Journal of the International Neuropsychological Society (2009), **15**, 1–8.

doi:10.1017/S1355617708090036

Cognitive sequelae of blast-related *versus* other mechanisms of brain trauma

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(RECEIVED March 17, 2008; FINAL REVISION August 25, 2008; ACCEPTED August 28, 2008)

Abstract

The use of improvised explosive devices has become the hallmark of modern warfare and has resulted in an ever-increasing number of blast-related traumatic brain injuries (TBIs). Despite this fact, very little is actually known about the cognitive sequelae of blast-related TBIs. The purpose of the current study was to compare patterns of performance on neuropsychological measures in subjects who have sustained TBIs as a result of blast (or explosion) with those who have sustained TBIs from non-blast or blunt force trauma (motor vehicle accident, fall, assault, etc.). Participants were categorized as blast-related TBI or non-blast-related TBI and according to severity of injury (mild or moderate-to-severe). No main effects were observed in analysis of covariance between blast-related TBI participants and non-blast-related TBI participants across any of the neuropsychological variables, although an interaction was observed on a visual memory test showing stronger performance for mild blast-related and poorer performance for moderate-to-severe blast-related participants compared with both non-blast groups. Overall, the results do not provide any strong evidence that blast is categorically different from other TBI mechanisms, at least with regard to cognitive sequelae on select measures. Additional findings included a marginally increased incidence of reported posttraumatic stress disorder symptoms among blast-injured participants. (*JINS*, 2009, *15*, 1–8.)

Keywords: Blast injury, Traumatic brain injury, Mild TBI, Neuropsychological, Concussion, PTSD

INTRODUCTION

Explosive mechanisms (e.g., improvised explosive devices [IEDs], landmines, rocket-propelled grenades) account for 78% of injuries in servicemen and women injured in Afghanistan and Iraq, which is the highest proportion seen in any large-scale conflict (Owens et al., 2008). A recent study found that 88% of military personnel treated at a medical unit in Iraq had been injured by IEDs or mortar (Murray et al., 2005). Furthermore, a Veterans Affairs (VA)–based study found that 56% of its war-injured sample had been injured by blasts (Sayer et al., 2008). While blast-related injuries are not new (Coupland & Meddings, 1999), it is the use of IEDs with ever-increasing amounts of explosive (and sometimes toxic) materials that have become the hallmark of these wars. IEDs and other explosive munitions can cause injury *via* high-force blast waves (primary blast injuries) or by the mechanical aftermath of the explosion such as expelled missile fragments, being forcefully thrown, or being crushed by collapsing objects (secondary, tertiary, or quaternary blast injuries) (DePalma et al., 2005; Taber et al., 2006). As such, exposure to blast-level forces can result in a multitude of injuries, including damage to internal organs, multiple fractures, amputations, burns, and traumatic brain injury (TBI).

The potential neuropsychological implications of exposure to blast are still uncertain. The Defense and Veterans Brain Injury Center reported that 59% of an "at-risk" group of injured

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soldiers returning from Afghanistan or Iraq from 2003 to 2004 suffered at least a mild TBI while in combat (Okie, 2005; Warden et al., 2005). A recent survey of returnees from Iraq revealed that nearly 15% reported an injury involving loss of consciousness (LOC) or altered mental status (Hoge et al., 2008). Of those, blast or explosion was the most common mechanism of injury. So, for instance, 79% of those reporting an injury involving LOC were injured *via* blast explosion. Clearly, blast-related TBI is not uncommon.

Our understanding of how blast affects the brain is limited. An explosive blast, with its over-pressurization or primary blast wave, is a different mechanism of injury than an acceleration–deceleration injury. Injuries caused by primary blast waves may result from discrepancies between the external atmospheric pressure and the internal pressure of air-filled organs such as the ear, lungs, and gastrointestinal tract or organs surrounded by fluid-filled cavities such as the brain and spinal cord (Elsayed, 1997; Mayorga, 1997). Despite limited human studies, an increasing number of animal studies suggest that primary blast waves can cause structural injuries to the brain. For example, animal exposure to primary blast waves results in damaged brain tissue and consequent cognitive deficits (Cernak et al., 1996; Kaur et al., 1995). More specifically, recent studies have found the formation of cytoplasmic vacuoles and myelin alterations in the hippocampus of primary blast-exposed rodents (Cernak et al., 2001). Such changes were even noted in rodents with blast to the thorax while the head was protected.

In contrast to injury from the primary blast, secondary, tertiary, and quaternary blast injuries are mechanical injuries and would therefore likely be similar to brain injuries sustained from falls or motor vehicle accidents (MVAs). For example, secondary blast injuries occur when flying debris or projectiles strike or penetrate any part of the body, while tertiary blast injuries can result when an individual is thrown by high-energy shock waves. Finally, quaternary blast injuries include a wide variety of conditions such as burns, toxic inhalations, or crush injuries from collapsed structures or displaced heavy objects (DePalma et al., 2005; Scott et al., 2005; Warden, 2006).

Very little is known about the cognitive sequelae of blast-related brain injuries in humans. The existing TBI literature was created almost exclusively using data from patients having sustained TBIs from blunt force trauma, such as those resulting from MVAs. With regard to mild TBI, the literature has consistently demonstrated improvement to baseline in the majority of cases by 3–6 months post-injury (Belanger et al., 2005; Binder et al., 1997; Schretlen & Shapiro, 2003). Moderate-to-severe injury, on the other hand, tends to result in long-standing impairment despite initial recovery (Dikmen et al., 2003), although this is not uniformly the case (Barnfield & Leathem, 1998; Dikmen et al., 1995; Millis et al., 2001). To date, no human studies have been published on the cognitive sequelae of blast-induced TBI. Sayer et al. (2008) found that mechanism of injury did not predict outcomes such as changes in motor or cognitive functioning as measured by the Functional Independence Measure. However, performance on neuropsychological tests was not examined in that study. The purpose of this study is to compare performance on neuropsychological measures in patients who have sustained a TBI primarily due to blast (or explosion) to performance in demographically comparable patients who have sustained TBI due to other, non-blast-related mechanisms (MVA, fall, assault, etc.).

METHODS

Participants

Participants were consecutively assessed individuals from the Tampa VA Medical Center and selected research volunteers from the Mid-Atlantic Mental Illness Research, Education and Clinical Center (MIRECC), which includes the Richmond, Salisbury, and Durham VA medical centers. Participants were excluded (n = 31) if they were suspected of poor effort or malingering based on clinical presentation and/or if they failed certain measures of symptom validity (Word Memory Test [Green et al., 1996] at the Mid-Atlantic MIRECC and Medical Symptom Validity Test [Green, 2003] and California Verbal Learning Test-II [CVLT-II] Long-Delay Forced-Choice Recognition [Delis et al., 2000] at Tampa). Participants were additionally excluded if they were known to suffer from other neurological disorders (e.g., stroke) apart from TBI (n = 1) or if they sustained a brain injury due to gunshot (n = 3). The final sample (N = 102) consisted primarily of returning active-duty or veteran military personnel who were injured in Afghanistan or Iraq (i.e., 68 were active duty [67%]). The average participant was 28.7 ± 7.7 years of age (range = 19–57 years), had 12.9 ± 2.0 years of education (range = 7–18 years), and had a Wechsler Test of Adult Reading (WTAR; Wechsler, 2001) predicted full-scale intelligence quotient (FSIQ) of 97.2 ± 13.7 (range = 68–125, n = 95). Additional basic demographic information is provided in Table 1. Patients recruited from the Tampa (n = 56) and Richmond (n = 27) VAs were participants in brain injury rehabilitation programs through their Polytrauma/TBI Rehabilitation Centers (P/TRCs), either inpatient or outpatient, and had been referred for a neuropsychological evaluation. Subjects from the Salisbury (n = 12) and Durham (n = 7) VAs were all post-deployed military personnel or VA outpatients. Participants were consented under research protocols approved by each facility's institutional review board.

TBI severity

Severity of TBI was based on self-report and/or documentation of LOC and length of posttraumatic amnesia (PTA). Self-report of PTA is often necessary in returning combat personnel due to the lack of detailed medical records from the theatre, although this means of assessment occurs almost exclusively in the case of mild TBI. In contrast, LOC is generally documented, although again momentary LOC is often only ascertained through questioning the patient about the events surrounding the injury. Only participants who had LOC of less than 30 min and PTA of less than 24 hr were

https://doi.org/10.1017/S1355617708090036 Published online by Cambridge University Press

Table 1. Demographic and injury information

	Sample (N = 102)
Gender	
Male	98
Female	4
Ethnicity	
Caucasian	76
African American	16
Hispanic	8
Other	2
Handedness	
Right	93
Left	7
Ambidextrous	2
Setting	
Inpatient	64
Outpatient	38
Injury type	
Blast	61
MVA	26
Fall	7
Other	8
LOC	
None to momentary	21
<30 minutes	37
<6 hours	10
>6 hours	26
Missing	8

included in the mild TBI group (n = 51). This categorization is based on widely accepted criteria of mild TBI (Kay et al., 1993). Participants meeting criteria for mild TBI with abnormal neuroimaging findings constituted 18% of that group (n = 9: six blast and three non-blast). These findings on magnetic resonance imaging (MRI) or computed tomography included variants of the following: questionable low signal suggesting possible shear injury, a cyst, nonspecific hyperintensity, abnormal morphology of the amygdala, and possible small-focus subarachnoid hemorrhage. Participants experiencing LOC greater than 30 min and/or PTA greater than 24 hr were included in the moderate-to-severe TBI group (n = 51). Demographic breakdowns as a function of TBI severity are presented in Table 2. The mild TBI group was significantly older at the time of evaluation ($p < .005$), and a significantly longer time had elapsed since injury ($p < .01$). No significant differences were observed for age at time of injury, level of education, or predicted FSIQ based on the WTAR (all ps > .05).

TBI etiology

Sixty-one subjects were exposed to blast as their primary mechanism of injury. Of these, 12 also sustained secondary injuries due to MVA. No differences were observed on any variable between those with pure injuries and those with secondary injuries from MVAs; subjects were therefore combined for the remaining analyses. Fifty-one subjects in the blast-related TBI group had closed-head injury; 10 subjects had open-head injury. All but one of the subjects with open-head injury was in the moderate-to-severe group. No differences were observed between subjects with open-*versus* closed-head injury on any variable, and thus, groups were combined for the remaining analyses. Forty-one subjects suffered injuries from non-blast types of mechanisms, including MVA (n = 26), fall (n = 7), motorcycle accident (n = 5), assault (n = 2), and helicopter crash (n = 1). Demographic information on groups as a function of blast *versus* non-blast etiology is presented in Table 3. No significant differences were observed for any variable. However, whereas blast victims were relatively evenly distributed between P/TRC (50/83) and non-P/TRC (11/19; $\chi^2 = 0.04$, $df = 1$, $p > .85$) facilities, a significantly larger percentage of moderate-to-severe TBI was observed in P/TRCs (48/83) compared with non-P/TRCs (3/19; Fisher's exact $p = .002$).

Procedures

The participants were administered a battery of neuropsychological tests. For the purposes of this study, measures known to have greater sensitivity to brain injury and administered in largest number across all sites were analyzed to maximize power to detect potential group differences. These measures included the Trail Making Test (Reitan & Wolfson, 1985), Digit Symbol-Coding subtest of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III; Wechsler, 1997), Brief Visuospatial Memory Test-Revised (BVMT-R; Benedict, 1997), and CVLT-II (Delis et al., 2000). T scores or age-corrected scaled scores based on normative comparisons presented in the manuals were used as dependent measures to control for age and education effects. For the Trail Making Test, Heaton et al.'s (1991) normative data were used. Participants also completed the WTAR (Wechsler, 2001) and a self-report measure of current posttraumatic symptomatology: the posttraumatic stress disorder (PTSD) CheckList (PCL; Weathers et al., 1991). Except for the PCL, not all subjects received each measure, resulting in differing cell sizes for analyses.

Statistics

Group differences on demographic variables and the WTAR were examined using t-tests or contingency table analysis depending on the variable's level of measurement. To determine whether the groups differed on cognitive functioning, we compared normative scores on the four neuropsychological tests using general linear model (GLM) multivariate analysis of covariance (MANCOVA): Trail Making Test Part A and Part B time to completion, Digit Symbol-Coding total symbols, BVMT-R Total Recall and Delayed Recall, and CVLT-II Total Recall (i.e., Trials 1–5 Free Recall Total) and Long-Delay Free Recall (LDFR) Total. TBI etiology (blast, non-blast) and TBI severity (mild, moderate-to-severe) were entered as class variables, and the etiology × severity interaction was examined. Repeated-measures modeling was applied for the Trail Making Test (Part A, Part B), BVMT-R (Total

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Table 2. Demographic variables by TBI severity

	Mild (n = 51)	Moderate/severe (n = 51)	Significance
Age at evaluation (mean)	30.9 (9.2)	26.4 (5.2)	$t_{[79.1]} = 3.06$, $p < .005$[a]
Age at injury (mean)	28.2 (7.7)	25.7 (5.0)	$t_{[86.2]} = 1.95$, $p > .06$[a]
Days since injury (mean)	1021.4 (1730.0)	275.5 (973.6)	$t_{[78.8]} = 2.68$, $p < .01$[a]
<90 days	13	39	Fisher's exact $p < .0001$
90 days to 1 year	5	6	
>1 year	33	6	
Years of education (mean)	13.1 (2.2)	12.8 (1.7)	$t_{[100]} = 0.72$, $p > .47$
WTAR FSIQ (mean)	98.1 (14.6)	96.2 (12.8)	$t_{[93]} = 0.70$, $p > .35$
n	49	46	

[a]Satterthwaite t-tests due to unequal variance.

Recall, Delayed Recall), and CVLT-II (Total Recall, LDFR). To control for significant differences between groups, time since injury (<90 days = 1, 90 days to 1 year = 2, >1 year = 3) was entered as a covariate.

RESULTS

Participants with blast injury were much more likely to be categorized with mild (n = 38) as opposed to moderate-to-severe TBI (n = 23), whereas subjects with non-blast etiologies were more likely to be categorized with moderate-to-severe (n = 28) as opposed to mild TBI (n = 13) ($\chi^2 = 9.18$, $df = 1$, $p < .005$). Twenty participants had history of concussion prior to the index TBI for this study, but no differences were observed in the number suffered by participants with blast injury (n = 13) *versus* those with non-blast etiologies (n = 7; $\chi^2 = 0.28$, $df = 1$, $p > .59$).

MANCOVA conducted on PCL scores yielded a highly significant GLM ($F_{[4,97]} = 21.35$, $p < .0001$). Participants with blast injury exhibited a marginally higher score on the PCL (41.1 ± 18.0) compared with subjects with non-blast etiologies (32.9 ± 17.2; $F_{[1,97]} = 3.60$, $p < .07$). The effect of time since injury was also significant ($F_{[1,97]} = 49.97$, $p < .0001$), reflecting progressively more severe PTSD symptomatology with the passage of time. Due to the near-significant difference between groups on this variable, a highly significant difference between severity groups (mild: 45.5 ± 17.2, moderate-to-severe: 30.1 ± 15.5; $t_{[100]} = 4.76$, $p < .0001$), and the potential for PTSD symptoms to influence neuropsychological performance, particularly memory (Brewin et al., 2007), PCL score was entered as a covariate in all subsequent analyses.

Unadjusted means and standard deviations for neurocognitive variables as a function of TBI etiology and severity are presented in Table 4. Statistically significant results for TBI severity were found for all dependent measures at $p < .05$ with the exception of the Trail Making Test Part B, which achieved borderline significance at $p < .09$. Outcomes for covariate-adjusted analyses were as follows.

Speed/flexibility

Results for the Trail Making Test (n = 92) revealed no significant between-subjects difference or interactive effect for any variable (all ps > .10). The repeated-measures effect for task difficulty was marginally significant, reflecting slightly higher T scores for Part B compared with Part A ($F_{[1,86]} = 3.47$, $p < .07$). Similarly, for WAIS-III Digit Symbol-Coding (n = 83), the overall model was nonsignificant ($F_{[5,77]} = 1.28$, $p > .28$).

Learning/memory

Results for the BVMT-R (n = 93) failed to show main effects for TBI etiology or severity but did yield a significant interaction between TBI etiology and TBI severity ($F_{[1,87]} = 4.31$,

Table 3. Demographic variables by TBI etiology

	Blast (n = 61)	Non-Blast (n = 41)	Significance
Age at evaluation (mean)	29.0 (7.9)	28.2 (7.5)	$t_{[100]} = 0.53$, $p > .59$
Age at injury (mean)	27.9 (7.3)	25.6 (5.2)	$t_{[99.5]} = 1.81$, $p > .07$[a]
Days since injury (mean)	443.3 (835.1)	953.7 (2018.6)	$t_{[49.3]} = -1.53$, $p > .13$[a]
<90 days	28	24	Fisher's exact $p = .43$
90 days to 1 year	8	3	
>1 year	25	14	
Years of education (mean)	13.1 (2.1)	12.6 (1.7)	$t_{[100]} = 1.24$, $p > .21$
WTAR FSIQ (mean)	98.5 (14.2)	95.2 (13.0)	$t_{[93]} = 1.17$, $p > .24$
n	56	39	

[a]Satterthwaite t-tests due to unequal variance.

https://doi.org/10.1017/S1355617708090036 Published online by Cambridge University Press

Table 4. Cognitive variables by TBI severity and etiology group

	Blast		Nonblast	
	Mild	Moderate-to-severe	Mild	Moderate-to-severe
Trail Making Test				
Part A	46.2 (11.6)	37.9 (7.0)	45.8 (14.8)	40.4 (9.9)
Part B	45.6 (9.4)	41.7 (7.9)	49.1 (15.0)	45.0 (9.4)
Digit Symbol-Coding[a]	8.9 (2.5)	7.2 (2.4)	8.3 (2.7)	7.6 (2.4)
BVMT-R				
Total Recall	50.1 (10.1)	38.7 (14.6)	45.2 (12.3)	45.2 (13.0)
Delayed Recall	50.7 (10.7)	40.0 (15.7)	48.6 (12.8)	48.4 (15.6)
CVLT-II				
Total Recall	54.0 (8.1)	48.0 (11.8)	52.8 (10.5)	45.7 (10.2)
LDFR	50.5 (11.4)	41.8 (12.7)	48.3 (9.1)	41.3 (13.3)

Note. Values presented are mean *T* scores (with standard deviations in parentheses).
[a]Digit Symbol-Coding scores represent WAIS-III age-corrected scaled scores (mean = 10, standard deviation = 3).

$p < .05$). Inspection of results indicated that blast-injured patients with mild TBI had the highest means, whereas blast-injured patients with moderate-to-severe TBI had the lowest means (i.e., worst performance) and non-blast patients had means intermediate between the two. Interactions with the repeated measure (Total Recall *vs.* Delayed Recall) were also significant in relation to PCL score ($F_{[1,87]} = 6.07, p < .05$) and time since injury ($F_{[1,87]} = 4.15, p < .05$). The interaction with PCL score reflected a significant correlation with Total Recall ($r = .21$, $p < .05$) but not Delayed Recall ($r = .08$, $p > .42$), and the interaction with time since injury reflected a somewhat steeper increase in performance with greater time since injury for Delayed Recall ($T = 44.7 \pm 14.7$ to 46.0 ± 14.7 to 51.2 ± 12.4) compared with Total Recall ($T = 43.2 \pm 13.3$ to 43.6 ± 16.1 to 49.0 ± 10.8). Finally, results for the CVLT-II ($n = 94$) indicated no between-subjects effect for TBI etiology ($F_{[1,88]} = 0.75$, $p > .38$) but did reveal a significant effect for TBI severity ($F_{[1,88]} = 6.63$, $p < .05$), reflecting better performance for the mild group compared with the moderate-to-severe group. The effect was noted for both Total Recall ($F_{[1,88]} = 8.09, p < .01$) and LDFR ($F_{[1,88]} = 4.44, p < .05$). A significant effect of the repeated measure was also observed ($F_{[1,88]} = 12.75, p < .001$), reflecting substantially better performance for learning trials (Total Recall) compared with LDFR.

DISCUSSION

To our knowledge, this is the first study comparing cognitive profiles of blast *versus* non-blast mechanisms of TBI. Our results suggest that cognitive sequelae following TBI are determined more by severity of injury than mechanism of injury on verbal learning and memory measures. Inspection of means indicated that cognitive performance was uniformly worse for moderate-to-severe TBI compared with mild TBI, with statistically significant results observed for all measures except for Part B of the Trail Making Test and significant findings when covariates were included for the CVLT-II, a verbal learning and memory measure. Statistical significance of TBI severity on neuropsychological measures other than the CVLT-II was lost with the addition of covariates (i.e., time since injury and PCL scores), illustrating the importance of these variables on outcomes. Other studies have found no differences on neuropsychological variables between mild and moderate-to-severe TBI groups (Barnfield & Leathem, 1998). Most outcome studies have found significant heterogeneity on neuropsychological measures across TBI severity, with many TBI survivors performing within normatively normal ranges at follow-up (Millis et al., 2001) and with many showing significant recovery months to years post-injury (Dikmen et al., 1995). Our sample was nearly 2 years post-injury, on average, which may have attenuated any effect of TBI severity or mechanism of injury on neuropsychological outcomes when time since injury was entered into the model.

Comparison of blast TBI with non-blast etiologies did not yield significant differences with the exception of an etiology × severity interaction on the BVMT-R. For Total Recall and Delayed Recall, blast-injured participants with mild TBI had the highest means, whereas blast-injured participants with moderate-to-severe TBI had the lowest means (i.e., worst performance) and non-blast participants had means intermediate between the two. Overall, the results do not provide any strong evidence that blast is categorically different from other mechanisms, at least with regard to cognitive sequelae on select measures.

Our sample of blast-injured participants was more likely to have mild rather than moderate-to-severe TBI. This pattern is consistent with findings of a recent survey of Iraq war returnees with a history of mild TBI who were more likely to have been injured in a blast/explosion than any other mechanism (Hoge et al., 2008). Clearly, additional efforts should focus on identifying the cognitive sequelae related to the more common cause of mild TBI in returning veterans: exposure to blast.

An important finding of this study was that participants with blast injury compared with non-blast etiologies showed a near-significant tendency to endorse a greater number of PTSD symptoms on the PCL. Various contextual and neural

https://doi.org/10.1017/S1355617708090036 Published online by Cambridge University Press

underpinnings may help explain why blast-related TBI victims in our sample more frequently evidenced PTSD symptomatology compared with non-blast victims. With the increasing threat of IEDs, the physiological level of arousal of these veterans would be expected to be heightened at the time when the blast event transpired (as compared with MVA where the victim is less likely to be hyperaroused pre-event). A heightened limbic arousal and multisensory inputs in the time immediately preceding the blast ("fight or flight response") may strengthen the encoding of survival-based memories following the blast, even with momentary LOC (Glaesser et al., 2004; van der Kolk, 1996). Because most blasts in our sample resulted in a mild TBI, it stands to reason that these individuals had an increased likelihood of being able to encode memories immediately following the blast. The events following blasts are often marked by perceptions of horror, vulnerability to attack (e.g., by snipers or additional blasts), or by witnessing injury/death of others in the blast vicinity. These experiences, more so than MVA and other blunt force mechanisms, are beyond the realm of ordinary human experience.

The high prevalence of PTSD and other psychiatric disturbances secondary to the Afghanistan and Iraq wars has been well documented (e.g., Erbes et al., 2007; Friedman, 2006; Hoge et al., 2006, 2008; Jakupcak et al., 2007; Kolkow et al., 2007; Milliken et al., 2007). Future studies are required to determine whether the rates of PTSD following blast-induced TBI are greater (or diminished) relative to individuals exposed to blast but without suffering TBI. With regard to PTSD symptoms, it has long been debated whether PTSD can follow TBI given the frequent period of retrograde and anterograde amnesia surrounding the traumatic event (Glaesser et al., 2004; Greenspan et al., 2006; Jones et al., 2005; Moore et al., 2006; Warden et al., 1997). In this sample, those injured *via* explosions were more likely to have sustained a mild TBI and presumably therefore better able to remember the traumatic event. Given the limitations of a singular self-report measure, a diagnosis of PTSD cannot be made, nor should it be inferred in interpreting these results. Rather, these findings suggest that individuals suffering from mild blast injuries tend to endorse more PTSD-related symptomology than individuals from other groups, including those suffering from mild injuries from non-blast-related events.

A number of possible hypotheses may explain the increasing PCL scores over time. First, recovery following brief LOC may be associated with recovery of memories surrounding the event. When these memories return, they may be experienced as intrusive and distressing, whether they are factually based or otherwise. Second, physiological changes (e.g., vestibular changes, hearing loss, tinnitus) may persist and trigger increased anxiety symptoms over time (e.g., increased startle response, hypervigilance). Finally, PCL scores may increase over time due to increased awareness and recognition of post-injury sequelae affecting quality of life, particularly as the combatant transitions back into civilian life. Indeed, Milliken et al. (2007) found that soldiers reported more mental health concerns several months after their return from Iraq as compared with their initial report upon returning home. Obviously, these hypotheses are speculative and require further exploration.

Several weaknesses of the current study warrant attention. By necessity, the presence of LOC and/or PTA was often based on self-report in cases of mild TBI. While careful questioning about the details surrounding the event can frequently shed light on these variables, objective data from emergency personnel (e.g., Glasgow Coma Scale scores) are obviously preferable. Furthermore, participants were recruited from different sites, possibly leading to unwanted variance across sites. Our numbers were too small and institutional settings too aligned with severity groupings (most moderate-to-severe subjects came from P/TRCs) to correct for these potential differences. A larger sample, with greater geographic diversity, may elucidate effects that were too small to detect in the current sample. Participants from Tampa were also treatment-seeking individuals evaluated under clinical protocols, whereas those from Richmond were treatment-seeking individuals who consented to participate in prospectively designed research studies and those from Salisbury and Durham were non-treatment-seeking individuals who consented to research-driven protocols.

Also, given that the blast-injured group included some patients with open-head injury and the non-blast-injured group did not, a potential confound may be present, although statistical analyses did not reveal formal differences. As this was a sample of convenience, a more controlled study will be needed to confirm our findings. Finally, TBI that is exclusively due to blast may be unusual. The force of the blast may propel the individual or nearby objects, thereby increasing the likelihood of secondary injuries (that are due to blunt force trauma rather than the pressure wave). Indeed, in the present study, 12 of 61 participants injured primarily due to blast exposure were also injured *via* other mechanisms. We would expect these cases to generate more cognitive sequelae relative to non-blast-injured, but this was not the case.

Overall, however, it appears that mechanism of injury does not have a significant differential effect on cognitive performance, at least on selected measures of speed/flexibility and learning/memory. It may be that while pathological changes differ within the brain due to mechanism, the behavioral manifestation of those changes is similar and varies more as a result of the extent or severity of injury to the brain. These findings are consistent with a recent study suggesting that mechanism of injury does not predict functional outcomes (Sayer et al., 2008). On the other hand, more physiologically based measures (like functional MRI [fMRI]) might reveal differences not apparent on neuropsychological measures, particularly in those cases with both brain injury and psychiatric sequelae (Trudeau et al., 1998). For instance, Chen et al. (2008) found no differences between concussed athletes and non-concussed athletes with and without depressive symptoms on behavioral cognitive measures but did find differences in brain activation on fMRI measures. Larger studies with all cognitive domains assessed are still needed and are underway in some centers (Mid-Atlantic MIRECC). These studies are specifically addressing the functional,

https://doi.org/10.1017/S1355617708090036 Published online by Cambridge University Press

neuroanatomical, and cognitive correlates in blast injury. Additional research focus should include much larger sample sizes in light of the heterogeneity of TBI in the current combat theatre. In the current study, those injured *via* blast were more likely to have sustained mild injuries and to report PTSD-related symptoms. Given that blast-injured soldiers constitute the largest portion of TBI survivors in the current military conflicts, efforts directed at mild TBI education and therapy, as well as prevention of PTSD symptom escalation, seem warranted.

ACKNOWLEDGMENTS

This material is the result of work supported with resources and the use of facilities at the James A. Haley Veterans' Hospital (Tampa VA), Mid-Atlantic (VISN 6) MIRECC, the W.G. (Bill) Hefner VA Medical Center (Salisbury VA), the Hunter Holmes McGuire VA Medical Center (Richmond VA), and the Durham VA Medical Center. The views expressed herein are those of the authors and do not necessarily reflect the views of the Department of Veterans Affairs.

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