes); and (f) significant risk of suicidal or homicidal behavior. Participants with any known history of "complicated" concussion (i.e., those concussive injuries that are accompanied by demonstrable intracranial findings via brain neuroimaging study) also were not included. Exclusion criteria relevant to general medical histories were assessed by trained psychology research staff, who conducted preliminary interviews with prospective participants. The consensus team of clinical neuropsychologists confirmed that traumatic brain injuries that were any greater than mild in severity as defined by acute-stage injury symptoms (described below) were not included. Doctoral-level research psychologists

and trained psychology research staff used the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID; First, Spitzer, Gibbon, & Williams, 2007) to assess exclusion criteria and participants' self-reported medical and mental health histories. One-hundred and four participants were included in a previous neuropsychological outcomes study (Nelson et al., 2012), 221 were included in a study that examined PTSD as a mediator of subjective and objective cognition (Mattson, Nelson, Sponheim, & Disner, in press), and the sample as a whole was utilized in a previous study that examined functional outcomes in U.S. military Veterans (Disner et al., 2017). Background characteristics of the current sample are summarized in Table 1.

Concussion Assessment—Concussion assessment followed the same protocol that was implemented in a previous neuropsychological outcomes study (Nelson et al., 2012). Regular consensus meetings were held by a team of clinical neuropsychologists (NWN, GJL, CRA, BMD, JH, KM) to review frequencies of self-reported combat activities and to ascertain whether any history of blast *exposure* (as defined by 'felt a pressure wave from an explosion') was more likely than not to have resulted in blast-related *concussion*. The Minnesota Blast Exposure Screening Tool (MN-BEST; Nelson et al., 2011), which is an instrument that was developed as a complement to the VA Traumatic Brain Injury Clinical Reminder, was used to maintain a uniform approach to the assessment of the concussion frequencies and severities. 'Concussion' was operationalized by American Congress of Rehabilitation Medicine (ACRM; Kay et al., 1993) criteria: (a) LOC extending no more than 30 minutes; (b) PTA extending no more than 24 hours; (c) any alteration of mental status (AMS), such as feeling dazed, disoriented, or confused; and (d) abrupt onset of focal neurologic symptoms or signs. The consensus group reviewed the three blast events that Veterans deemed most significant during deployment and the three non-blast-related head injuries that participants identified as most significant (whether before, during, or after deployment), allowing for a range of 0 to 6 assessed concussions during one's lifetime (i.e., 3 blast-related and 3 non-blast-related). The rationale for assessing the 3 most significant BRC's (and NBRC's) was informed by previous concussion research (e.g., Guskiewicz et al., 2003), which suggests that experiencing two or more concussions may increase risk of sustaining additional concussion and the possibility that they may result in more extended recoveries relative to those who sustain a single injury. Time constraints precluded the assessment of any more than 6 lifetime concussions. Consensus participants were blinded to psychiatric diagnostic status.

Consensus members offered impressions as to whether a given event was 'more likely than not' or 'less likely than not' to have contributed to BRC and/or NBRC. External information (e.g., emergency medical records; eyewitness accounts) corroborating self-reported blast exposures and other injury events were not available for review in the current sample. As such, the determination as to whether a given blast exposure was more likely than not to have contributed to blast concussion was based largely on clinical judgment and review of self-reported acute-stage symptoms and signs (ACRM; Kay et al., 1993), which were necessary but not sufficient conditions for concussion. The likelihood of concussion was also considered in light of the overall context and coherence of described events. For example, as discussed in more detail elsewhere (Nelson et al., 2014), the MN-BEST

consensus team relies upon the quality and *specificity* of self-reported blast events (e.g., as to when and how injuries were sustained). Thus, a blast exposure that reportedly transpired at a specific time and date, in a specific place, and in the company of specific individuals, would be seen as more plausible relative to an event that was sustained in the absence of eyewitnesses, or could not be located in time or place. As another example, blast exposures associated with combat activity (e.g., unanticipated assault with rocket-propelled grenade, RPG) that resulted in acute symptoms would be more likely to contribute to concussion than blast exposure associated with an intentional detonation (e.g., following discovery of improvised explosive device, IED) that did not result in any acute symptoms. Proximity from the blast source (Howe, 2009), the significance of injuries in addition to concussion (e.g., orthopedic or peripheral injuries), such as tympanic membrane perforation (Xydakis et al., 2007), are examples of additional factors that informed the likelihood that blast exposure resulted in concussion.

Next, using criteria outlined by Ruff and Richardson (1999), each of up to three individual blast concussions explored during the MN-BEST consensus process were classified according to severity. Blast injuries that did not contribute to LOC or PTA were classified as ‘Type 0’; those contributing to AMS without clear LOC or PTA as ‘Type I’; injuries resulting in definite LOC (up to 5 minutes) and/or PTA (up to 12 hours) classified as ‘Type II’; and injuries that resulted in LOC (> 5 to 30 minutes) and/or PTA (> 12 hours to 24 hours) classified as ‘Type III’. These indicators of concussion severity were combined with concussion frequencies to arrive at a composite index of BRC. The same scheme was implemented for each of up to three individual non-blast concussions, yielding two composite indices, one representing an index of overall BRC burden and another representing an overall index of NBRC burden (please see Nelson et al., 2011 for a more detailed summary of the MN-BEST consensus process). The BRC and NBRC composite indices were used in the primary structured equation modeling analyses summarized below.

Psychological Diagnostic Assessment—Participants underwent the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1995) to ascertain whether previous combat experiences resulted in psychological and emotional symptoms (e.g., re-experiencing; avoidance) that satisfied formal diagnostic criteria for PTSD as defined by DSM-IV-TR criteria. Each symptom item was scored separately for frequency and intensity using a 5-point scale (0–4) and the sum total of frequency and intensity across the 17 DSM-IV-TR symptoms, across specific PTSD symptom clusters (i.e., intrusive thoughts, avoidance, dysphoria, and hyperarousal), was used to determine the CAPS severity score. PTSD diagnosis was determined based on DSM-IV-TR criteria, although diagnostic status was only used for descriptive purposes, and not in any subsequent models. Participants also underwent the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID; First, Spitzer, Gibbon, & Williams, 2007) to assess any additional psychological and emotional conditions (i.e., those in addition to PTSD) related to previous combat experiences. The CAPS and the SCID were administered by doctoral-level clinical psychologists and trained and supervised psychology research staff. Research staff completed formal CAPS training under direction of doctoral-level clinical psychologists who specialized in the assessment of trauma-related disorders. Formal DSM-IV-TR diagnoses were then determined by doctoral-

level clinical psychologists and advanced doctoral psychology graduate student trainees with expertise in the assessment of mental health disorders. The consensus process focused on the review of reported symptomatology, incorporation of ancillary information from medical or military records that were available, and determination of whether specific symptom-based criteria were met by participants. Research staff who administered the CAPS and the SCID were not aware of the MN-BEST consensus process at the time of diagnostic consensus meetings (see Table 1 for a summary of psychological diagnoses in the current sample). While formal psychological diagnoses were determined by consensus, the overall CAPS PTSD severity score was used for purposes of present analyses.

Performance-Based Tasks

Performance Validity—Performance invalidity is a significant source of diminished cognitive performance among combat Veterans with self-reported histories of concussion. While frequencies of invalid presentation on standard performance validity tests (PVTs) tend to be highest in clinical and forensic evaluation settings (Ashendorf et al., 2017; McCormick et al., 2013; Nelson et al., 2010), some Veteran research samples who undergo cognitive testing have also been shown to demonstrate invalid performances on PVTs. Frequencies of invalid performance in one recent study of 198 OEF/OIF research participants (Clark et al., 2014), for example, ranged from 4% to 9% across multiple PVTs, with an overall base rate of 5.6%. Results like these support the inclusion of multiple PVTs in concussion research to identify the degree to which limited engagement/effort, as opposed to remote history of BRC(s), may account for diminished cognitive performances in Veteran samples. In the current study, recommended cut-scores developed for the Victoria Symptom Validity Test (VSVT; Slick et al., 1997), the forced-choice trial of the CVLT-II (Moore & Donders, 2009), WAIS-III Digit Span (Babikian et al., 2006), and Trail Making Test A (Iverson et al., 2002) were used to inform performance validity in the current sample (please refer to respective studies for the specific cut-scores themselves). Participants who demonstrated questionable effort on two or more of these indices were excluded, and on this basis, four participants (1.4%) were not included in subsequent analyses related to questionable effort observed during testing¹.

Cognitive Ability—Participants completed neuropsychological tests across several cognitive domains. As premorbid ability is among the most significant predictors of cognitive functioning in healthy and clinical samples alike, including OEF/OIF Veterans with histories of concussion (Stewart-Willis et al., 2017), participants completed the Wechsler Test of Adult Reading (WTAR; The Psychological Corporation, 2001) to ensure that any potential impairments or relative weaknesses were not erroneously ascribed to brain injury as opposed to relative weaknesses that might have pre-existed the time of injury. Other cognitive domains included auditory attention/working memory (Wechsler Adult Intelligence Scale – 3rd Edition, WAIS-III, Digit Span scaled score; Wechsler, 1997); cognitive efficiency (WAIS-III Coding scaled score); processing speed/set-shifting (Trail Making Tests A & B T-scores [TMT-A & TMT-B], Reitan & Wolfson, 1993, using the

¹An additional 33 participants failed exactly one effort measure. A post hoc replication of the subsequent results excluding these individuals did not significantly alter any of the associations between the presented variables.

Heaton, Miller, Taylor, & Grant, 2004 normative comparison sample); and verbal learning/memory (California Verbal Learning Test – 2nd Edition, CVLT-II list 1–5 recall z score, Delis et al., 2000). As described in more detail below, collective performances were used to form a Cognitive Performance composite as an index of overall ability.

Analytic Approach

The first component of the analysis used confirmatory factor analysis (CFA) to test a one-factor measurement model of Cognitive Performance. Five neuropsychological measures were included in the CFA in order to represent a range of cognitive processes (e.g. attention, memory, executive functioning) that are commonly impacted by psychopathology. Standardized scores from the following measures were used: WAIS-III Coding and Digit Span subtests, TMT-A, TMT-B, and CVLT-II recall over Trials 1–5. The second component of the analysis used the Cognitive Performance factor score from the previous measurement model and incorporated it into a structural equation model (SEM) along with observed PTSD symptom severity, BRC, and NBRC severity measures derived from the MN-BEST. All analyses were conducted using the SEM function in Stata (StataCorp, College Station, TX). All models used the full information maximum likelihood method, which utilizes all available (i.e. non-missing) information. Adequate model fit was determined using the following criteria: root mean square error of approximation (RMSEA) < 0.08, standardized root mean residual (SRMR) < 0.08, and comparative fit index (CFI) > 0.90 (Byrne, 2013). Mediation was assessed within the SEM using bootstrapped estimation of the indirect effects that was resampled 1000 times with replacement (Hayes, 2009). Post hoc bivariate correlations were calculated to determine whether each PTSD symptom cluster (intrusive thoughts, avoidance, dysphoria, and hyperarousal) may be specifically linked to any observed associations.

Results

Neither gender nor ethnicity was significantly associated with BRC (gender: $t = -1.69$, $p = .09$; ethnicity: $\beta = .005$, $p = .93$), NBRC (gender: $t = 0.90$, $p = .37$; ethnicity: $\beta = -.018$, $p = .77$), or the Cognitive Performance factor (gender: $t = 0.83$, $p = .41$; ethnicity: $\beta = -.036$, $p = .56$). As might be anticipated, WTAR-estimated premorbid ability was significantly correlated with most cognitive tasks, including TMT-B t score ($r = .19$, $p < .01$); WAIS-III Coding scaled score ($r = .28$, $p < .001$); WAIS-III Digit Span scaled score ($r = .38$, $p < .001$); and the CVLT-II Trials 1–5 z-score ($r = .18$, $p < .01$).

As shown in Table 2, BRC and NBRC frequencies were not significantly correlated with any of the cognitive tasks, nor were the overall MN-BEST BRC and NBRC composite indices. Among participants with a history of BRC or NBRC, performances among those whose injuries were accompanied by any period of LOC/PTA were not significantly different relative to those whose injuries did not result in LOC/PTA ($p > .05$). Cognitive performances also did not vary as a function of LOC ($p = .19$) or PTA ($p = .85$) among those with a history of NBRC. PTSD symptom severity (i.e., overall CAPS score) was significantly associated with TMT-A t score ($r = -.18$, $p < .01$); TMT-B t score ($r = -.13$, $p = 0.04$); Coding scaled

score ($r = -.21, p < .001$); Digit Span scaled score ($r = -.16, p = .01$); and the CVLT-II Trials 1–5 z score ($r = -.18, p < .01$).

Overall fit for the CFA loading the five neuropsychological measures on to the latent Cognitive Performance factor was excellent (RMSEA = 0.001, CFI > 0.999, SRMR = 0.020). The SEM linking the latent Cognitive Performance factor with PTSD symptom severity and the concussion variables is presented in Figure 1. Fit was good for the SEM based on RMSEA (0.014), CFI (0.995), and SRMR (0.035). Of the three observed predictors of Cognitive Performance, PTSD symptom severity had the only significant direct effect ($\beta = -0.27, p = 0.004$; see Figure 1). There was no significant effect on Cognitive Performance for either BRC ($\beta = 0.01, p = 0.842$) or NBRC ($\beta = 0.06, p = 0.618$). Self-reported blast exposure frequency was not significantly associated with PTSD symptom severity. However, BRC did have a significant effect on PTSD symptom severity ($\beta = 0.24, p < 0.001$; see Figure 1) though NBRC did not ($\beta = -0.03, p = 0.732$). BRC also showed a significant indirect effect via the BRC > PTSD symptom severity > Cognition path ($B = -0.02, SE = 0.007, p = 0.033$, bootstrapped 95% CI $[-.029, -.001]$), suggesting that remote BRC impacts cognition by virtue of its impact on PTSD symptoms. There was no such indirect effect for NBRC ($p = 0.644$). Using post hoc bivariate correlation, each PTSD symptom cluster was significantly correlated with Cognitive Performance (intrusive thoughts [$r = -.236, p = .004$], avoidance [$r = -.169, p = .021$], dysphoria [$r = -.162, p = .027$], and hyperarousal [$r = -.216, p = .003$], though there was no significant difference between the correlation coefficients for any of the four factors (Steiger's $Z = -0.19, p = .848$). Similarly, each PTSD symptom cluster was significantly correlated with BRC (intrusive thoughts [$r = .298, p < .001$], avoidance [$r = .218, p = .003$], dysphoria [$r = .227, p = .002$], and hyperarousal [$r = .163, p = .029$]). There was no significant difference between the correlation coefficients for any of the four factors (Steiger's $Z = 0.76, p = .446$).

Discussion

While the previous wars in Iraq and Afghanistan are now complete, many OEF/OIF Veterans continue to express cognitive limitations that they attribute to previous combat experiences. Identification of which combat experiences and injuries are ultimately most predictive of neuropsychological functioning in these combat Veterans is an essential component of effective clinical-decision making to ensure that they receive individualized and appropriate care. The aim of the current study was to examine the relative roles of BRC, NBRC, and PTSD symptom severity on neuropsychological performances in a diverse OEF/OIF combat Veteran sample.

First, we examined whether Veterans' histories of BRC during deployment were more predictive of neuropsychological impairment than a history of NBRC. While there is little question that explosive blast represents a novel injury mechanism (DePalma et al., 2005; Mayorga et al., 1997; Taber et al., 2006), the current results do not support the notion that BRC directly contributes to distinct forms of cognitive impairment relative to NBRC in the late post-deployment period. Correlates of BRC and NBRC with cognitive performances were comparable and neither was associated with a robust index of Cognitive Performance in a structural equation model. These results, which are reminiscent of several previous

research investigations (e.g., Belanger et al., 2009; Lange et al., 2012; Luethcke et al., 2011), suggest that *if* blast itself contributes to distinct and persistent central nervous system involvement (e.g., Newsome et al., 2016; Scheibel et al., 2012; Sullivan et al., 2018), any direct residua of such involvement could not be appreciated on standard neuropsychological measures in the current sample.

Second, in consideration of the potential effect that recurrent concussion may have on neuropsychological performances relative to a history of a single concussion alone or no concussion (cf., Belanger et al., 2012; Kontos et al., 2013), we explored whether a dose-response relationship might exist between *recurrent* concussion and neuropsychological impairment. Irrespective of whether concussive injuries were sustained as a result of blast during deployment, or via other (non-blast) mechanisms before, during, or after deployment during one's lifetime, concussion frequency and severity were not significantly associated with the Cognitive Performance factor. Relevant to the favorable patterns of neuropsychological recovery repeatedly documented in cases of NBRC (Belanger et al., 2005; Frencham et al., 2005; Iverson, 2005), current results support the notion that long-term prognosis for neuropsychological functioning, regardless of mechanism (blast, non-blast, or both) or recurrence, is generally quite encouraging, and imply that factors other than concussion history as such are likely to drive continued expression of cognitive limitation in the late post-deployment period.

Finally, we examined whether chronic symptoms of PTSD and their severity mediated the relationship between BRC and neuropsychological performances in the current sample. Although there was no direct effect between BRC and cognitive performance, the significant indirect effect linking BRC to cognition via PTSD symptoms is sufficient to meet the criteria for mediation (Hayes, 2009). The link between BRC and PTSD, PTSD's ensuing mediation between BRC and cognitive performance, and the absence of such a relationship with NBRC was similar to effects found by other research groups (e.g., Belanger et al., 2009; Kontos et al., 2013; Troyanskaya et al., 2015; Verfaillie et al., 2014). Symptoms of PTSD, in turn, represented a significant source of neuropsychological performance in the current sample, consistent with the known attenuating effect that trauma symptoms have on cognitive abilities (Scott et al., 2015). That NBRC was not meaningfully associated with either PTSD symptoms or neuropsychological functioning in the current sample is perhaps unsurprising in light of the favorable pattern of psychological recovery that is typically observed following conventional concussive injuries (Panayiotou et al., 2010). In addition, it is notable that correlations were observed between Cognitive Performance and each individual PTSD symptom cluster, although there was no difference between correlations across clusters. This latter result likely stems from the high degree of covariance between symptom clusters (all r 's > 0.53 , all $p < 0.001$). As such it appears that the cognitive consequences of PTSD are borne not by any specific symptoms, but rather by the gestalt of the clinical presentation.

Implications, Limitations, and Future Directions

Extending these results to clinical practice, findings suggest that OEF/OIF Veterans can be encouraged that a history of concussion, blast-related or otherwise, does not typically result in direct, long-term neuropsychological impairment. Clinicians might consider incorporating

these findings, and those of another recent study that identified PTSD symptoms as a significant mediator between subjective cognitive complaints and cognitive performances (Mattson et al., in press), into their work with OEF/OIF/OND Veterans. Specifically, clinicians are encouraged to provide psychoeducation and reassurance that persisting cognitive limitations are less likely to represent a byproduct of concussion itself, and are more likely to extend from unresolved PTSD symptoms and other psychological adjustment difficulties that followed in the post-deployment years. Findings also warrant the provision of treatment interventions (e.g., psychotherapeutic, psychotropic) specifically directed to PTSD symptoms in OEF/OIF samples, particularly those with a history of blast exposure, in the interest of promoting psychological health and well-being, and improving cognitive functioning.

Limitations of the current study should also be noted. Perhaps the most significant weakness was the exclusive reliance on retrospective self-report information to inform concussion history. Despite the current researchers' best efforts to obtain detailed information pertaining to previous combat-related injuries through research interviews (e.g., dates, years, locations, nature and extent of medical care), the reality is that many combat Veterans experience understandable difficulty providing a fully accurate summary of historical blast exposures and other combat events particularly given the extended duration of time that had transpired since these phenomena were encountered. As with most other studies that have been conducted in OEF/OIF samples, medical records and other collateral information (e.g., eyewitness accounts) that might corroborate self-reported combat experiences were not presently available for review. As such, some proportion of the current participants may have been classified as having sustained BRC and NBRC when they did not, and conversely, an unknown proportion of Veterans may not have sustained BRC and/or NBRC when, in fact, they did. It is certainly possible that the limited association noted between BRC and NBRC and neuropsychological performances in the current study was at least partially reflective of the limited reliability of self-report information.

In fact, a number of recent studies have raised serious concerns regarding the reliability of self-reported concussion in some military and Veteran samples (cf., Alosco et al., 2015; Polusny et al., 2011; Russo & Fingerhut, 2017; Van Dyke et al., 2013), and some research (e.g., Alosco et al., 2015; Nelson et al., 2015) suggests that chronic emotional symptoms, including but not limited to PTSD symptoms, may diminish Veterans' abilities to represent combat-related concussions reliably over time. Future research that integrates acute-stage injury characteristics documented through medical record systems (e.g., through the Department of Defense) with accounts of BRC during post-deployment (e.g., through the VHA) may afford a greater ability to assess the reliability of self-reported concussion and the impact that this factor has on outcomes neuropsychological and otherwise.

The test battery administered in the current study, though in some ways consistent with previous studies (e.g., Belanger et al., 2009) and inclusive of measures that are ostensibly sensitive to chronic effects of acquired brain injury, was nevertheless somewhat limited in scope. Use of an expanded number of instruments across additional cognitive domains not assessed in the current work (e.g., visual memory; verbal fluency) might be considered in future studies.

Another important limitation relates to the homogeneous demographic composition of the current sample, which consisted of predominately Caucasian, male, and well-educated Veterans from the Midwestern region of the United States. As such, we cannot speak to the generalizability of these findings to OEF/OIF Veterans of more diverse backgrounds. Women, for example, comprised only 5% of the current sample, which is significantly under-representative of the approximate 12% of the total number of military Veterans who were screened for traumatic brain injury from 2007 to 2013 across the United States (Whiteneck et al., 2015). Regarding race/ethnicity, fewer than 11% of the current Veteran sample identified as minorities, compared to approximately 40% of Veterans assessed for traumatic brain injury through VA in the above study. Future studies that examine the potentially unique effects of BRC and/or PTSD in the way of neuropsychological functioning in more diverse Veteran samples is clearly warranted.

Another consideration is that while the number of blast *exposures* reported in the current sample was substantial (e.g., some reported up to 1000 previous blast exposures), most participants sustained no more than one previous BRC and one previous NBRC. The relative infrequency of BRC and NBRC may have attenuated the ability to detect a genuine ‘recurrent concussion’ effect in the current sample. Moreover, only the three most significant BRCs and NBRCs were investigated in the current sample; it is possible that a minority of participants sustained more than the number formally assessed, and this may have limited the ability to capture other potential events that were relevant to the question of recurrence. Continued investigations of neuropsychological functioning among OEF/OIF Veterans with a more significant history of recurrent BRC and NBRC would be of benefit, particularly in the context of continued debate surrounding chronic traumatic encephalopathy (CTE; McKee & Robinson, 2014) and the relative risk of developing neurodegenerative dementias status-post recurrent traumatic brain injury (Nordstrom & Nordstrom et al., 2018).

Future research directed to neuropsychological outcomes following BRC, PTSD symptoms, and other non-concussion-related factors that may complicate recovery in OEF/OIF samples is needed. For example, while the present results suggest that PTSD symptoms represent a significant source of neuropsychological performance in the current sample, we did not have the ability to examine consistency in subjective cognition relative to objective cognitive performances and the role that chronic PTSD symptoms and other unresolved psychological difficulties might play in maintaining persistent expressions of cognitive limitation (see Jak et al., 2015, for example). Other non-concussion factors that are worthy of continued research investigation in OEF/OIF concussion samples include: poor sleep quality and fatigue (Rau et al., 2017; Verfaellie et al., 2016); secondary gain and performance validity issues (Ashendorf et al., Clark et al., 2014); and resiliency (Reid et al., 2018). The widespread discussion of “TBI” in the popular media, and the suggestion that it may increase risk of various health conditions (e.g., CTE or other neurodegenerative process), also raises the possibility of social influence as a significant source of perceived limitations in OEF/OIF (and other) concussion samples (Merz et al., 2017). Future researchers might examine these social influence factors as they relate to neuropsychological functioning in OEF/OIF concussion samples. Finally, the observed association between BRC and PTSD symptoms raises key questions about the mechanisms that link these conditions. Whether the association stems from biomechanistic properties (e.g. the unique characteristics of blast

force on brain tissue) or psychological properties (e.g. the traumatizing nature of blast events compared to non-blast) is an important area for future study.

Conclusion

In conclusion, OEF/OIF Veterans and clinical providers can be encouraged by the lack of direct association between remote concussion (BRC and NBRC) and neuropsychological performances in the post-deployment phase. Present results suggest that BRC does contribute to cognitive functioning, but only indirectly through its significant association with chronic PTSD symptoms in the years that followed deployment in the current sample. Clinical neuropsychologists are encouraged to consider these findings as a source of psychoeducation regarding long-term outcomes following BRC when attempting to conceptualize the cognitive concerns of war Veterans.

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Public Significance Statement:

While many Veterans of the wars in Iraq and Afghanistan continue to express cognitive limitations in the years after deployment, it is unclear whether these difficulties relate to previous histories of blast-related concussion, posttraumatic stress, or some combination of these factors. In the current study, we found that while blast concussion did not predict Veterans' cognitive performances, blast concussion did predict posttraumatic stress, which in turn contributed to cognitive impairments. These findings support psychotherapy and other interventions tailored to treat posttraumatic stress in combat Veterans.

Figure 1.

Structural equation model portraying the contribution of blast-related concussion on posttraumatic stress and posttraumatic stress on Cognitive Performance. The decision to use a single latent Cognitive Performance factor is based off model fit indices from a separate confirmatory factor analysis of cognitive variables.

Note. *denotes $p < .001$. All other values were non-significant ($p > .05$). CVLT = California Verbal Learning Test – 2nd Edition; BRC = blast-related concussion; NBRC = Non-blast-related concussion; PTSD symptoms = posttraumatic stress disorder.

Table 1.

Sample characteristics.

Variable	<i>n</i>	<i>M (SD)</i>
Age (years)	277	33.6 (8.3)
Education (years)	275	14.4 (2.0)
WTAR (SS)	275	103.3 (8.5)
CAPS Severity (raw)	254	32.0 (28.2)
Time since last BRC (months)	154	63.6 (30.2)
Time since last NBRC (months)	176	139.1 (103.9)
Self-reported blast exposures (#)	273	9.5 (27.7)
Consensus-based BRC severity	263	1.4 (2.0)
Consensus-based NBRC severity	140	2.1 (2.5)
Trail Making Test A (T)	275	49.5 (11.1)
Trail Making Test B (T)	275	49.8 (10.1)
WAIS-III Digit Span (SS)	275	9.9 (2.4)
WAIS-III Coding (SS)	275	9.7 (2.5)
CVLT-II Trials 1–5 (z)	274	0.1 (0.9)
<i>n (%)</i>		
Gender		
Male	262 (94.2)	
Female	16 (5.8)	
Ethnicity		
White/Caucasian	247 (89.2)	
African American	8 (2.9)	
	<i>n (%)</i>	
Hispanic	4 (1.4)	
Other	18 (6.5)	
BRC Frequency		
0	154 (56.2)	
1	84 (30.7)	
2	27 (9.9)	
3 or more	9 (3.3)	
Any BRC with LOC and/or PTA	76 (27.7)	
NBRC Frequency		
0	121 (44.2)	
1	104 (38.0)	
2	38 (13.9)	
3 or more	11 (4.0)	
Any NBRC with LOC and/or PTA	112 (40.9)	
Primary Psychological Diagnosis		
PTSD+	70 (25.0)	

Variable	<i>n</i>	<i>M (SD)</i>
Other Anxiety Disorder	58 (20.7)	
Adjustment Disorder	2 (0.7)	
Alcohol Use (partial remission)	8 (2.9)	
Major Depression	17 (6.1)	
Dysthymia	3 (1.1)	
Bipolar II Disorder	2 (0.7)	
Other	2 (0.7)	
None	118 (42.1)	

Note. BRC = Blast-related concussion; CAPS = Clinician-Administered PTSD Scale (Blake et al., 1995); CVLT-II = California Verbal Learning Test – 2nd Edition (CVLT-II; Delis et al., 2000); NBRC = Non-blast-related concussion; WAIS-III = Wechsler Adult Intelligence Scale = Third Edition (WAIS-III; Wechsler, 1997); WTAR = Wechsler Test of Adult Reading (WTAR; The Psychological Corporation, 2001); Participants in the ‘PTSD+’ category met formal criteria for current posttraumatic stress disorder and/or other primary psychiatric condition according to diagnostic consensus review of information derived from the CAPS and the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID; First et al., 2007).

Table 2.

Pairwise correlates of cognitive performance.

Variable	TMT-A	TMT-B	Coding	Digit Span	CVLT-II Trials 1–5
PTSD Total Symptom Severity	-.18 **	-.13 *	-.21 ***	-.16 **	-.18 **
PTSD Intrusion Cluster	-.15 *	-.14 *	-.20 **	-.22 ***	-.22 ***
PTSD Avoidance Cluster	-.18 *	-.06	-.14	-.19 **	-.11
PTSD Dysphoria Cluster	-.12	-.08	-.20 **	-.11	-.10
PTSD Hyperarousal Cluster	-.16 *	-.13	-.17 *	-.15 *	-.17 *
Self-reported blast event frequency	.02	-.01	-.10	.13	-.06
Blast-related concussion (BRC) frequency	.00	-.05	-.03	-.08	.03
Non-blast concussion (NBRC) frequency	.10	.06	-.01	-.03	.14
MN-BEST BRC severity	-.01	-.02	-.06	-.09	-.05
MN-BEST NBRC severity	.10	.05	-.05	-.02	.10

Note. PTSD = Posttraumatic Stress Disorder, defined by the Clinician Administered Assessment of PTSD (CAPS) Symptom Severity Score. Blast-related concussion (BRC) and non-blast-related concussion (NBRC) frequencies included only the three most significant of each that participants described during their lifetimes. The Minnesota Blast Exposure Screening Tool (MN-BEST; Nelson et al., 2011) was used to establish composite indices of BRC and NBRC burden that were based upon acute-stage symptom severities and frequencies.

*
p < .05;

**
p < .01;

p < .001.