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THE EFFECTS OF POSTTRAUMATIC STRESS DISORDER, MILD TRAUMATIC BRAIN INJURY, AND COMBINED POSTTRAUMATIC STRESS DISORDER/MILD TRAUMATIC BRAIN INJURY ON RETURNING VETERANS

THESIS

A thesis submitted in partial fulfillment of the
requirements for the degree of Master of Science in the
College of Arts and Sciences
at the University of Kentucky

By

Hannah Lane Combs

Lexington, Kentucky

Director: Dr. David T. R. Berry, Professor of Psychology

Lexington, Kentucky

2013

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ABSTRACT OF THESIS

THE EFFECTS OF POSTTRAUMATIC STRESS DISORDER, MILD TRAUMATIC BRAIN INJURY, AND COMBINED POSTTRAUMATIC STRESS DISORDER/MILD TRAUMATIC BRAIN INJURY ON RETURNING VETERANS

Veterans of the Iraqi and Afghanistan conflicts have frequently returned with injuries such as mild traumatic brain injury (mTBI) and posttraumatic stress disorder (PTSD). More recently, concern has been raised about the large number of returning soldiers who are diagnosed with both. Literature exists on the neuropsychological factors associated with either alone, however far less research has explored the effects when combined (PTSD+mTBI). With a sample of 206 OEF/OIF veterans, the current study employed neuropsychological and psychological measures to determine whether participants with PTSD+mTBI have poorer cognitive and psychological outcomes than participants with PTSD-o, mTBI-o, or veteran controls (VC), when groups are matched on IQ, education, and age. The PTSD+mTBI and mTBI-o groups exhibited very similar neuropsychology profiles, and both PTSD+mTBI and mTBI-o performed significantly (α=.01) worse than VC on executive functioning and processing speed measures. There were no significant differences between VC and PTSD-o on any notable neuropsychology measures. In contrast, on the psychological measures, the PTSD+mTBI and PTSD-o groups were identical to each other and more distressed than either mTBI-o or VC. These findings suggest there are lasting cognitive impairments following mTBI that are unique to the condition and cannot be attributed to known impairments associated with distress.

KEYWORDS: Posttraumatic Stress Disorder, Mild Traumatic Brain Injury, Veteran, OEF/OIF, Neuropsychological Assessment

Hannah L. Combs

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Chapter 1: Introduction

Traumatic brain injury (TBI) constitutes a significant health concern in most developed countries; among high income nations it is one of the leading causes of death and disability among people under the age of 45 (Maas, Stocchetti, & Bullock, 2008). In civilian settings most TBI is secondary to a vehicle accident or falls (NINDS, 2002). TBI ranges in severity from moderate to severe with poor outcome, to mild with generally good recovery. In military settings mild traumatic brain injury (mTBI) is gaining attention due to its label as the "signature injury" in veterans of the current conflicts of Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF). Recent studies (Hoge, McGurk, Thomas, Cox, Engel, & Castro, 2008; Schneiderman, Braver, & Kang, 2008) report mTBI incidence rates of approximately 12-16% in deployed veterans. The vast majority of these mTBIs are the result of blast exposures from an improvised explosive device (IED), which are common in contemporary combat zones (Galarneau, Woodruff, Dye, Mohrle, and Wade, 2008).

Posttraumatic stress disorder (PTSD), a severe anxiety disorder that may develop after exposure to a traumatic experience, is also common in veterans. Rates of PTSD in returning service personnel are roughly comparable to rates of mTBI, ranging from 13-17% (Hoge, Castro, Messer, McGurk, Cotting, & Koffman, 2004; Hoge, Terhakopian, Castro, Messer, & Engel, 2007). Research suggests that the development of PTSD in veterans is more highly specific to combat experience and being injured rather than simply to being deployed to a war zone (Kennedy, Jaffee, Leskin, Stokes, Leal, & Fitzpatrick, 2007; Smith, Ryan, Wingard, Slymen, Sallis, & Kritz-Silverstein, 2008).

Consequently, military personnel who serve in combat areas may be at greater risk for both mTBI and PTSD than soldiers without such service. In fact, recent data suggest that there have been an increasing number of veterans returning with both mTBI and PTSD. Vanderploeg, Belanger, & Curtiss (2009) indicated that approximately one-third of OIF veterans with mTBI also have PTSD (or depression). To date, there is extensive literature on the neuropsychological factors associated with PTSD or mTBI alone; however, far less research has explored the psychological effects of the disorders combined.

Instead of referring to the two conditions occurring at once as "comorbid PTSD/mTBI," the current study will refer to this classification as PTSD+mTBI. This reflects a more accurate description of the overall condition as the two disorders have many developmental differences (discussed below). In addition, veterans with current PTSD but no mTBI history will be referred to as PTSD-only (PTSD-o) and veterans with history of deployment related mTBI, but no PTSD will be referred to as mTBI-only (mTBI-o).

Mild Traumatic Brain Injury

The National Center for Injury Prevention and Control (NCIPC) describes mild TBI as a traumatically induced brief alteration of mental status, loss of consciousness for less than 30 minutes, and/or post-traumatic amnesia for less than 24 hours following an impact, to or forceful motion, of the head (2003). The American Congress of Rehabilitation Medicine stipulates that the initial Glasgow Coma Scale (a measure of level of consciousness) scores must not be less than 13 and post-traumatic amnesia may not exceed 24 hours (1993). As noted earlier, in civilian populations, a mTBI is generally

a result of a closed head injury sustained as a result of a fall or a motor vehicle accident. In veterans, most mTBIs are caused by exposure to a blast and it is estimated that approximately 15-20% of veterans returning from Iraq and Afghanistan have sustained a mTBI (Hoge et al., 2008).

Neuropsychological Deficits Associated with mTBI

In civilian contexts, even though many individuals experience at least some cognitive difficulties immediately following mTBI including impairments in attention, memory efficiency, and processing speed measures (Belanger, Curtiss, Demery, Lebowitz, & Vanderploeg, 2005), evidence suggests that for most people the cognitive effects of mTBI resolve within days to at most 3 months post-injury (Iverson 2005; Schretlen and Shapiro 2003). A recent re-evaluation of three prior meta-analyses of mTBI by Rohling, Binder, Demakis, Larrabee, Ploetz, & Langhinrichsen-Rohling (2011) found the largest deficits related to verbal and visual memory at 1 week post-injury, however, at 3 months post-injury, all specific neurocognitive domains returned to pre-morbid levels.

Nevertheless, small subsets of civilians with mild TBI report the subjective experience of chronic cognitive deficits despite a positive long-term prognosis (e.g., Dikmen, McLean, & Temkin, 1986; Vanderploeg et al. 2009). There are several theories about the experience (subjective and objective) of persistent cognitive decline after mTBI. The first theory is that approximately 4-6% of persons with mTBI experience lasting deficits in attention (Binder, Rohling, & Larrabee, 1997), but many studies simply dismiss these findings as outliers (Bigler, Young, Kane, & Nicholson, 2006). A second theory is that most individuals with mTBI experience a very small (4-6%) measurable but

subjectively significant decline in attention compared to pre-injury ability levels. Another theory is that there is no objective decline in attention and other cognitive functions long-term, but the subjective experience of impaired attention can be explained through other mechanisms, such as psychological distress, problematic coping style, compensation-seeking status, iatrogenic effects, and substance abuse (Ettenhofer & Abeles, 2008; Marsh & Smith, 1995). However, proponents of the first two theories that support the possibility of long-term cognitive decline would argue that these alternative factors cannot account for all individuals showing chronic cognitive complaints.

Posttraumatic Stress Disorder (PTSD)

The DSM-IV-TR (APA, 2000) requires that six criteria be met in order for an individual to be diagnosed with PTSD. Criterion A is twofold; an individual must have exposure to a traumatic event (A1) that is accompanied by a fear response (e.g. feelings of fear, helplessness, horror etc.) (A2). Criterion B necessitates the traumatic event be re-experienced in a persistent, intrusive manner in at least one way (e.g. dreams, memories, flashbacks, etc.). Criterion C requires a minimum of three symptoms of avoidance of trauma-related stimuli or emotional numbing (e.g. avoiding activities that may remind the individual of the trauma, use of substances to numb strong emotions, or an inability to or decrease in experience of emotion). Criterion D stipulates that the individual have at least two symptoms of hyperarousal such as difficulty sleeping, abnormal startle reaction, or hypervigilance. The onset of all Criterion B, C, and D symptoms must occur after the traumatic event. Criterion E requires the PTSD symptoms be present for at least one month. Criterion F specifies that the symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Factors Associated with Development of PTSD

Base rates indicate that most people will experience a stressor sufficient to meet DSM-IV-TR criterion at some point in their lives, but only a minority of individuals develop PTSD in response to such stressors. In a longitudinal study by Breslau, Lucia, and Alvarado (2006), it was reported that by age 17, over 75% of the 713 children in their study had experienced trauma of some sort, but only 6.3% subsequently developed PTSD.

Beyond trauma, a number of factors have been identified that may serve as risk factors for developing PTSD. Polusny, Erbes, Murdoch, Arbisi, Thuras, & Rath (2011) found increased prevalence of PTSD in National Guard soldiers who reported feeling less prepared for deployment and/or described experiencing more stressors before deployment to Iraq. Combat and combat aftermath exposure were also significantly related to PTSD (Polusny et al., 2011). Intelligence also appears to play a role in risk for developing PTSD. IQ contributes to prediction of PTSD severity beyond combat exposure and education, such that lower pre-deployment IQ was associated with more severe PTSD symptoms (McNally & Shin, 1995; Macklin, Metzger, Litz, McNally, Lasko, Orr, et al., 1998). Lastly, in a longitudinal study with 668 veterans from the OIF/OEF conflicts, Marx, Doron-Lamarca, Proctor & Vasterling (2009) showed that poor pre-trauma visual immediate memory performance was associated with greater post-deployment PTSD symptom severity.

Some possible protective factors for PTSD have also been identified. Research with children suggests high IQ may also serve as a protective factor against both exposure to trauma and against development of PTSD in those who were exposed

(Breslau, Lucia, and Alvarado, 2006). Similarly, recent work suggests that nonverbal memory scores may be higher in individuals who do not develop PTSD in response to trauma compared with those who do (Wingo, Fani, Bradley, and Ressler, 2010).

Neuropsychology of PTSD

There is extensive research regarding the performance of individuals with PTSD on neuropsychological testing. Although PTSD is often viewed primarily as dysfunctional regulation of fear conditioning, neuropsychological components play a key role in the disorder (Vasterling, Verfaellie, & Sullivan, 2009). In fact, impairments in memory and attention are crucial to the clinical presentation of PTSD and are included in the DSM-IV-TR diagnostic criteria (APA, 2000). Moreover, PTSD is highly associated with impairments on tasks assessing memory, attention, and executive functioning (Vasterling et al., 2009; Vasterling & Brailey, 2005; Brewin, Kleiner, Vasterling, & Field, 2007).

Memory. A recent meta-analysis (Brewin et al., 2007) found a small to moderate association between PTSD symptoms and immediate and delayed verbal memory impairments and a weaker association with visual memory. Johnsen and Asbjørnsesn (2008) concluded that these memory impairments were seen in both military and civilian samples, although the strongest effects were seen amongst veterans. Samuelson, Neylan, Metzler, Lenoci, Rothlind, Henn-Haase, et al. (2006) found significant verbal memory impairments in veterans with PTSD, even after controlling for depression and substance abuse. Because, as noted earlier, IQ is thought to be a risk factor for developing PTSD (and often studies are not well-matched on this variable), Neylan and colleagues (2004) conducted a study matching groups on IQ, education level, and other psychological

comorbidities. No differences in memory impairments were found in a well-matched sample of combat veterans with chronic PTSD and non-PTSD participants. Although these groups were closely matched the average education level was approximately 15 years, much higher than the average veteran. Using a more representative sample, Samuelson, Krueger, Burnett, and Wilson (2010) evaluated whether intelligence and education differences account for the memory impairments seen with PTSD. After controlling for IQ score, Samuelson et al. (2010) found that the PTSD group still performed significantly worse than controls on the California Verbal Learning Test, suggesting that memory impairments cannot be accounted for solely by IQ differences.

Attention and Executive Functioning. Patients with PTSD also show deficits in attention and executive functioning. In two studies that tested a four-domain model of attention (Mirsky et al. 1991), Gulf War and Vietnam veterans with PTSD performed worse than warzone-exposed veterans without PTSD on sustained attention and encoding tasks, but not on a focus-execute or a shifting task (Vasterling et al. 1998, 2002). These findings are representative of other studies with war veterans in which PTSD has been associated with deficits on encoding (Barrett, Green, Morris, Giles, & Croft, 1996; Beckham, Crawford, & Feldman, 1998; Gilbertson et al. 2001), but not set-shifting (Sullivan et al. 2003) or focus-execute tasks (Litz et al. 1996). Persons with PTSD also tend to perform worse on some tests of executive functioning (e.g. Jenkins, Langlais, Delis, & Cohen, 2000; Hart, Kimbrell, Fauver, Cherry, Pitcock, Booe, et al., 2008).

PTSD+mTBI

Neuropsychologists have only recently begun to study PTSD and mTBI as "comorbid" conditions. Clinical and research interest is high given the great co-

occurrence of these disorders in returning veterans. As noted above, earlier research suggested that these disorders result in comparable deficits, at least initially, in neuropsychological performance (Vasterling, Verfaellie, & Sullivan, 2009) and are often complicated by factors such as substance abuse (Stein & McAllister, 2009). Despite these similarities, the paths to recovery are quite distinct (Vasterling et al., 2009). While PTSD symptoms and associated neuropsychological deficits are typically present for years (Beckham et al., 1998), in civilian populations mTBI symptoms generally only last a few weeks to months (Ponsford, Willmott, Rothwell, Cameron, Kelly, Nelms, et al., 2000). Some studies have reported deficits that are considered to be unique to their co-occurrence. These include different levels of severity of deficits related to PTSD or mTBI, as well as further impairments not classically associated with either (Dolan, Martindale, Robinson, Kimbrel, Meyer, Kruse, et al., 2012).

Mild TBI and PTSD Development

mTBI is associated with greater risk for developing PTSD than found with more severe brain injuries (Bryant, Creamer, O'Donnell, Silove, & Clark, 2009; Vasterling et al., 2009). Studies by Belanger, Kretzmer, Yoash-Gantz, Pickett, and Tupler (2009) and Lippa, Pastoerk, Benge, and Thornton (2010) suggested that blast-related TBI (most common in combat areas) was related to greater likelihood of development of PTSD. However, Luethcke, Bryan, Morrow, & Isler (2011) found no significant differences between acute blast- versus nonblast-induced mTBI. This inconsistency may be attributed to a difference in samples: Lippa et al. (2010) and Belanger (2009) both found relationships between TBI and PTSD at least one year after injury, while Luethcke et al. (2011) studied at veterans within 72 hours after injury.

Vasterling and colleagues (2009) propose possible ways in which mTBI could negatively impact development of and recovery from PTSD. Potential mechanisms include early mTBI symptoms affecting trauma-coping and memory encoding or persistent postconcussive symptoms affecting post-trauma adjustment. Because the consolidation of memory occurs within 24 hours of an event, acute cognitive impairments related to mTBI may interfere with this process. This could result in improper integration of the traumatic event into memory, facilitating the development of PTSD (Vasterling et al., 2009). Others suggest that the high comorbidity may be a result of an increased vulnerability to the development of PTSD by depletion of a person's ability to cope with negative emotions following trauma (Bryant, Felmingham, Kemp, Das, Hughes, Peduto, et al., 2008).

Neuropsychological Deficits Associated with PTSD+mTBI

Studying the influence of PTSD+mTBI on neuropsychological functioning has proven challenging. Findings are conflicting, especially as to whether or not the co-occurrence of PTSD+mTBI leads to deficits over and above their individual effects (Gordon, Fitzpatrick, and Hilsabeck, 2011). Brenner, Terrio, Homaifar, Gutierrez, Staves, Harwood et al. (2010) examined the performance of veterans with PTSD on neurocognitive tasks and compared the results between a group with PTSD-o and a group with PTSD+mTBI. 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 differences between any of the groups on the tests administered. Gordon, Fitzpatrick, and Hilsabeck (2011) found similar null results.

Although few studies are available, there has been some neuropsychological evidence indicating neuropsychological deficits unique to patients with PTSD+mTBI. One study demonstrated lower Stroop Word Reading scores in veterans with PTSD+mTBI compared to veterans diagnosed with PTSD-o (Brenner et al. 2010). This finding supported an earlier study by Nelson, Yoash-Gantz, Pickett, & Campbell (2009) who looked at OIF/OEF veterans with history of mild to moderate TBI-o. The PTSD+mTBI group scored worse than the mild-moderate TBI-o group on the Stroop Color (measures speed of information processing) and Color/Word tests (measures response inhibition). The authors speculated that the results were suggestive of an effect of PTSD on executive functioning and processing speed. Barrett et al. (1996) also found evidence for PTSD+mTBI individuals performing worse on set-shifting, an executive function task, using PTSD-o and PTSD+comorbid psychiatric diagnosis comparison groups.

These studies suggest that the acute cognitive effects of exposure to mTBI are comparable to those observed in veterans who endorse significant symptoms of PTSD, and the co-occurrence may be associated with greater cognitive difficulties. However, there are several issues present in the current literature that must be addressed.

Gaps in the PTSD+mTBI Literature

Not only is the literature on PTSD+mTBI quite limited, but it is also fraught with methodological problems. The effect sizes for the PTSD+mTBI groups in the Brenner et al. (2010) study and Nelson et al. (2009) imply important differences in neuropsychological performance between veterans with co-morbid PTSD+mTBI and veterans with only mTBI; however, both studies lacked a PTSD-o control group, creating

a major limitation to the findings. Given the large effect sizes related with PTSD on neuropsychological testing, it is important to see whether their results will be replicated in an independent sample, with comparable group sizes and adequate power. The Campbell et al. study (2009) was the first to include a critical PTSD-o control group; however, the small size of the group likely affected statistical power.

Given the compensable nature of PTSD diagnoses in veterans, another noteworthy limitation to the current literature on the combined effects of PTSD+mTBI is that most neuropsychological studies fail to use measures of psychiatric symptom validity, instead utilizing only measures of neurocognitive symptom validity. This limitation, combined with the reliance on brief self-report questionnaires for diagnosing PTSD, may call the validity of the PTSD diagnoses into question.

Only one study using neuropsychological testing has incorporated a combat-exposed comparison group (Shandera-Ochsner, 2012). This group is essential because the possible effect of combat stress on neuropsychological profile characteristics is unknown. A combat-exposed control group would be the most appropriate comparison for both veterans with mTBI-o (at least 3 months post injury) and veterans with PTSD. It is important to compare the effects of PTSD to the effects of typical combat stress exposure that does not result in a psychological disorder. However, as mentioned earlier, research suggests there may be other important factors related to the development of PTSD (e.g. pre-deployment stress, extent of combat exposure, pre-morbid IQ).

Shandera-Ochsner (2012) were the first researchers to look at the neurocognitive and psychiatric impairments following PTSD+mTBI, PTSD-o, and mTBI-o, compared to a Combat Control group. Their study of 81 OIF/OEF veterans suggests that PTSD has the

greatest effect on neuropsychological functioning post-deployment. There were no significant differences between the PTSD+mTBI and the PTSD-o groups on any neuropsychological measure. A second major finding was that deployment concussion did not make a significant difference in long-term cognitive outcome. The mTBI group scored comparably to the combat control group on all neuropsychological measures. However, the PTSD+mTBI group was significantly more psychologically distressed than the mTBI-o or the PTSD-o group. The mTBI-o and PTSD-o groups were comparable and both significantly more distressed than the control group on measures of anxiety and depression, while the PTSD+mTBI group was significantly more distressed than all other groups. Although this study provides strong evidence for the notion that PTSD contributes more to neurocognitive impairments than mTBI, the groups were not equivalent on estimated pre-morbid IQ, education level, combat exposure, lifetime mTBI, and current psychiatric disorders, which raises questions about the proper interpretation of these results.

Purpose of the Present Study

The present study employs neuropsychological and psychological assessment measures to determine whether veterans with PTSD+mTBI have poorer cognitive and psychological outcomes than veterans with PTSD-o, mTBI-o, or veteran controls (VC). Based on the previous literature the following hypotheses were tested:

1. There are no differences between the PTSD+mTBI group and the PTSD-o group, suggesting that the cognitive impairments are mostly accounted for by the PTSD diagnosis.

2. There are no differences between the mTBI-o group and the VC group on neuropsychological measures.
3. The PTSD+mTBI and PTSD-o groups perform more poorly on the neuropsychological measures than the mTBI-o and VC groups.
4. The PTSD+mTBI group is more distressed than PTSD-o, mTBI-o, and VC on diagnostic measures.

Matching groups based on pre-deployment IQ, education, combat exposure, and number of lifetime mTBIs will address methodological concerns identified in the previous study.

Chapter 2: Methods

Participants

The present study utilized archival data from the VA's TBI Clinical Reminder and Comprehensive TBI Evaluation database that included four hundred and thirty eight OIF/OEF veterans. All were English-speakers with combat exposure. Participants were excluded from the study if they met any of the following criteria: psychosis, ADHD/ADD diagnosed in childhood, significant neurologic history (other than mTBI in the mTBI-o and PTSD+mTBI groups) such as stroke, epilepsy, or brain tumor, post-deployment TBI (mild or worse), <93% correct on the Letter Memory Test, >6 total score on the Miller Forensic Assessment of Symptoms Test total score, or >80T on MMPI-2-RF VRIN, TRIN, or L scales. Due to the particularly high rates of other psychological and substance abuse diagnoses in OIF/OEF veterans (over 85% of veterans with deployment mTBI and over 40% of those without) reported by Carlson et al. (2010), participants with co-morbid diagnoses such as these will be allowed in the study. Estimates from the literature indicate that more than two-thirds of individuals with PTSD have at least one additional Axis I diagnosis (Brady, 1997; Kesler et al., 1995), therefore, self-report data on current psychiatric and substance abuse diagnoses were obtained.

Study participants were obtained from a multi-site VA study examining the effectiveness of the VA's Comprehensive TBI Evaluation, which recruited all newly returned OIF/OEF personnel for research evaluations at the Lexington, KY, Tucson, AZ, and Chicago, IL VAMC. Veterans in this study were selected for the analysis in the current study if they met basic eligibility criteria described above. Group assignment was based on the veteran's responses to the Structured Interview for TBI Diagnosis and the

Clinician-Administered PTSD Scale (CAPS; Blake, Weathers, Nagy, Kaloupek, Gusman, Charney, et al., 1995). For purposes of this research study, a veteran was considered to have sustained a deployment mTBI if the criteria for mTBI provided by the American Congress of Rehabilitation Medicine (ACRM; Mild Traumatic Brain Injury Committee, 1993) were met by his or her responses to the TBI interview questions with likelihood of mTBI rated as "almost certainly" or "very likely." Similarly, "no history of deployment mTBI" was defined as responses to TBI structured interview questions resulting in rating of "not at all likely" or "very unlikely." Veterans who reported alteration, but not loss, of consciousness were queried to obtain detailed descriptions of their endorsement of this symptom. In some cases, the veteran described "alteration" of consciousness as feeling fearful or otherwise emotionally distressed. In cases where emotional distress was the exclusive reported experience, the interviewer over-ruled the veteran's endorsement of alteration of consciousness (AOC) and did not classify the event as a mTBI. A veteran was considered to have PTSD based on the lenient scoring rule (described below) provided in the CAPS manual.

Measures

Diagnostic measures.

Clinician Administered PTSD Scale (CAPS). Regarded as the "gold standard" diagnostic assessment tool for PTSD, the Clinician Administered PTSD Scale (CAPS) (Blake, Weathers, Nagy, Kalouplek, Charney, & Keane, 1995) is a structured interview that follows the criteria set forth by the DSM-IV. The measure has 30 items and takes approximately 45 minutes to 1 hour to administer. CAPS administration includes use of a self-report form (given at the beginning of the interview) called the Life Events Checklist

(LEC) to identify exposure to traumatic events in the interviewee's lifetime. The examinee's responses on the LEC assist the interviewer in focusing the first few questions of the CAPS, which deal with Criterion A (fear response after exposure to significant stressor). The psychometric characteristics of the CAPS are strong. After reviewing the literature on the CAPS, Weathers, Keane, and Davidson (2001) concluded the measure has excellent interrater reliability (r = .90 and higher), two to three day test-retest reliability (r =.89), and internal consistency (r =.80-.90). Weathers et al. (2001) also found strong evidence of convergent validity (.70 and higher) with self-report measures of PTSD.

Structured Interview for TBI Diagnosis in OEF/OIF Veterans (SITDOV). The original version of this unpublished interview was piloted by Donnelly and colleagues at the Buffalo VA (Donnelly, Donnelly, Dunnam, Warner, Kittleson, Constance, Bradshaw, & Alt, 2011). The form was modified by researchers at the Lexington, Tucson, and Hines VAs for use in a multi-site study on the validity of the VA's Second Level Clinical Reminder tool for diagnosing mTBI. The psychometric properties of the SITDOV have not yet been investigated. A copy of the modified SITDOV is provided in Appendix A.

Beck Depression Inventory (BDI-II). The BDI-II (Beck, Steer, & Brown, 1996) is a 21-item self-report measure that assesses the presence and severity of symptoms of depression. The BDI-II has excellent reliability, an internal consistency alpha of .92, and one week test-retest correlation of .93 The BDI-II correlates more strongly with other measures of depression (r = .71 with the Hamilton Psychiatric Rating Scale for Depression) than with measures of anxiety, a construct shown to be associated with but distinct from depression (Beck, Steer, Ball, & Ranieri, 1996).

Beck Anxiety Inventory (BAI). The BAI (Beck, Epstein, Brown, & Steer, 1988) is a 21-item self-report measure that assesses the presence and severity of anxiety symptoms. The BAI has high internal consistency (alpha = .92) in outpatients and good test-retest reliability after one week (r = .75). The BAI correlates with other measures of anxiety (r = .51 with the Hamilton Anxiety Rating Scale – Revised) and with measures of depression (r = .48 with the BDI-II; Beck, Steer, & Beck, 1993).

Insomnia Severity Index (ISI). The ISI (Bastien, Vallieres, & Morin, 2001). Is a 7-item self report measure that assesses the nature, severity, and impact of insomnia. The ISI has high internal consistency (alpha = .90) in outpatients and good test-retest reliability after 2 weeks (r = .79). The ISI correlates with other measures of sleep quality such as sleep diaries (r = .59) and the Pittsburgh Sleep Quality Index (PSQI) (r = .80; Morin, Belleville, Belanger, & Ivers, 2011).

Neuropsychological measures.

Wechsler Test of Adult Reading (WTAR). The WTAR (Wechsler, 2001) was used to estimate global intelligence level (IQ). The WTAR uses irregular word reading ability and demographic information to estimate pre-morbid Full Scale IQ (FSIQ). The WTAR has excellent internal consistency (*r* = .90 to .97) and test-retest stability (*r* = .90 to .94, test-retest average interval of 35 days). The WTAR correlates highly with other measures of reading recognition, and has high correlations with WAIS-III Verbal IQ (*r* = .66 to .80), Full Scale IQ (*r* = .63 to .80) and moderate correlations with Performance IQ (*r* = .45 to .80).

California Verbal Learning Test (CVLT-II). The CVLT-II (Delis, Kramer, Kaplan, & Ober, 2000) involves oral presentation of a 16-item word list over 5 learning

trials, an interference trial, short-delay recall (free and cued portions), 20-minute "long-delay" recall, and recognition trials. The CVLT-II has excellent split-half reliability (r = .94). Evidence for the construct validity for the first version of the CVLT has been provided by numerous publications and Delis et al. (2000) indicate the CVLT-II has a high degree of concurrent validity with the CVLT.

Conners' Continuous Performance Task (CPT-II). The CPT-II (Conners & MHS Staff, 2000) 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." When an x appears on the computer screen, the examinee must abstain from responding until the next letter appears. The computer program varies the rate at which the stimuli appear throughout the test. Thus, the CPT-II provides measures of response speed and variability, errors in failing to inhibit a response, and errors in failing to respond. The CPT-II has strong test-retest reliability (correlations of r = .89 to .92 across a three month interval) and has been shown to reliably discriminate between individuals with a "clinical" condition believed to affect attention (ADHD, certain neurological conditions) and those without such a condition (Conners & MHS Staff, 2004).

Delis-Kaplan Executive Function System (D-KEFS). The D-KEFS (Delis, Kaplan, & Kramer, 2001) is a collection of "classic" neuropsychological tests of executive functioning (e.g. Trails, Verbal Fluency, Tower, Stroop) mixed with newly-developed tests designed to measure abstract reasoning, application of concepts, and verbal deduction. The D-KEFS provides a standardized method of examination of executive function sub-systems and a consistent normative group on which to base interpretations. 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 days) 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 validity of the "core" subtests is well recognized in that these are practically identical to well researched tests such as Trails B, the Stroop Task, and Controlled Oral Word Association (Delis et al., 2001).

Wechsler Adult Intelligence Scale-IV (WAIS-IV): Processing Speed Index. The WAIS-IV (Weschler, 2008) is known as the "gold standard" intelligence test in the assessment of adults. Administration of 2 of the 10 core subtests - Coding and Symbol Search – allows for the calculation of the Processing Speed Index (PSI). Reliability values for both subtests are very good. Internal consistency is α = .86 (Coding) and α = .81 (Symbol Search). Test-retest reliability, with an average of three weeks between testing, is r = .86 (Coding) and r = .81 (Symbol Search). The subtests have good evidence for validity as well.

Effort measures. Several tests of feigning or inadequate effort were incorporated in the test battery. As noted earlier, most of the current research ignores the issue of effort so it was imperative to include these measures of effort and symptom exaggeration. It is projected that approximately 40% of mTBI claims (Mittenberg, DiGiulio, Perrin, & Bass, 2002) contain probable symptom exaggeration. In addition, Lees-Haley (1997) showed 20-30% of individuals being evaluated for PTSD claims produced test responses consistent with symptom exaggeration or faking. Furthermore, the DSM-IV-TR cautions that the clinician should rule out malingering before coming to a diagnosis of PTSD.

Minnesota Multiphasic Personality Inventory-2-Restructured Form (MMPI-2-RF). The MMPI-2-RF (Ben-Porath, & Tellegen, 2008) 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. The MMPI-2-RF has sound psychometric properties. One-week test-retest reliability for the validity scales ranges from .40 (TRIN-r) to .84 (K-r). The MMPI-2-RF validity scales are revised versions of those from the MMPI-2 and the performance of these scales has been found to be on par with the previous validity scales (Ben-Porath, & Tellegen, 2008).

Letter Memory Test (LMT). The LMT (Inman, Vickery, Berry, Lamb, Edwards, and Smith, 1998) The LMT is a 45-item, forced-choice recognition task that uses consonant letters as stimuli and manipulates apparent difficulty level along 2 dimensions: the number of letters to be remembered and the number of choices from which the target stimulus must be selected. Inman et al. (1998) found that the LMT discriminated poorly motivated from well-motivated groups at a moderately high level of accuracy, which was comparable to that of the Digit Memory Test. The internal consistency reliability of the LMT was also found to be high.

Miller Forensic Assessment of Symptoms Test (M-FAST). The M-FAST (Miller, 2001) is a 25-item structured interview designed to screen for malingered psychiatric symptoms. Previous research has shown that a total cutoff score of 6 (sensitivity = 0.93, specificity = 0.83) is effective for correct classification of malingering with forensic and clinical samples (Miller, 2001).

Procedure

Approval for the study was obtained from the University of Kentucky IRB, and the Lexington, Tucson, and Chicago VA Medical Center R&D Boards. The archival database utilized in the present study was collected at three sites: the VA Medical Center in Lexington, Kentucky, the VA Medical Center in Tucson, Arizona, and the VA Medical Center in Chicago, Illinois. Informed consent and HIPAA authorization were obtained from all study participants. Veterans were required to complete full-day clinical or research test batteries that involved many (but not all) of the same measures of interest in the current study. Eligible patients were offered the opportunity to participate in the current research study and were paid $160 for their participation in the original multi-side VA study.

Power Analysis

As noted earlier, a recent meta-analysis found a large overall effect size (d = .82) for verbal memory deficits in groups with PTSD due to war trauma compared to controls (Johnsen and Asbjornsen, 2008). A-priori power calculations indicate that a total of 160 subjects in a 4-group design provides approximately 95% power to detect a large effect size (alpha = 0.05). 80% power is considered acceptable (Cohen, 1992). The present database consists of 235 subjects, well above the necessary sample size.

Chapter 3: Results

Data Analysis

Preliminary examination of the data showed significant departure from normal distribution (absolute values of skewness and kurtosis ratios to their SEs commonly exceeded 2.0) for approximately half of the dependent variables, suggesting assumptions of ANOVA were significantly violated. Thus, non-parametric tests were used instead. Analyses were performed with Kruskal-Wallis tests and follow-up contrasts with Mann-Whitney *U*. Except for demographic and diagnostic variables, where $p<.05$ was used, alpha was held at .01 to account for the large number of statistical tests conducted. Effect sizes are presented in Cohen's *d*.

Sample Description

Of the 438 veterans seen for clinical and/or research purposes at the Lexington, Tucson, and Chicago VAMCs during the 15-month duration of the study, 75 were excluded because they scored below the cutoff on one or more of the aforementioned effort tests or validity scales (33 scored less than 93% on LMT, 30 scored above 6 on M-FAST, 1 for elevated VRIN-R, 3 for elevated TRIN-R, and 8 for elevated L Scale), 36 were excluded due to post-deployment mTBI, 21 were excluded due to childhood ADHD/ADD. Upon closer examination of the four groups it was determined that there was a subset of control subjects who did not have a history of mTBI or PTSD but who did endorse military related trauma on the CAPS and elevated distress scales (n=65). It was unclear whether these subjects were experiencing normal levels of distress upon returning from the OIF/OEF conflicts or if they were experiencing subclinical levels of PTSD. Because of this, these veterans were not included in the final analysis.

Of the remaining 241 veterans, 35 subjects were excluded in order to match the four groups on age, estimated IQ, and education level. The following procedure was employed in order to match the groups: First, groups were compared to determine what differences lay between demographic variables (age, estimated IQ, and education). The main difference between the groups was that the VC group had significantly higher education levels and predicted FSIQ than the combined PTSD and mTBI group. Groups were matched on education first by limiting the range of education to 12-16 years. Next, individuals were removed from VC who had higher levels of education and higher predicted FSIQ in order to allow for similar variance between both demographic variables. Once IQ and education was matched, older individuals from PTSD+mTBI were removed in order to match for age.

The final sample included 62 OIF/OEF veterans with no history of military related trauma (VC), 51 OIF/OEF veterans with histories of deployment mTBI (mTBI-o), 38 OIF/OEF veterans with current PTSD (PTSD-o), and 55 OIF/OEF veterans with current PTSD and a history of deployment mTBI (PTSD+mTBI).

Table 3.1 presents demographics and other characteristics of the groups. The groups did not significantly differ in terms of age, education, predicted FSIQ, gender, ethnicity, months post-mTBI, number of pre-deployment civilian mTBIs, or number of deployment mTBI. However, analyses indicated there were significant group differences in Total Frequency and Intensity score on the CAPS. As would be expected, the PTSD-o and PTSD+mTBI groups had higher CAPS FI scores than the others. The PTSD-o and mTBI+PTSD groups were more likely to have current psychiatric diagnoses listed in their

VA medical record than the other two groups, consistent with the high psychological comorbidity with PTSD (Tanielian & Jaycox, 2008).

Neuropsychological Results

Table 3.2 presents neuropsychological results of the group differences. Initial analyses utilizing Kruskal-Wallis comparisons found overall group differences on several variables. The following tests were significant at the alpha = .01 level: D-KEFS Visual Scanning, D-KEFS Number Sequencing, D-KEFS Number-Letter Switching, WAIS-IV Digit Symbol, and WAIS-IV Processing Speed Index.

Follow-up Mann-Whitney U's were performed on the variables that exhibited significant overall group differences. All findings, non-significant and significant, can be found in Table 3.3. For D-KEFS Visual Scanning and Number Sequencing, both mTBI-o and PTSD+mTBI performed significantly worse than VC and PTSD+mTBI scored worse than PTSD-o. The PTSD+mTBI group had significantly poorer scores than VC on D-KEFS Number-Letter Switching. Both PTSD+mTBI and mTBI-o groups had significantly lower scores on WAIS-IV Digit Symbol and overall Processing Speed Index. Overall, the mTBI-o group performed similarly to the PTSD+mTBI group, although the latter group tended to have slightly worse performance than all other groups.

Effect size contrasts are presented in Tables 3.3. The PTSD+mTBI group has a large effect on performance for D-KEFS Visual Scanning and D-KEFS Number Sequencing. PTSD+mTBI has a moderate size effect on D-KEFS Number-Letter Switching, D-KEFS, WAIS-IV Digit Symbol, and WAIS-IV Processing Speed Index. The mTBI-o group has a moderate effect on D-KEFS Visual Scanning, D-KEFS Number Sequencing, D-KEFS Number-Letter Switching, D-KEFS, WAIS-IV Digit Symbol and

WAIS-IV Processing Speed Index. The effect sizes also demonstrate a small effect for PTSD-o on several variables (D-KEFS Visual Scanning, Number Sequencing, Number-Letter Switching, WAIS-IV Digit Symbol and Processing Speed Index).

Psychiatric Results

Tables 3.4 and 3.5 present the results of the psychiatric measures. Overall significant group differences were found for all measures. Follow-up contrasts revealed that the PTSD+mTBI group was not significantly different than PTSD-o on any measure, but was significantly higher than mTBI-o and VC groups on all psychiatric measures. The mTBI-o and PTSD-o groups had significantly higher scores than the VC group on all psychiatric measures. Lastly, PTSD-o had significantly higher scores on BDI-II, BAI-II, and CAPS, but not on ISI, than the mTBI-o group. As expected, presence of PTSD appears to have a greater impact on scores than mTBI, however unlike in previous studies, the combination of the two conditions does not appear to be associated with greater emotional distress and symptom complaints.

Examination of effect size contrasts in Table 3.5 illustrates the impact of PTSD diagnosis on psychiatric measures. The PTSD+mTBI and PTSD-o groups had very large effect sizes on all psychiatric measures. In addition, the mTBI-o had a large effect size on all psychiatric measures as compared to the VC group.

Supplemental Analyses

To determine whether mTBI interacts with PTSD on the neuropsychology measures, a 2 (mTBI diagnosis) by 2 (PTSD diagnosis) ANOVA was run on the variables that had significant group differences ($\alpha = .01$). Although the data are heavily skewed, ANOVA is considered to be robust against violations of normality. There was a

significant main effect for mTBI on Visual Scanning, F(1,202)= 20.003, p< .001, Number Sequencing, *F*(1,202)= 14.429, p < .001, Number-Letter Switching, F(1,202) = 11.221, p = .001, and Digit Symbol, F(1, 202)= 11.291, p = .001. There was an additional main effect nearing significance for mTBI on the WAIS-IV Processing Speed Index, F(1, 202)= 5.974, p = .015.

There were significant main effects for PTSD on Visual Scanning, F(1, 202)= 7.145, p = .008 and Number Sequencing, F(1, 202)= 7.008, p = .009. There were no significant interaction effects within the variables that showed group differences during the initial analyses. Figures 3.1-3.9 illustrate the 2x2 ANOVAs for each variable.

Table 3.1: Demographic Characteristics of Participants Included in Final Analyses

		VC n=62 Md M (SD)	mTBI n=51 Md M (SD)	PTSD-o n=38 Md M (SD)	PTSD+ mTBI n=55 Md M (SD)	*K* or *U* N=206	*p*
Male	*%*	83.9%	88.2%	86.8%	98.2%	6.732	.081
Age	*Med.*	30	27	29	27	3.33	.343
	M	30.90	29.36	30.71	30.00		
	SD	7.54	6.73	6.93	7.47		
Years of Education	*Med.*	14	14	14	14	2.66	.448
	M	13.90	14.00	14.11	13.56		
	SD	1.57	1.48	1.93	1.34		
Race						5.76	.124
Caucasian	*%*	75.8%	68.6%	65.8%	87.3%		
Afr. Amer.	*%*	8.1%	13.7%	23.7%	3.6%		
Other	*%*	16.1%	17.7%	10.5%	9.1%		
Ethnicity						3.03	.387
Hispanic	*%*	19.4%	19.6%	15.8%	10.9%		
Non-Hispanic	*%*	75.8%	68.6%	71.1%	78.3%		
Unknown	*%*	3.2%	9.8%	13.2%	9.1%		
WTAR Predicted FSIQ	*Med.*	104.00	102.00	101.00	104.00	4.20	.241
	M	103.21	102.33	100.87	103.07		
	SD	6.87	6.76	8.14	8.81		
# Deployment Related	*Med.*	-	1.00	-	1.00	1336.00	.643
mTBI	*M*	-	3.02	-	2.96		
	SD	-	13.72	-	13.21		
Prior Hx of mTBI	*%*	16.1%	35.3%	34.2%	27.3%	6.616	.085
# Months Post mTBI	*Med.*	-	43	-	42	1097.50	.878
	M	-	46.30	-	45.15		
	SD	-	27.09	-	23.98		
CAPS Frequency +	*Med.*	3.5	34.5	58.00	63.00	87.35	.000
Intensity Score	*M*	5.8	32.39	59.55	67.29		
	SD	6.8	15.36	19.70	20.63		

Table 3.2 Results of the Neuropsychology Measures

Variable	Descriptives				Omnibus Test	
	VC n=62 M SD	mTBI n=51 M SD	PTSD-o n=38 M SD	PTSD+mTBI n=55 M SD	*K* N=206	*p*
D-KEFS Visual Scanning	11.05 2.00	9.86 2.43	10.55 2.37	8.31 3.69	24.08**	.000
D-KEFS Number Seq.	11.08 2.03	9.90 2.66	10.32 2.70	8.76 2.81	24.47**	.000
D-KEFS Letter Seq.	10.90 1.84	10.18 2.32	10.53 2.39	9.51 2.94	10.53*	.015
D-KEFS N-L Switching	10.61 2.00	9.41 3.01	10.11 2.09	8.80 3.19	12.44**	.006
D-KEFS Motor Speed	11.65 1.52	11.08 2.21	11.11 1.64	10.75 2.19	8.20*	.042
D-KEFS Letter Fluency	10.35 2.98	9.47 3.03	9.66 3.00	9.69 3.01	3.52	.318
D-KEFS Categ. Fluency	11.81 3.10	11.51 3.57	10.89 2.96	10.09 3.00	10.24*	.017
D-KEFS Categ. Switch	10.98 3.36	10.47 3.35	9.87 3.40	9.51 3.86	6.29	.098
D-KEFS Inhibition	9.97 2.96	9.76 3.12	9.29 3.42	9.62 3.75	.821	.844
CPT (T Score) Omissions	47.84 7.91	47.10 7.37	46.18 5.36	55.07 28.65	2.90	.408
CPT (T Score) Commissions	48.66 9.16	50.47 9.66	49.71 7.34	50.75 10.53	1.70	.637
CPT Hit Rate	47.11 10.76	46.01 8.69	47.12 8.47	48.89 12.77	.38	.944
CPT Standard Error	46.68 10.71	49.09 8.96	52.06 10.04	54.14 13.68	10.71*	.013
CVLT Trials 1-5	54.31 8.41	52.90 7.66	50.92 10.30	49.36 10.07	9.20*	.027
CVLT Short Delay	.11 .95	.15 .99	.00 .908	-.25 1.15	5.23	.156
CVLT Long Delay	.04 .93	.05 .90	-.13 1.05	-.48 1.19	7.63	.054
WAIS-IV Digit Symbol	10.76 2.18	9.49 1.95	10.05 2.42	9.05 2.88	15.92**	.001
WAIS-IV Symbol Search	10.95	10.06	9.92	9.82	8.51*	.037

Table 3.2 (continued) Results of the Neuropsychology Measure

	2.17	2.17	2.49	3.01		
WAIS-IV						
PSI	103.98	98.67	99.76	97.02	13.70**	.003
	10.21	9.71	11.21	14.70		

(**p < .05; **p < .01)*

Table 3.3: Group Comparisons Among Significant Neuropsychology Measures

	VC v. mTBI-o *U* *p* *d*	VC v. PTSD-o *U* *p* *d*	VC v. PTSD+mTBI *U* *p* *d*	mTBI-o v. PTSD-o *U* *p* *d*	mTBI v. PTSD+ mTBI *U* *p* *d*	PTSD-o v. PTSD+mTBI *U* *p* *d*
D-KEFS						
Visual	1086.50**	1029.50	919.50**	779.00	1051.00*	635.00**
Scanning	.004	.282	.000	.111	.025	.001
	0.545	0.235	0.947	0.290	0.497	0.703
D-KEFS						
Number	1131.50**	993.00	840.00**	857.50	1032.00*	683.00**
Sequencing	.009	.182	.000	.351	.018	.004
	0.510	0.333	0.964	0.159	0.420	0.570
D-KEFS						
Num-Letter	1220.00*	972.50	1094.00**	911.00	1198.00	816.00
Switching	.035	.139	.001	.626	.192	.071
	0.483	0.248	0.695	0.266	0.198	0.524
WAIS-IV						
Digit	1103.00**	936.00	1052.00**	884.50	1187.00	796.50*
Symbol	.005	.083	.000	.478	.169	.050
	0.616	0.315	0.681	0.262	0.179	0.374
WAIS-IV						
Processing	1105.50**	879.50*	1106.50**	953.50	1228.00	892.00
Speed Index	.006	.033	.001	.897	.268	.231
	0.536	0.402	0.561	0.106	0.133	0.207

(*$p < .05$; **$p < .01$)

Table 3.4 Results of the Psychiatric Tests (Descriptives and Omnibus Tests)

Variable	Descriptives				Omnibus Test	
	VC n=62 M SD	mTBI n=51 M SD	PTSD-o n=38 M SD	PTSD+mTBI n=55 M SD	*K* N=206	*p*
BDI-II	5.27 5.85	10.59 7.64	18.11 10.68	21.55 10.56	83.00**	.000
BAI-II	2.65 4.32	8.49 7.63	12.87 7.66	15.11 9.35	88.26**	.000
CAPS	5.88 6.82	32.39 15.36	59.55 19.70	67.29 20.63	87.35**	.000
ISI	7.21 6.63	12.27 6.36	14.79 6.36	15.11 6.90	42.87**	.000

(*$p < .05$; **$p < .01$)

Table 3.5: Group Comparisons Among Psychiatric Tests

	VC v. mTBI-o *U* *p* *d*	VC v. PTSD-o *U* *p* *d*	VC v. PTSD+mTBI *U* *p* *d*	mTBI v. PTSD-o *U* *p* *d*	mTBI v. PTSD+mTBI *U* *p* *d*	PTSD-o v. PTSD+mTBI *U* *p* *d*
BDI-II	889.50** .000 0.799	277.00** .000 1.617	293.00** .000 1.955	554.00** .001 0.840	566.50** .000 1.193	821.50 .080 0.328
BAI-II	631.50** .000 0.976	213.50** .000 1.777	234.50** .000 1.761	611.50** .003 0.580	778.50** .000 0.780	924.50 .346 0.260
CAPS	32.50** .000 2.330	1.00** .000 4.093	1.00** .000 4.134	213.50** .000 1.584	221.00** .000 1.923	799.00 .054 0.386
ISI	866.50** .000 0.784	476.00** .000 1.173	686.00** .000 1.179	747.50 .066 0.401	1068.00* .034 0.431	1012.00 .796 0.048

(*$p < .05$; **$p < .01$)

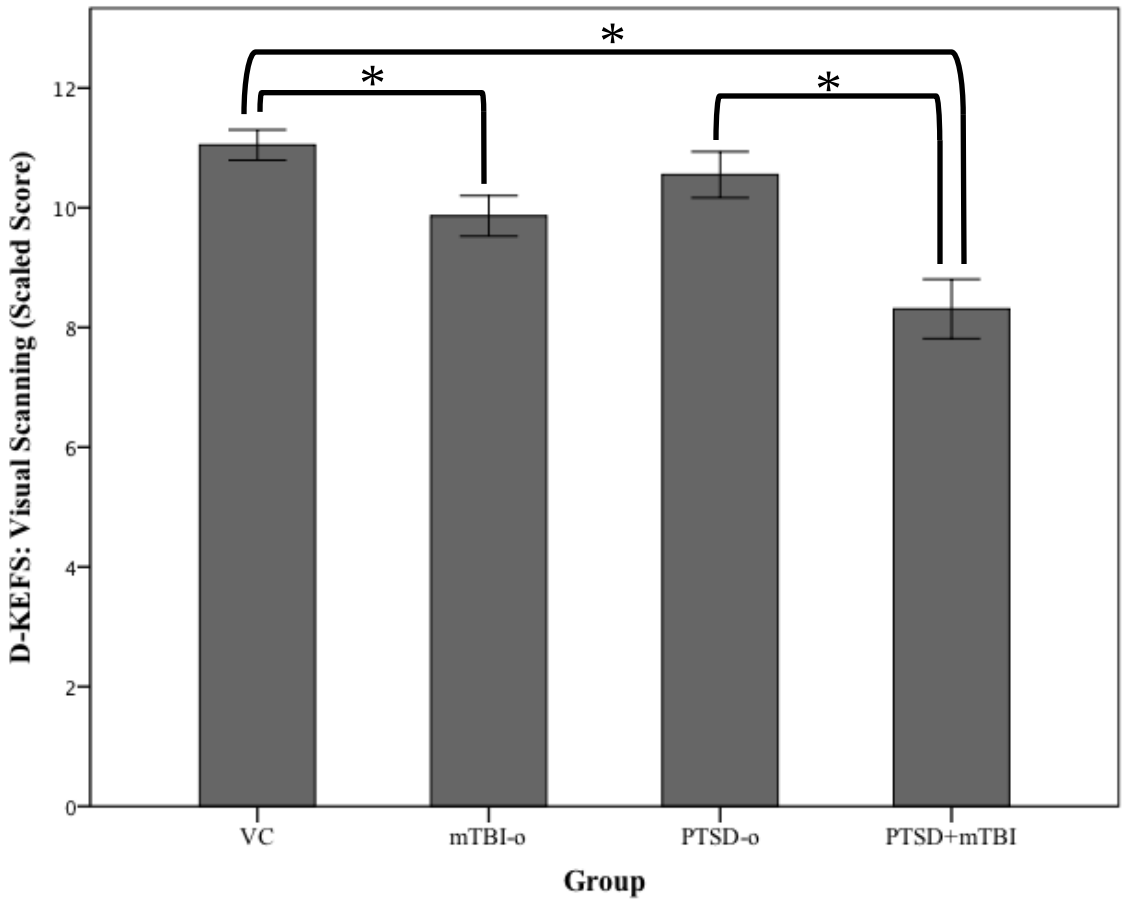

Figure 3.1 D-KEFS Visual Scanning Group Means. Standard errors are represented in the figures by error bars.
*p<.01

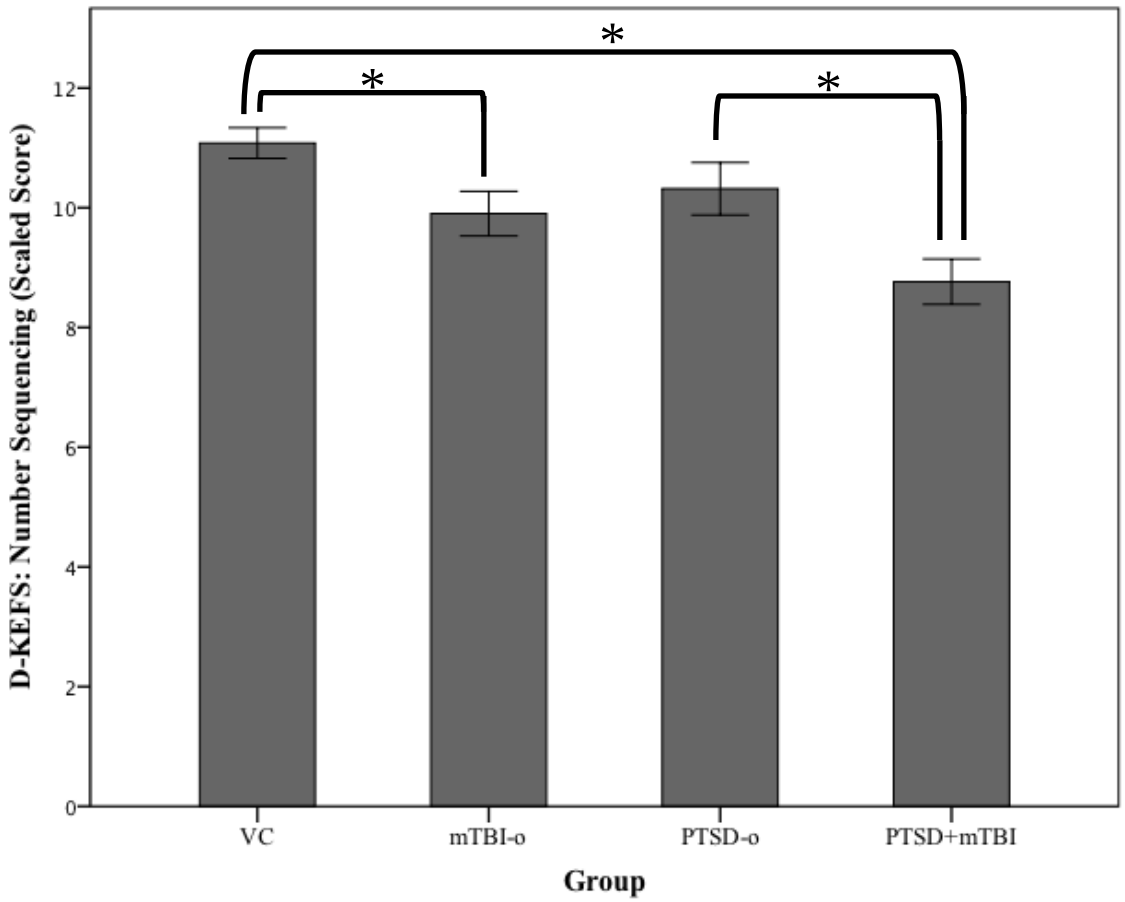

Figure 3.2 D-KEFS Number Sequencing Group Means. Standard errors are represented in the figures by error bars.
*p<.01

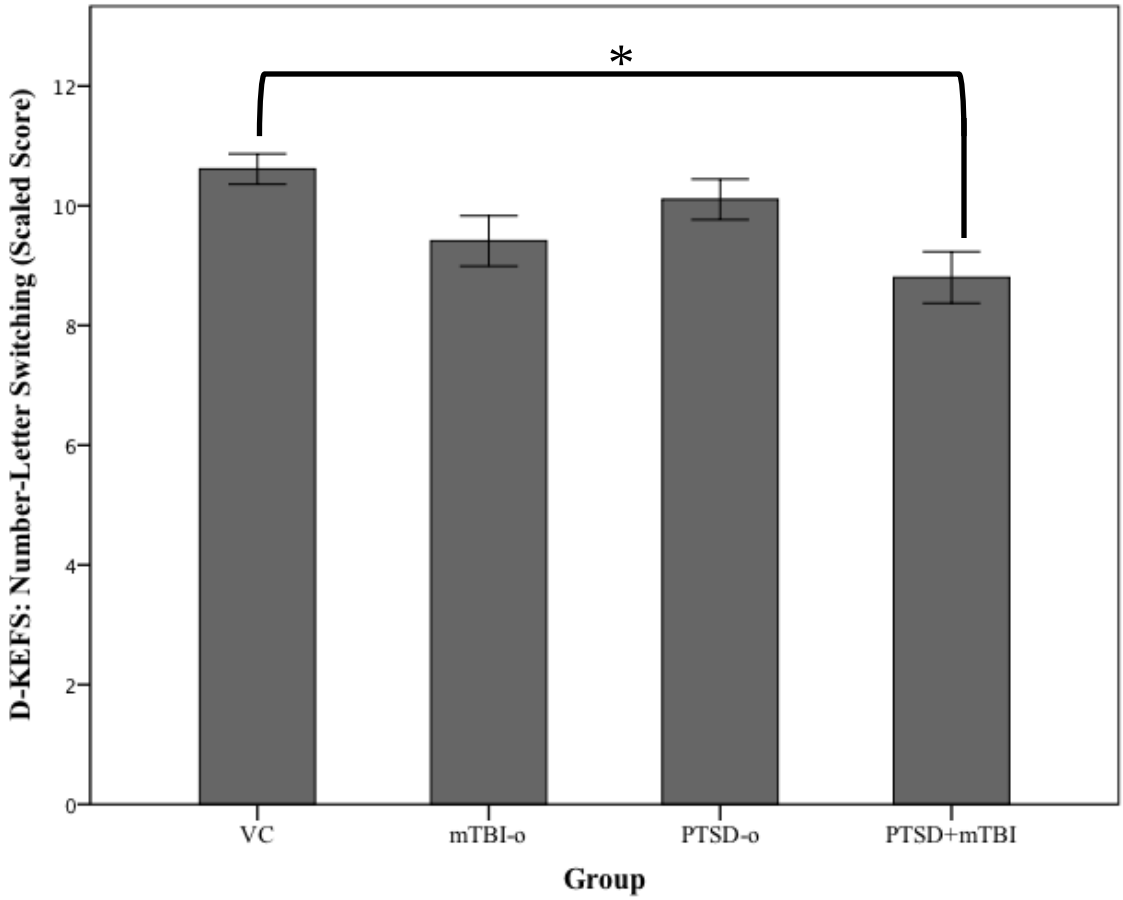

Figure 3.3 D-KEFS Number-Letter Switching Group Means. Standard errors are represented in the figures by error bars.
*p<.01

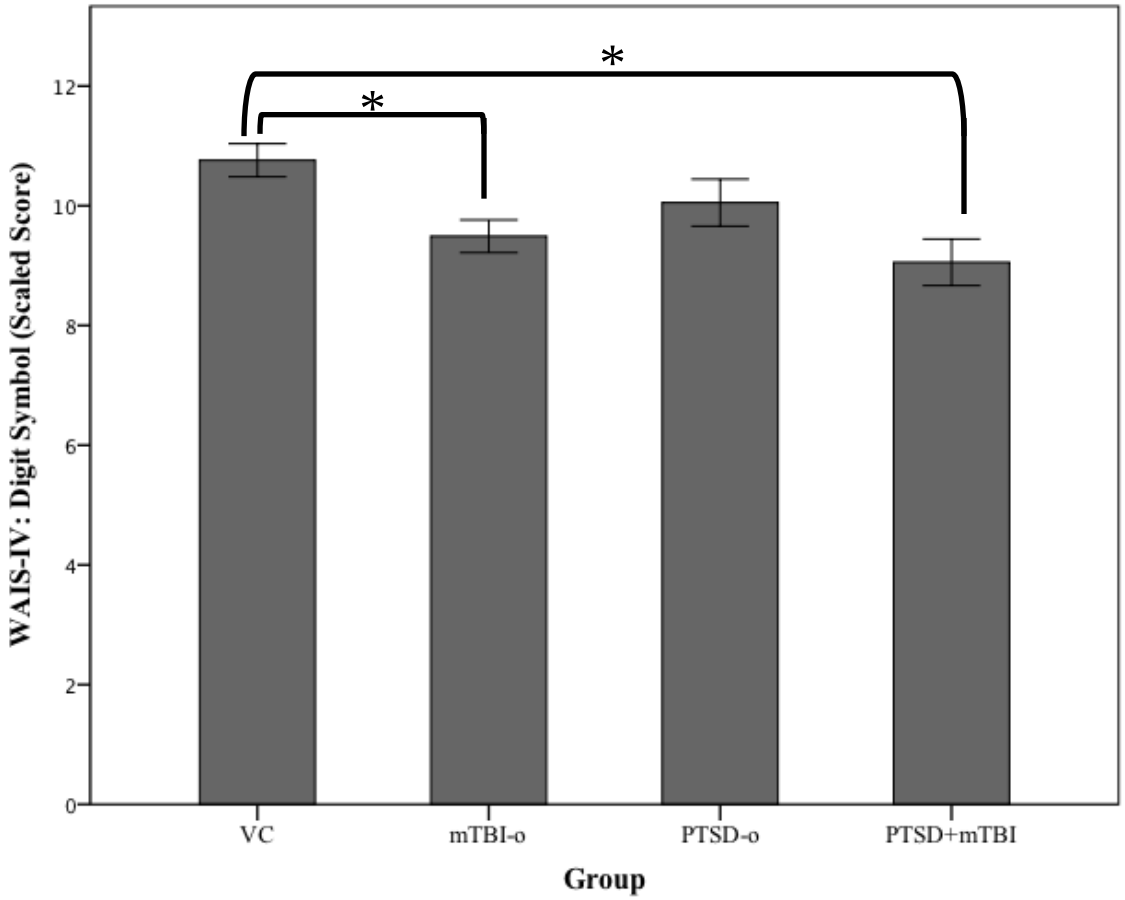

Figure 3.4 WAIS-IV Digit Symbol Group Means. Standard errors are represented in the figures by error bars.
*p<.01

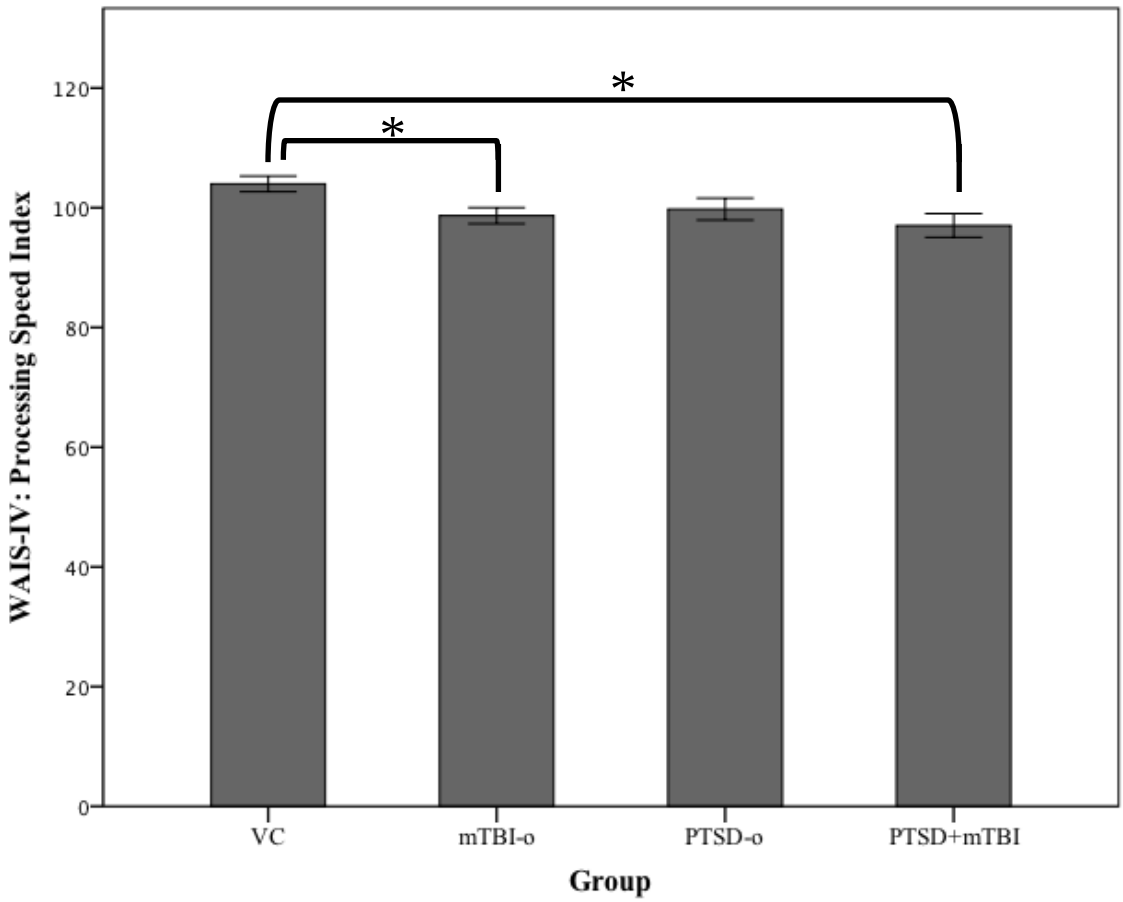

Figure 3.5 WAIS-IV Processing Speed Index Group Means. Standard errors are represented in the figures by error bars.
*p<.01

Chapter 4: Discussion

Overview of Findings

The present study used a neuropsychological test battery to examine the neuropsychological and psychological impairments associated with mTBI, PTSD, and combined mTBI and PTSD in returning veterans. This study is innovative in that it explored the relationship between the cognitive and emotional factors of PTSD and mTBI using carefully matched groups. It is essential to determine the extent of potential cognitive impairments following mTBI and PTSD while controlling for possible intelligence and education confounds, because these are key demographic variables that are often related to neuropsychological performance. The current study included a comprehensive battery of neurocognitive, psychiatric, and validity tests using a matched sample that controls for these potential confounds.

The present study found that the PTSD+mTBI group performed more poorly on several neuropsychological measures than the other three groups. Based on previous research it was predicted that there would be no differences between the PTSD+mTBI group and the PTSD-o group, however differences were found on two noteworthy neuropsychology measures of visual scanning and visual attention, with the combined group producing lower scores. A second noteworthy finding was that there were significant differences between the mTBI-o group and the VC group on several neuropsychological measures, contrary to what was originally predicted. The mTBI-o group performed more poorly on measures of visual scanning and visual attention as well as measures of ability to process routine or complex visual information. Another result in contradiction of study hypotheses was that there were no significant differences on any neuropsychology measures between the PTSD-o group and the VC group. Additionally,

there are no significant differences on neuropsychology measures between mTBI-o and PTSD+mTBI groups. While not significantly different, there was a small effect size for the differences between these two groups, with the combined group performing worse than the mTBI-o group. Additionally, differences are evident when considering the effect sizes that mTBI-o and PTSD+mTBI groups have relative to the VC group. The mTBI-o group has a moderate effect on the neuropsychology measures while the PTSD+mTBI group has a large effect.

Lastly, it was predicted that the PTSD+mTBI group would report more psychopathology than the three other groups. Though this was true for the mTBI-o and VC groups, the PTSD+mTBI and PTSD-o groups were not significantly different on measures of psychopathology. Nevertheless, the trend of severity for every psychiatric measure followed as such: PTSD+mTBI > PTSD-o, PTSD-o > mTBI-o, and mTBI-o > VC.

Implications

The results from the present study demonstrate that PTSD+mTBI produces greater impairments in cognitive functioning than PTSD alone. These effects seem to be additive, as the small to moderate effect sizes present in both PTSD-o and mTBI-o groups translate to large effect sizes when the two issues are combined. Furthermore, the cognitive impairments related to PTSD+mTBI group cannot be attributed to greater levels of distress as there were no significant differences on any psychiatric measures between PTSD+mTBI and PTSD-o. It is important to note that the mean scaled scores for all groups on the significant neuropsychology measures fell within the average range, and thus these score may not translate into clinical impairments.

Additionally, the results provide evidence for long-term processing speed and visual scanning deficits associated with mTBI-o as compared with controls, contrary to current findings in the civilian mTBI literature. Given what is known about the demographic and psychiatric characteristics of this sample, three possible explanations for the disparity between this finding and typical findings in the civilian mTBI literature are offered.

First, the veterans in the mTBI-o group all reported having experienced a deployment concussion. A deployment concussion, as defined in the introduction, occurs in the midst of the experience of chronic stress. Civilian mTBI findings are based on concussions and other injuries that occur outside of the confines of combat, where the environment is presumably lower in chronic stress. Thus, it is possible that the differences found here can be attributed to the environment in which the mTBI occurred.

A second possibility is that in the current study sample, those in the mTBI-o group had significantly higher psychiatric distress than the control 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 control group, but there were no accompanying differences in visual scanning and processing speed, suggesting it is unlikely that psychiatric distress above accounts for the novel finding of differences between mTBI-o and control group in this present study.

A final alternative explanation for why impairments were seen for the mTBI-o group is that there may be evidence of higher rates of diffuse axonal injury within this group than in prior civilian groups. Diffuse axonal injury (DAI) is related to slower

processing speed and attention, and has been identified in even the mildest forms of traumatic brain injury. The impairments found in the present study are most consistent with measures of both processing speed and visual attention, suggesting evidence of DAI.

Another noteworthy finding from the present study was that there were no differences between PTSD-o and VC groups on any neuropsychological measure. This was contrary to what was expected based on previous literature. As this was the first study to compare the four groups (VC, mTBI-o, PTSD-o, and PTSD+mTBI) when they were matched for 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.

Limitations

While this study provides an important contribution to the current body of literature on neuropsychological functioning in OEF/OIF veterans with PTSD and deployment mTBI, important limitations must be acknowledged. Though care was used to arrange demographically and diagnostically clean groups, matching based on psychiatric distress was not possible.

A second limitation to the present study is that it was not possible to assess differences in combat exposure between the four groups. It would be expected that PTSD+mTBI would have the greatest amount of combat exposure (Shandera-Ochsner, 2012); however, future studies will need to include measures of combat exposure in order to determine what, if any, influence this variable has on the impairments of interest.

A third major limitation to the present study is the subjective nature of the structured face-to-face interview process. 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 comorbid with PTSD) on cognitive functioning may be more severe and long-lasting than previously thought, especially on measures of visual scanning and processing speed. Clinically, as more and more veterans are returning from the current OEF/OIF conflicts complaining of both PTSD and mTBI, it is important to recognize that the subjective impairments veterans report may in fact translate into objective cognitive impairments.

Script for Structured Interview for TBI Diagnosis

- **Complete a separate form for each TBI-related event, starting with the most severe (as identified by the Veteran) and moving down the reported severity scale as needed to evaluate all potential TBIs.**
- **If the most severe reported event is rated as "very likely" or "almost certainly" to reflect a true TBI, continue with a separate form to evaluate the next most severe event.**
- **Repeat the interview, on separate forms, until all "very likely" or "almost certainly" TBI events have been evaluated.**
- **Once an event does not meet the TBI criterion of "very likely" or "almost certainly," no other, less severe events need to be evaluated.**

Most of the questions below have parenthetical follow ups. You might not always need to ask these questions, but in matters of clinical uncertainty they should be helpful.

Discussing the combat events in a structured manner may be mildly uncomfortable for some Veterans, but most will be accustomed to talking about experiences that resulted in an injury. In the unlikely event a Veteran becomes very distressed during the interview, implement local safety procedures for evaluation and intervention.

Introduce the interview by saying:

1.) *"Some Veterans of OIF/OEF report being exposed to things LIKE blast waves, or having been hit on the head in motor vehicle accidents or combat situations. Did you experience ANYTHING LIKE THIS during your deployment, where you might have injured your head?" (***Goal is to cast a broad net to see if Veteran has had exposure to any events that may have resulted in loss or alteration of consciousness)**

YES→ *'Okay, I know you may have several events in mind, but for now I'd like you to think about the most significant event that happened during your OEF/OIF service.'*

(Some Veterans report a very high number of events initially (>10). When this happens, the interviewer will need to prompt the Veteran to be sure he or she clearly understands what is meant by 'significant.' Ex. *Yes, we've had several people tell us they experienced blasts very frequently, sometimes daily. Right now, we're interested in finding out the details of the ones that <u>really stand out to you</u>.* **Clarify until Veteran understands question)**

NO→ Discontinue structured Interview.

(If a participant relates an event that was psychologically troubling or traumatizing, please remind them that we will be covering those events during a later interview. The goal is for the participant to report those experiences that were [or could have been] physically injurious or could have resulted in a head injury. Query the participant regarding their combat experiences, duties in the military, etc. The interviewer will need to clarify that the veteran was never in the vicinity of an IED, mortar, landmine, grenade, or other blast explosion. If satisfied that no event occurred, code answer as 'No' and conclude interview.)

2.) ***What was the cause of the event? (Was it an IED, vehicle accident, etc?)***

(Check cause below. Use the generic "Blast" option only for blast-related injuries **not** covered by more specific options [IED, RPG, Mortar, Landmine, Grenade]).

Blast	Mortar	Vehicular accident
IED	Landmine	Fall
Bullet above shoulder	Grenade	Assault
RPG	Blow to the head	Other
If Other, specify the nature of the event below:		

For each event, ask the following questions:

3.) ***In what month and year did this event occur?*** / (mm/yyyy)

(If the Veteran is unable to spontaneously answer this question, follow up with *'What year was it?'* and then *'What season was it?'* Then follow up with the month options for that season [e.g., *'was it December, January, February or March?'*]. **If necessary, encourage the Veteran to make the best guess.**)

4.) ***What happened during the event itself?*** (Elicit as many details as possible, such as *'Who was with you?' 'What was going on around you?'* Keep probing.)

_____

4a.) ***Do you remember this or did someone tell you about it?***

I remembered I was told

4b.) (If the Veteran remembered, **Ask** *'How clearly do you remember the event?*)

No amnesia for what happened during the event

Amnesia for what happened during the event

5.) ***Were you wearing a helmet at the time of the event?*** Yes No

6.) ***If you were exposed to a blast, how close were you from the explosion?***

0-25 feet 51-75 feet

26-50 feet >76 feet NA

(Select N/A [not applicable] if no blast was related to the event.)

7.) ***If you were exposed to a blast, was there any object between you and the explosion?*** Yes No N/A

7a.) ***If so, what was the object?*** (If the response is ambiguous, ask for more detail. For example, "a wall" may be a single sheet of plywood or several feet of concrete.)

_____

No objects

Objects smaller than a vehicle

Vehicle

Objects larger than vehicle but smaller than a building

Building or larger

Veteran was in a vehicle

Veteran was in a building

8.) ***Did you lose consciousness?*** Yes No

8a.) ***If yes, for how long?***

Seconds Minutes Hours Days Weeks Months

8b.) ***Did anyone see you lose consciousness??***

Yes No N/A Veteran was alone

Notes:

9.) ***Were you disoriented or confused after the event?*** Yes No

(Ask for details and examples of the sensation of disorientation or confusion to clarify if the experience was truly injury-related cognitive clouding vs. an affective/physiological response to an unexpected and frightening experience.)

_____

_____

9a.) *If yes, for how long?*

Seconds Minutes Hours Days Weeks Months

(Probe for the duration as described above. **Ask** *'How long after the event did it take until you felt like you knew what was going on again?'*)

9b.) ***Did anyone tell you they noticed that you were acting differently?***

Yes No N/A Veteran was alone

(If yes, **Ask** *'What were you told?' 'How were you acting?'*)

10.) ***What happened leading up to the event?*** (If the Veteran seems confused by the question, **Ask** *'What were you doing right before the event?'* Elicit as many details as possible.)

_____

10a.) ***Do you remember this or did someone tell you about it?***

I remembered I was told

10b.) (If the Veteran was told, **Ask** *'What is the last thing **you** remember before the event?' 'When was that?'* Elicit as many details as possible to help determine how clearly the event is recalled and if there was any retrograde amnesia.)

No amnesia for what happened prior to the event

Amnesia for what happened prior to the event

11.) ***How well do you remember what happened right after the event? Do you have any gaps in your memory?*** (Again, elicit as many details as possible and assess the clarity with which this information is recalled.)

_____

Amnesia for what happened after the event (PTA)

No amnesia for what happened after the event (PTA)

11b.) If positive to either question above, **Ask** *"How long until you started remembering clearly after the event?'*Elicit as many details as possible to help determine how clearly the event is recalled and if there was any anterograde amnesia.)

Notes:_____

_____

Duration of PTA: Seconds Minutes Hours Days Weeks Months

12.) ***Did you notice anything different about yourself after the event?*** If veteran does not understand what is being asked, say: ***Did you have any symptoms/problems after the event?*** **It's best to ask this as an open**

question, rather than to ask about specific post-concussive symptoms. Rephrasing as *'Have you noticed any physical changes, emotional changes, or changes in your thinking abilities since your injury?'* might be necessary.

Yes No

If so, what did you notice? When did it start? (Use columns to prompt for clarification of onset and symptom course. Check all that apply. For example, if a participant began experiencing a symptom 'within one month of injury'; symptom continued throughout deployment and the symptom is still 'current' all columns should be checked.)

Symptom	Within 1 month of injury	More than 1 month past injury	After returning home	Current
Feeling Dizzy				
Loss of balance				
Poor Coordination, Clumsy				
Headaches				
Nausea				
Vision problems, blurring, trouble seeing				
Sensitivity to light				
Hearing difficulty				
Sensitivity to noise				
Numbness or tingling on parts of my body				
Change in taste and/or smell				
Loss of appetite or increase appetite				
Ringing in ear, Tinnitus				
Poor concentration, can't pay attention				
Forgetfulness, can't remember things				
Difficulty making decisions				
Slowed thinking, difficulty getting organized, can't finish things				
Fatigue, loss of energy, tire easily				
Difficulty falling or staying asleep				
Feeling anxious or tense				
Feeling depressed or sad				

Irritability, easily annoyed				
Poor frustration tolerance				
Drowsiness				

13.) ***Did you receive/seek any medical treatment after the event?*** Yes No

Details:

(Include location and duration of treatment, who provided it, any diagnoses that the Veteran is aware of, etc. Some Veterans might not consider being treated at the scene as "treatment." Ask about any evaluation or medical care given by a medic, corpsman, etc. after the event.)

RATING SHEET

Rate the Injury(ies):

How likely is it that the Veteran sustained at least one TBI?

Not at all likely (ACRM criteria clearly not met) Very unlikely (ACRM criteria do not appear to be met; veteran may be inconsistent, poor historian, etc) Somewhat unlikely (Unclear due to complicating factors*, but veteran's report is largely inconsistent with criteria) *Complicating Factors: e.g. extreme stress, emotional distress, somnolence, or substance use at the time of the event	Somewhat likely (ACRM criteria may be met, but complicating factors* prevent diagnostic clarity) Very likely (ACRM criteria met; veteran may have complicating factors*, but clinician is able to separate them out with reasonable degree of certainty) Almost certainly (ACRM criteria clearly met, no complicating factors* present at time of event)
How many TBIs (Very likely or Almost certainly) did this Veteran experience?	

If it is likely that the Veteran sustained one or more TBIs, how severe was each? (Check the appropriate box(es) and note the quantity in the column to the right)

1. Transient confusion, no loss of consciousness, concussion symptoms or mental status abnormalities resolved in less than 15 minutes.
2. Transient confusion, no loss of consciousness, concussion symptoms or mental status abnormalities lasted more than 15 minutes but no more than an hour.
3. Transient confusion, no loss of consciousness, concussion symptoms or mental status abnormalities lasted between one and 24 hours.
4. Transient confusion, no loss of consciousness, concussion symptoms or mental status abnormalities last more than 24 hours.
5. Loss of consciousness, from very brief (seconds) to several minutes. Concussion symptoms or mental status abnormalities resolve in less than 15 minutes.
6. Loss of consciousness, from very brief (seconds) to several minutes. Concussion symptoms or mental status abnormalities lasted more than 15 minutes.

7. Loss of consciousness over one hour but less than one day.

8. Loss of consciousness more than one day.

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Vita

PERSONAL INFORMATION

Place of Birth: Ruston, Louisiana

EDUCATION

August 2011-Present	University of Kentucky Clinical Psychology Doctoral Program
2007-2011	University of Texas, at Austin Psychology, B.S. (Minor in Biology) Graduated with Honors

RESEARCH INTERESTS

Traumatic Brain Injury and Post Traumatic Stress Disorder: Cognitive impairments and rehabilitation.

FELLOWSHIPS, SCHOLARSHIPS, AND AWARDS

2010-2011	Undergraduate Research Fellowship
2010-2011	Psychology Departmental Honors Program
2008- 2011	University Honors
2008-2010	College of Liberal Arts Dean's List
2004-2007	National Honor Society

PUBLICATIONS

Combs, H.L., Adkins, D. L., Kozlowski, D.A., & Jones, T. A. (2011). Skill training, exercise and constraint-like therapy together promote major functional reorganization of remaining motor cortex after controlled cortical impact injury in rats. [Abstract]. *Journal of Neurotrauma, 28*(6), A-106.

O'Bryant, A. J., Adkins, D. L., Sitko, A. A., Combs, H., Nordquist, S. K., Jones, T. A. (Submitted). Enduring post-stroke motor functional improvements by a well-timed combination of motor rehabilitative training and cortical stimulation in rats. *Experimental Neurology. Manuscript submitted for publication.*

PRESENTATIONS

O'Bryant, A., Combs, H., Nordquist, S., & Jones, T. A. (2010). "Effects of transcranial cortical stimulation and motor rehabilitative training on functional recovery following unilateral cortical infarcts in rats." Poster presented at the Neuroscience 2010 conference of the Society for Neuroscience, San Diego, CA.

Combs, H. L., Adkins, D. L., & Jones, T. A. (2010). "Motor learning, forced exercise rehabilitation, and functional motor cortex neuroplasticity following traumatic

brain injury in rats." Poster presented at the Psychology Departmental Honors poster session.

Combs, H.L., Adkins, D. L., & Jones, T. A. (2011). "Motor learning, forced exercise rehabilitation, and functional neuroplasticity following controlled cortical impact." Poster presented at the annual meeting of the University of Texas' Institute of Neuroscience Symposium, Austin, TX.

Combs, H.L., Adkins, D. L., Kozlowski, D.A., & Jones, T. A. (2011). "Skill training, exercise and constraint-like therapy together promote major functional reorganization of remaining motor cortex after controlled cortical impact injury in rats." Poster presented at the annual meeting of the National Neurotrauma Symposium, Ft. Lauderdale, FL.

PROFESSIONAL SOCIETIES

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