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The Effect of Comorbid Traumatic Brain Injury and Posttraumatic Stress Disorder on Cognitive Performance and Social Functioning among Treatment-Seeking Active Duty US Service Members

by

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ABSTRACT

The Effect of Comorbid Traumatic Brain Injury and Posttraumatic Stress Disorder on Cognitive Performance and Social Functioning among Treatment-Seeking Active Duty US Service Members:

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TBI and PTSD have been labeled “signature wounds” of the conflicts in Iraq and Afghanistan and can result in considerable distress for a significant number of service members. Despite their frequent comorbidity and overlapping symptoms, there is a dearth of knowledge regarding the combined effects of TBI and PTSD on cognitive performance as well as how they impact social functioning. The present study first examined potentially synergistic effects of comorbid TBI and PTSD symptoms on cognitive performance in a sample of treatment-seeking service members with PTSD symptoms and/or TBI. While service members in the TBI-only, PTSD symptoms-only, and comorbid groups performed significantly below average compared to norms in regards to cognitive performance, service members with TBI-only did not significantly differ from those with PTSD symptoms-only. However, individuals with both TBI and PTSD symptoms performed worse than those with either condition alone. The study further

explored the contributions of cognitive performance, neurobehavioral symptoms, and emotional distress on social functioning in a subsample of these service members. Results indicated a significant predictive relationship among cognitive performance, neurobehavioral symptoms, and emotional distress on social functioning. Additionally, neurobehavioral symptoms were found to completely mediate the relationship between emotional distress and social functioning. Findings highlight the importance of the symptom relationships between TBI and PTSD.

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CHAPTER 1: INTRODUCTION

Since September 11, 2001, more than 2.8 million United States military service members have deployed to Iraq and Afghanistan in support of Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF, later renamed Operation New Dawn [OND]; Meadows, Tanielian, & Karney, 2016). Fortunately, due in part to advances in modern medicine and improvements in body armor, the fatality rate of these conflicts has been lower than it was in earlier wars. However, many service members who survive previously fatal wounds are now left with debilitating injuries. As of September 2018, more than 52,000 service members have been physically wounded in combat (Department of Defense, 2019) and over 1,600 have lost limbs (Fischer, 2015).

Not all wounds sustained by service members in these conflicts are visible to the eye. In fact, rates of "invisible wounds," such as traumatic brain injury (TBI) and posttraumatic stress disorder (PTSD), have been high. Close to 500,000 service members have returned from deployments with varying severity of TBI and PTSD (Fischer, 2015). Thus, both of these conditions were quickly labeled the "signature wounds" of these wars (Howlett & Stein, 2016) and are known to be debilitating health concerns for a significant number of service members deployed to these recent conflicts (Betthauser et al., 2018).

TRAUMATIC BRAIN INJURY

The Department of Defense (DoD) and the Defense and Veterans Brain Injury Center (DVBIC) estimate nearly a quarter of all combat casualties from the conflicts in Iraq and Afghanistan are brain injuries. According to DVBIC, nearly 384,000 service members were diagnosed with a TBI between January 2000 and April 2018, including those sustained TBIs through mechanisms other than combat (Defense and Veterans

Brain Injury Center, 2018a). In 2017 alone, 17,841 service members were diagnosed with a TBI (Defense and Veterans Brain Injury Center, 2017). Notably, these numbers only include those evaluated and diagnosed with TBI by a medical provider; therefore it is likely the actual prevalence rate is substantially higher.

In 2009, the Department of Veterans Affairs (VA) and the DoD released a diagnostic matrix to help standardize the classification of the severity of different TBIs (see Figure 1). Concussions, or mild traumatic brain injuries (mTBI), are the most common form of TBI (Ryan & Warden, 2003; Centers for Disease Control and Prevention, 2003). Typically for mTBI, loss of consciousness (LOC) is minimal, ranging from none at all to 30 minutes; alteration of consciousness (AOC; e.g. feeling dazed, confused, or disoriented) is also marginal, lasting from only a moment to 24 hours. Post-traumatic amnesia (PTA) is relatively short and there is no known structural damage to the skull or brain. Individuals with mTBI will typically be rated on the Glasgow Coma Score (GCS), a measure of level of consciousness, as 13 or more upon hospital admission. LOC in individuals with moderate TBIs generally lasts between 30 minutes and 24 hours, AOC is greater than 24 hours, PTA can last between 1 and 7 days, and abnormal brain structure is possible. A GCS rating of 9-12 upon hospital admission is indicative of a moderate TBI. Individuals with severe TBIs experience LOC and AOC for longer than 24 hours, PTA for at least one week, and structural damage to the skull or brain is sometimes evident. Additionally, a GCS score of less than 9 is generally reported for individuals with severe TBI (Department of Veterans Affairs & Department of Defense, 2016).

Strictly speaking, a TBI refers solely to the anatomical location of injury. However, TBI often leads to cognitive, physical, mood, and behavioral difficulties that persist over time for the individuals who have suffered such injuries. Collectively, these symptoms have been referred to as "neurobehavioral symptoms." Cognitive difficulties are among the most common complaints after a TBI and often include reports of problems with attention, executive functioning, and memory (Dikmen et al., 2009). Specifically, individuals who have sustained a TBI often complain of an inability to concentrate, difficulty with maintaining focus, trouble performing more than one task at a time, and feeling less "cognitively efficient" (Riggio, 2010). They may also experience challenges with processing speed, problem solving, and inhibition as well as with planning and organization (McAllister, 2008). Physical complaints are also frequent and include headaches, dizziness, and fatigue (King & Kirwilliam, 2011). Individuals with TBI also commonly acutely experience nausea and more chronically experience sensitivity to light and sounds and difficulty sleeping (Riggio, 2010; King & Kirwilliam, 2011). Many individuals who have sustained a TBI also undergo various mood and behavior changes. They may become frustrated with perceived deficits in cognition and physical abilities and this frustration may be expressed through anxiety or depression reactions or by becoming more irritable or apathetic (Riggio, 2010). Additionally, emotional lability is also common as individuals who have sustained a TBI often have a more exaggerated display of emotions and their reactions to certain stimuli may be out of proportion (as compared to their previous reactions (McAllister, 2008). Individuals who have sustained a TBI may also become more impulsive than their pre-injury selves related to poorer judgement and decreased quality in decision-making (McAllister, 2008).

Importantly, the severity of the initial TBI does not necessarily correlate to the severity of the symptoms described above (Al-Hassani et al., 2018; Arciniegas et al., 2005). However, nearly every individual who has experienced a TBI will report at least some neurobehavioral symptoms in the acute phase after injury. Typically, neurobehavioral symptoms related to the TBI resolve within one month. However, in a small minority of individuals, they can last months or even years after the initial injury. The persistence of these symptoms is known as postconcussive syndrome (PCS; Ryan & Warden, 2003; Carroll et al., 2004).

Neurobehavioral symptoms related to TBI can have a significant impact on individuals in a multitude of domains. Symptoms resulting from TBI can impact close relationships and marriages, elevating the risk for social isolation (Godwin, Chappell, & Kreutzer, 2014). Suicide risk is also increased as is the development of mood disorders (Dree et al., 2018). Longer term, individuals who have sustained repeated or more severe TBI are more susceptible to the subsequent development of Parkinson's disease (Gardner et al., 2018; Bower et al., 2003), Alzheimer's disease (Weiner et al., 2013; Fleminger, Oliver, Lovestone, Rabe-Hesketh, & Giora, 2003; Plassman et al., 2000; Guo et al., 2000), chronic traumatic encephalopathy (CTE; McKee et al., 2013; McKee & Robinson, 2014), and other neurodegenerative disorders. Furthermore, service members with a history of TBI are significantly more likely to be discharged from the military for substance abuse reasons than service members without a history of TBI (Tanielian and Jaycox, 2008).

Societal costs of TBI in the military are also great. TBI affects a service member's ability to return to work, their productivity if they are able to work, and any future job

opportunities they may have (Weber, Spirou, Chiaravalloti, & Lengenfelder, 2018; Temkin, Corrigan, Dikmen, & Machamer, 2009). A national study of OEF/OIF/OND veterans who received treatment in the VA found those with a TBI had a four times higher median health services costs ($5,831) compared to those without a TBI ($1,547; Taylor, et al., 2012). In 2010, the estimated societal and economic cost of TBI in both civilian and military populations was approximately $76.5 billion (Centers for Disease Control, 2017).

POSTTRAUMATIC STRESS DISORDER

PTSD among military personnel is also pervasive, affecting 11-20% of service members returning from OEF/OIF/OND (National Center for PTSD, 2018). This translates to between 242,000 and 440,000 service members who have returned home from combat theaters experiencing PTSD. According to the American Psychiatric Association's (2013) *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), in order to be diagnosed with PTSD one must meet several criteria. An individual must first be exposed to an upsetting traumatic event, such as death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence (Criterion A). The individual must further experience symptoms across four categories. These are intrusion symptoms (e.g. re-experiencing the traumatic event by way of spontaneous memories, dreams, or flashbacks; Criterion B), avoidance symptoms (e.g. persistent evasion of stimuli relating to the event such as memories, thoughts, feelings, or external reminders like objects, people, or places; Criterion C), negative alterations in cognitions and mood (e.g. persistent blame of self or others, diminished interest in previously pleasurable activities, inability to recall certain features of the traumatic event;

Criterion D), and alterations in arousal and reactivity (e.g. irritable, aggressive, self-destructive, or reckless behavior, concentration issues, sleep disturbances, exaggerated startle response; Criterion E). To meet full criteria for PTSD diagnosis per DSM-5, individuals must exhibit one or more symptoms from Criterion B, one or both symptoms from Criterion C, two or more symptoms from Criterion D, and two or more symptoms from Criterion E. The symptoms must be present for at least one month, cause the individual significant distress or functional impairment (e.g. in social or occupational domains) and cannot be explained by medication, substance use, or other medical or psychological illnesses (American Psychiatric Association, 2013).

PTSD has been associated with high rates of psychiatric comorbidity, particularly major depression, anxiety (Ginzburg, Ein-Dor, & Solomon, 2010; Spinhoven, Penninx, van Hemert, Rooij, & Elzinga, 2014), substance use disorders (Swendsen et al., 2010), and, especially among military personnel, TBI (Wall, 2012; Kessler, 2000). PTSD also increases the risk of suicide (Jakupcak et al., 2009; Pietrzak et al., 2010) and homelessness (O'Connell, Kasprow, & Rosenheck, 2008). Individuals experiencing PTSD are more susceptible to developing medical complications, such as cardiovascular diseases (Coughlin, 2011; Edmondson & vin Kanel, 2017). Additionally, research has suggested PTSD is associated with a lower quality of life and reduced well-being (Magruder et al., 2004). Individuals with PTSD also report greater difficulties in their marriages or other romantic relationships, less social support, and perceive less cohesion in their families (Tsai, Harpaz-Rotem, Pietrzak, & Southwick, 2012). Service members with PTSD are more likely than the general population to develop anger problems and exhibit violence (Jakupcak et al., 2007; Taft et al., 2005).

The economic and societal burden of PTSD is also heavy. According to the Sidran Institute (2016), PTSD is noted to have one of the highest treatment costs of any psychiatric disorders primarily due to the high rates of healthcare service use by those with the disorder. In the first year of PTSD treatment, the Veterans Health Administration spent an average of $8,300 per veteran. The average cost of treatment for a patient without a diagnosis of PTSD was $2,400 (Congressional Budget Office, 2012). In 2012, the total PTSD costs for active duty service members with PTSD was $294.1 million (Institute of Medicine, 2014).

PTSD also leads to lost productivity. It has a substantial negative effect on labor-market outcomes (Tanielian & Jaycox, 2008), including lower incomes (Savoca & Rosenheck, 2000) and difficulty in attaining additional education (Tanielian & Jaycox, 2008). Unemployment rates also increase (Savoca & Rosenheck, 2000). Tanielian and Jaycox (2008) estimated that 50,000 service members returning from deployment with PTSD in 2008 cost society up to $204.7 million, even when they were receiving effective treatment.

COMORBIDITY OF TBI AND PTSD

TBI and PTSD frequently co-occur in service members (Betthauser et al., 2018), as many brain injuries are sustained during traumatic events (Bryant, 2011). Because of the substantial overlap in symptoms (Stein & McAllister, 2009; Howlett & Stein, 2016), the prevalence of this comorbidity is difficult to confirm; thus, estimates have greatly varied (Defense and Veterans Brain Injury Center, 2017). Studies conducted using military and veteran samples place the prevalence rates of this comorbidity as ranging between 10-40% (Defense and Veterans Brain Injury Center, 2017). For example, in a

study conducted by Hoge (2008), 32.6% of US Army soldiers who screened positive for mTBI after returning from deployment also screened positive for PTSD. Brenner and colleagues (2010) found similar results, with 26% of soldiers screening positive for *both* mTBI and PTSD.

Although TBI and PTSD have distinguishing characteristics in symptomatology, their symptoms also greatly overlap (Carlson et al., 2011). This makes it incredibly difficult for clinicians and researchers as many of the defining characteristics of TBI are also trademark symptoms of PTSD, particularly irritability, sleep disturbances, and concentration and memory difficulties (Stein & McAllister, 2009; Hoge et al., 2008). Other symptoms such as fatigue, depression, and anxiety are also common across both conditions. Additionally, dissociative reactions often characteristic of PTSD have been frequently observed after TBI, including manifestations of derealization, depersonalization, decreased situational awareness, emotional numbing, and amnesia (Bryant, 2011). In regards to the overlap of the two conditions among military personnel specifically, returning service members frequently present with a combination of symptoms that are features of both PTSD and persistent symptoms of TBI (i.e. PCS; Stein & McAllister, 2009). Some studies have even noted that service members with mild TBI report symptoms of PTSD twice as often as those without a TBI (Hoge et al., 2008; Schneiderman, Braver, & Kang, 2008).

With the United States' involvement in the conflicts in the Middle East, it has become clear that TBI and PTSD have an important and complex relationship (Howelett & Stein, 2016). However, the details of this relationship are not yet well understood and despite their comorbidity and intersecting symptomatology, there is a paucity of research

regarding how TBI in the post-acute and chronic phases combined with PTSD symptoms affects cognitive performance (Betthauser et al., 2018). The few studies that have been conducted in this area reveal mixed results. Vasterling and colleagues (2006) examined the effects of self-reported PTSD symptoms and mTBI status on cognitive performance among soldiers after deployment to Iraq. They found that higher levels of reported PTSD symptoms were associated with cognitive deficits on several objective measures of neuropsychological functioning, yet the presence of TBI did not significantly impact cognitive performance. Interestingly, the authors also found that higher frequency or severity of PTSD symptoms along with experiencing a mTBI were associated with better performance on a simple reaction time test.

In a later study, Vasterling and colleagues (2012) also found that higher levels of reported PTSD symptoms were associated with worse cognitive performance on several cognitive tasks, including code substitution learning, and code substitution delayed, even after adjusting for a TBI sustained during the previous deployment. However, in this study, more severe PTSD was related to worse performance on the same simple reaction time test. The authors also found that a mTBI occurring during the previous deployment was not related to post-deployment cognitive performance, including on the simple reaction time test.

In 2018, Betthauser and colleagues found that a combination of mTBI and PTSD in a sample of active duty soldiers completing post-deployment assessments was associated with worse performance on an objective cognitive measure than either condition alone. They concluded that although mTBI alone impacts cognitive functioning for some individuals returning from deployment, current PTSD symptoms appear to

exacerbate cognitive deficits for a nontrivial minority. To date, this is the only study to examine the effect of comorbid TBI and PTSD symptoms on cognitive performance.

The long-lasting impacts of TBI and PTSD, and the unique contribution of each condition, thus remains unclear. The few studies that have provided glimpses of these relationships are limited in that they only included members of the US Army, excluded TBI severities greater than mild, and consisted of individuals who were on normal duty status and undergoing routine post-deployment assessment (i.e. were not treatment-seeking). This makes it difficult to generalize to a clinical population of military service members.

IMPACT OF TBI AND PTSD ON FUNCTIONING

Beyond the potential effects on cognitive performance, the impact of TBI and PTSD on functional outcomes is of utmost clinical importance. In fact, both the DoD and VA emphasize a focus on functional impairment in the assessment and subsequent treatment of TBI and PTSD. The impact of TBI on various domains of functioning has been previously discussed in sections above and is also well-documented elsewhere (e.g. Dams-O'Connor et al., 2013; Schonberger, Ponsford, Olver, & Ponsford, 2010; Svestkova, Angerova, Sladkova, Bickenback, & Raggi, 2010; Schretlen & Shapiro, 2003; Hoofien, Gilboa, Vakil, & Donovick, 2001). However, the mechanisms by which this relationship operates are less understood, particularly as they pertain to military personnel.

One mechanism that has been suggested is patients' subjective perception of their own cognitive functioning and difficulties. In a sample of US Army Special Operations Command personnel diagnosed with mTBI, Kontos and colleagues (2013) determined a

history of mTBI was associated not only with objective neurocognitive deficits, but also the service members' perception of decreased cognitive functioning. A later study conducted by French, Lange, and Brickell (2014) extended these results and examined subjective cognitive complaints and neuropsychological test performance among a sample of active duty service members following military-related TBI. However, they found that self-reported cognitive complaints were not significantly correlated with overall objective neurocognitive functioning. On the other hand, subjective complaints were significantly correlated with psychological distress in that service members who had cognitive complaints had reliably higher scores on psychological distress measures. This was consistent with previous research demonstrating that emotional distress is more influential in the subsequent self-report of cognitive problems than objective neuropsychological/cognitive functioning measures among civilian (Chamelian & Feinstein, 2006; Satz et al., 1998; Gass & Apple, 1997) and veteran samples (Spencer, Drag, Walker, & Bieliauskas, 2010).

The relationship between PTSD and functional outcomes, particularly in the social domains, is well-recognized in the literature (e.g. Holowka & Marx, 2012; Rodriguez, Holowka, & Marx, 2012) and has also already been discussed above. As with TBI, the potential mechanisms by which PTSD leads to poorer functioning is not yet well understood. However, it has been established PTSD is indeed associated with mild neurocognitive deficits (Scott et al., 2015). Research has also found that individuals with PTSD report experiencing more cognitive problems (Blanck et al., 1995; Li, Yu, Long, Li, & Cao, 2015). Furthermore, higher levels of psychological distress are known to be associated with more self-reported cognitive deficits (Spencer et al., 2010). It is important

to note, however, that self-perception of cognitive difficulties is not always related to objective cognitive performance among patients with PTSD (Samuelson et al., 2016; Binder, Storzbach, Anger, Campbell, & Rohlman, 1999). This suggests there may be a misalignment between patients' own perceptions of cognitive problems and the actual level of impairment indicated by objective measures. Thus, similar to TBI, Samuelson and colleagues (2017) suggested negative self-perception of cognitive abilities may also be one of the mechanisms linking PTSD to poor functional outcome. More specifically, based on prior research (e.g. Sayer et al., 2011; Sayer, Carlson, & Frazier, 2014), Samuelson and colleagues proposed a strong association between PTSD and difficulties in aspects of social functioning, such as community engagement, self-care, and productivity.

In a study examining male and female veterans of the recent wars in Iraq and Afghanistan, Samuelson and colleagues (2017) found that perceived cognitive problems mediated the relationship between PTSD and psychosocial outcomes. Again, it was the *perception* of cognitive difficulties, not objective performance, that mediated the relationship between PTSD and functional abilities. Samuelson and colleagues suggested it is patients' own appraisals of attention, concentration, and memory problems, rather than deficits on objective cognitive performance measures that influence functioning in social and occupational domains.

At present, Samuelson and colleagues' (2017) is the only study to examine this relationship. To our knowledge, no research has been conducted to extend these findings to a treatment-seeking sample of active duty service members with mixed severity TBI and PTSD. Furthermore, the researchers did not examine the relationship between

objective cognitive performance and social functioning and whether this relationship was similarly mediated by perceived cognitive difficulties.

STUDY OVERVIEW AND SPECIFIC AIMS

The present study aims to add to the current understanding of the complex relationship between TBI and PTSD and their impact on functional outcomes. We examined several issues related to the impact of comorbid TBI and PTSD on cognitive performance and social functioning among treatment-seeking active duty service members with cognitive complaints. Our specific aims are outlined below:

Specific Aim 1

To compare performance on an objective cognitive assessment among three groups (a) active duty service members with both TBI and PTSD symptoms, (b) those with TBI alone, and (c) those with PTSD symptoms alone.

Hypothesis 1a

Service members with comorbid TBI and PTSD symptoms will perform worse on the objective cognitive assessment than service members with either condition alone.

Hypothesis 1b

Service members with PTSD-symptoms-only will perform worse on the objective cognitive assessment than service members with TBI-only on the cognitive assessment.

Specific Aim 2

To determine whether cognitive functioning, self-reported neurobehavioral symptoms, and emotional distress relate to social functioning among service members with TBI or PTSD symptoms.

Hypothesis 2a

Because the measure of social functioning is scored such that a greater score indicates greater perceived impairment, we expect there will be a negative correlation between scores on the cognitive assessment and scores on the measure of social functioning. Thus, poorer cognitive performance will be associated with more difficulties with social functioning.

Hypothesis 2b

Again, because the measure of social functioning is scored such that a greater score indicates greater perceived impairment, we expect there will be a positive correlation between scores on the measure of neurobehavioral symptoms and scores on the measure of social functioning. Thus, more neurobehavioral symptom endorsement will be associated with more difficulties with social functioning

Hypothesis 2c

There will be a positive correlation between scores on the measure of emotional distress and scores on the measure of social functioning. Thus, more symptom endorsement on the emotional distress measure will be associated with more difficulties with social functioning.

Specific Aim 3

To determine whether self-reported neurobehavioral symptoms mediate the relation between emotional distress and social functioning and the relation between cognitive performance and social functioning.

Hypothesis 3a

Scores on the measure of neurobehavioral symptoms will mediate the relation between scores on the emotional distress measure and the social functioning measure.

Hypothesis 3b

Scores on the measure of neurobehavioral symptoms will mediate the relation between cognitive performance and scores on the social functioning measure.

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CHAPTER 2: METHODS

OVERALL STUDY DESIGN AND SETTING

The present study was a cross-sectional design using data collected between 2008 and 2017 as part of a larger clinical assessment project. Data collection was conducted in the National Intrepid Center of Excellence's (NICoE) Brain Fitness Center (BFC) at Walter Reed National Military Medical Center (WRNMMC) and Fort Belvoir Community Hospital (FBCH). The overall goal of the BFC is to provide any patient with complaints of cognitive dysfunction the opportunity to use commercially available brain-training technology in a structured, supportive environment. This brain-training is used either as an adjunct therapy to ongoing rehabilitation treatments or as a stand-alone service for those discharged from cognitive rehabilitation or preparing for discharge. Male and female military healthcare beneficiaries aged 18 years and older are eligible to participate in the BFC and engage with its brain-training programs. Military healthcare beneficiaries include active duty service members, National Guard and Reserve members, military retirees, their families, survivors, certain former spouses, and others registered in the Defense Enrollment Eligibility Reporting System (DEERS).

Most patients are referred to the BFC by clinical providers, although self-referrals are also accepted. Patients must also report some concern regarding their cognitive functioning. Although the majority of patients in the BFC have been diagnosed with TBI using standard clinical diagnostic procedures, the BFC also serves patients with other medical and psychiatric conditions or subjective complaints of cognitive dysfunction following deployment. All patients complete an objective cognitive assessment measure and a variety of self-report questionnaires as part of the BFC intake procedure. These

data are collected as part of the normal standard of care for internal review as well as a means of providing feedback to patients. During their first visit, all BFC patients are offered the opportunity to have their data included in a database to be used for research. This database consists of de-identified data collected from the BFC's normal standard of care procedures.

Participants

Aim 1

To address Aim 1, data were analyzed from participants who met the following inclusion criteria: (a) patients who were diagnosed with TBI and/or scored a 35 or higher on the Posttraumatic Stress Disorder Checklist-Civilian version (PCL-C), (b) completed the Automated Neuropsychological Assessments Metrics (ANAM; the objective cognitive assessment), (c) were at least 18 years of age, (d) were an active duty service member treated at WRNMMC or FBCH, (e) had the ability to communicate well in English, and (f) were capable of providing informed consent. Individuals were excluded from the study if they (a) were unable to provide informed consent or HIPAA authorization, (b) suffered a penetrating TBI, or (c) had incomplete data on either the PCL-C or the ANAM.

A total of 211 participants met the inclusion criteria outlined above. Participants' age ranged from 19-years-old to 56-years-old, with a mean age of 34.5 (standard deviation = 9.09). Approximately, 28% of the sample was female, with the remaining 72% being male. Each branch of the military was represented (USA = 54.5%, USN = 19.9%, USMC = 14.7%, USAF = 9.5%, USPHS = .9%, USCG = .5%). Enlisted service members made up approximately 75% of the study sample and 23% were warrant or

commissioned officers. Roughly 2% of the sample was service members whose rank was coded as "other." Twenty-six percent of service members in the sample carried a TBI diagnosis, 31% had significant PTSD symptoms (PCL-C $\geq$ 35), and 43% met criteria for both. Of those with a TBI, 82% were classified as mild, 11% were moderate, and 7% were severe. These characteristics and other sample demographics for Aim 1 are presented in Table 1.

Using G*Power (Erdfelder, Faul, & Buchner, 1996), we conducted an analysis to determine the power available with our sample size of 211 service members. We had power (1 - β) of .23, α = .05, to identify a small effect (*f* = .10) and power of .91, α = .05, to determine a medium effect size (*f* = .25). In order to find a large effect (*f* = .40), we had power (1 – β) of .99, α = .05. Thus, our sample size of 211 participants would provide sufficient power to find medium and large effects for these analyses.

Aims 2 and 3

Patients from the larger BFC database were included in the analyses for Aims 2 and 3 if they met the inclusion criteria outlined in Aim 1 and also completed the Neurobehavioral Symptom Inventory (NSI) and the Mayo-Portland Adaptability Inventory-4 (MPAI-4). Exclusion criteria were the same as Aim 1. Additionally, patients were excluded if they had incomplete data on either the NSI or the MPAI-4, which led to a total of 71 eligible participants. The MPAI-4 was introduced as a BFC measure later in the data collection process and therefore many of the participants eligible for Aim 1 were not eligible for Aim 2 because they had not completed the MPAI-4.

Participants' age ranged from 20-years-old to 56-years-old, with a mean age of 36.1 and a standard deviation of 9.65. Approximately 37% of the sample was female with

the remaining 63% being male. All branches of the military were represented, except the Coast Guard (USA = 59.2%, USN = 19.7%, USAF = 12.7%, USMC = 7.0%, USPHS = 1.4%, USGC = 0%). Sixty-nine percent of the sample were enlisted service members and 31% were warrant or commissioned officers. Eighty-three percent of service members with TBI were mild severity, 11% were moderate, and 6% were severe. These characteristics and other sample demographics for Aims 2 and 3 are depicted in Table 2. There were no significant differences in regards to age between the sample for Aim 1 and the sample for Aims 2 and 3, $t(280) = -1.208$, $p = 0.228$. Additionally, no association was found between sample group and gender ($X^2(1) > 1.679$, $p = 0.195$), sample group and branch of service ($X^2(5) > 3.163$, $p = 0.606$), or sample group and enlisted/officer status ($X^2(1) > 1.487$, $p = 0.223$).

G*Power (Erdfelder et al., 1996) was also used to determine available power given our sample size of 71 service members. We had insufficient power ($1 - \beta = .14$, $\alpha = .05$) to determine a small effect ($f^2 = 0.02$) or a medium effect ($1 - \beta = .76$, $\alpha = .05$, $f^2 = 0.15$). In order to identify a large effect ($f^2 = 0.35$), we had power ($1 - \beta$) of .99, $\alpha = .05$. Thus, our sample size of 71 participants would provide sufficient power to detect large effects for these analyses.

Materials and Procedure

As part of the BFC intake process, participants underwent an initial intake interview following which they completed self-report measures and questionnaires as well as an objective cognitive assessment. At the end of the intake evaluation, all patients were asked if they were interested in participating in a research database study. Patients were reminded their participation was completely voluntary and that declining to

participate would not affect their course of treatment in the BFC. Data from patients who consented were entered into a larger database for research. For the present study, a dataset was created for analysis that included the baseline data of all eligible participants who were experiencing significant PTSD symptoms and/or had experienced a TBI. Data were analyzed via IBM Statistics 24 version 25.

Emotional Distress and PTSD Symptoms

The Posttraumatic Stress Disorder Checklist – Civilian Version (PCL-C; Weathers, Huska, & Keane, 1991) was one of several self-report measures administered to every patient during their first visit as part of the BFC's standard procedures and was used to assess emotional distress and PTSD symptom severity. This version of the PCL was selected for use in the BFC as it is not linked to a specific event, unlike the PCL-M which refers solely to a "stressful *military* experience." The PCL-C is a 17-item self-report measure of PTSD symptoms that refers more generally to a "stressful experience from the past." Respondents are asked to read a list of complaints and rate how much they have been bothered by each over the past month on a scale from 1 ("not at all") to 5 ("extremely"). Items include symptoms such as "repeated, disturbing memories, thoughts, or images of a stressful experience from the past," "avoiding thinking about or talking about a stressful experience from the past or avoiding having feelings related to it," and "feeling jumpy or easily startled."

The outcome of the PCL-C is a continuous score – the higher the sum of the scores on the items, the more PTSD symptoms the respondent has endorsed. For the purposes of this study, patients were considered to have significant levels of PTSD symptoms if they scored a 35 or higher on the PCL-C. We chose this cut-point for several

reasons. The VA National Center for PTSD recommends different cut-scores for different settings and purposes. In specialized medical clinics (such as a TBI or pain clinic) or a VA primary care setting, a cut-off score of 35 or greater is recommended. In contrast, for a VA or civilian specialty mental health clinic, a cut-off score of 45 or higher is recommended. Given the setting, referral concerns, referring providers and other considerations, we felt a cut score of 35 best represented the BFC. Additionally, previous research has also supported this cut-off score in similar settings (e.g. Murphy, Ross, Ashwick, Armour, & Busuttil, 2017; Bliese et al., 2008).

Previous research has demonstrated the PCL-C has high internal consistency (α = .94 to .97; Blanchard et al., 1996; Weathers, Litz, Herman, Huska, & Keane, 1993). It also had a similarly high internal consistency within our own sample with a Cronbach's α = 0.95. The PCL-C additionally has strong test-retest reliability (Blanchard et al., 1996; Ruggerio et al., 2003). Indications of its validity include positive correlations with both the Mississippi PTSD scale (convergent validity r =.85 to .93; Weathers et al., 1993) and the Clinician Administered PTSD Scale (CAPS; r =.92, Blanchard et al., 1996).

Cognitive Performance

Cognitive performance was measured using the Automated Neuropsychological Assessment Metrics version 4 TBI (ANAM-4 TBI), an objective cognitive assessment. The ANAM-4 TBI aims to evaluate domains impacted by TBI and is a battery of seven cognitive tests, including simple reaction time, code substitution (learning), procedural reaction time, mathematical processing, matching to sample, code substitution (delayed), and simple reaction time (repeated). Table 3 depicts these subtests and the cognitive functions targeted by each. For each test, reaction time, accuracy, and throughput are

documented. The throughput score is a composite of both accuracy and reaction time and thus was used in the present study to assess the effectiveness and efficiency of a participant's cognitive performance. Additionally, throughput is the score that is most often used in the literature when assessing cognitive performance and is considered a good measure of cognitive efficiency (Roebuck-Spencer, Vincent, Schlegel, & Gilliland, 2013; Thorne, 2006).

Overall cognitive performance was examined by using an ANAM composite score (ACS), which summarizes overall performance using all the throughput scores from each subtest. To create the ACS for this study, throughput scores on each of the subtests were converted to T-scores relative to an age- and gender-matched normative group (mean = 100, sd = 15). In this case, we employed military-specific norms (Vincent, Roebuck-Spencer, Gilliland, & Schlegel, 2012). These converted T-scores were then summed across the tests and a standard score of this summed T-score was computed relative to the summed T-score in the normative control group:

Standard Score = 100 +15 x [Raw Throughput Score – Throughput Mean of the Normed Group] / Throughput Standard Deviation of the Normed Group

The throughput standard scores for all seven subtests were then summed. The ACS was calculated using the following equation:

ACS = (Sum of the Standard Score – 700.9764524) / 67.4768974

The numeric values presented in this equation reflect the mean (700.98) and standard deviation (67.48) of the military normative control data. The composite score is reported in standard deviations with mean = 0 and standard deviation = 1. The ACS has a normal distribution.

Neurobehavioral Symptoms

Within the last few years, the DoD has chosen the Neurobehavioral Symptom Inventory (NSI; Cicerone & Kalmar, 1995) as an assessment tool in tracking recovery from TBI in treatment programs across all TBI clinics in the Military Healthcare System (MHS). The NSI is a 22-item self-report measure that assesses postconcussion symptoms (e.g. dizziness, balance, headaches, forgetfulness, irritability, etc.) and asks participants to rate how much each symptom has affected them over the past two weeks on a 5-point Likert scale ranging from 0 ("None – Rarely if ever present; not a problem at all") to 4 ("Very Severe – Almost always present and I have been unable to perform at work, school, or home due to this problem; I cannot function without help").

The NSI can be divided into several subscales. Originally, Cicerone and Kalmar (1995) used cluster analysis to group patient-endorsed symptoms on the NSI into four distinct categories: affective, cognitive, somatic, and sensory (King et al., 2012). More recently, however, researchers have demonstrated that a three-factor model provides a more parsimonious structure for clinicians and for clinical settings (Caplan et al., 2010). Thus, the NSI, in our study, is grouped into three subscales: somatic/sensory, affective, and cognitive. The somatic/sensory subscale assesses symptoms such as dizziness, loss of balance, sensitivity to light, and nausea. The affective subscale examines symptoms related to fatigue, anxiety, depression, and irritability. Symptoms including concentration difficulties and forgetfulness are assessed by the cognitive subscale (Caplan et al., 2010).

A total NSI score was obtained by summing the ratings for the 22 items (range from 0 to 88) which produces a continuous score. The higher the sum of the scores, the more symptoms the participant reported experiencing. In the present sample, the NSI

demonstrated high internal consistency (α = 0.93). The somatic/sensory, affective, and cognitive subscales all had high reliabilities, Cronbach's α = 0.85 to 0.89. This is very similar to previous research showing high internal consistency for the NSI (total α = 0.95; subscales α = 0.88 to 0.92; King et al., 2012) as well as seven-day test-retest stability (Silva et al., 2013).

Social Functioning

The Mayo-Portland Adaptability Inventory-4 (MPAI-4; Malec, 2005) is a global outcome measure often used in postacute (posthospital) rehabilitation settings to assess patient functioning after brain injury as well as to track progress in rehabilitation programs providing services to these individuals (Bellon et al., 2012). It is commonly used throughout the United States and the world (Malec et al., 2003; Malec, Moessner, Kragness, & Lezak, 2000; Kean, Malec, Altman, Swick, & Rasch, 2011) and is a standard outcome assessment used in the MHS (Kean et al., 2013).

The MPAI-4 is a self-report measure designed to assess a patient's functional abilities and covers a wide range of domains often troubling to those with brain injury, including physical, cognitive, emotional, behavioral, and social functioning. The current version consists of 35 items that examine key indicators of limitations in ability, activities and adjustment, and social/community participation. The first 29 items on the MPAI-4 represent the patient's current level of functioning across a variety of domains. The remaining six items reference pre- and post-injury information helpful in identifying circumstances that may impede rehabilitation efforts, such as symptoms of psychosis, alcohol and/or drug use, legal infractions, and any additional concerns leading to physical or cognitive impairment. These items, however, are not included in the total score, as

they do not necessarily represent the specific effects of the brain injury (Bellon, Malec, & Kolakowsky-Hayer, 2012) and thus were not included in the present analyses.

The MPAI-4 consists of three subscales – the Ability Index, the Adjustment Index, and the Participation Index. The Ability Index is made up of 13 items that examine impairment associated with mobility, use of hands, vision, audition, dizziness, motor speech, verbal and nonverbal communication, attention and concentration, memory, problem-solving, and visuospatial abilities. The Adjustment Index includes 12 items that assess anxiety, depression, irritability/anger/aggression, pain and headaches, fatigue, mild symptom sensitivity, social interaction, and self-awareness. The Participation Index consists of 8 items that focus on the patient's ability to initiate activities, social interaction, take care of themselves, manage responsibilities of their home, independently use transportation, engage in leisure activities, and manage their finances (Bellon et al., 2012).

We chose to focus on the Participation Index as a measure of functioning in the present study for several reasons. First, patients and their families are generally most concerned about social functioning and engagement when assessing recovery and outcome (Malec, Parrot, Altman, & Swick, 2014). Second, because gains in functionality assessed by the Abilities and Adjustment indices are often a "prerequisite" to gains in social engagement, participation outcome is a good assessment of overall functioning (Malec, 2004). Third, items assessed by the Participation Index on the MPAI-4 have been linked to health-related domains in the Internal Classification of Functioning (ICF; World Health Organization, 2001; Lexwell, Malec, & Jacobsson, 2012; Resnick & Plow, 2009). Finally, many items across the NSI are similar to those assessed by the Ability and

Adjustment indices of the MPAI-4; therefore we sought to reduce overlap between the two measures.

All items on the MPAI-4 are rated on a 5-point Likert scale ranging from 0 to 4. A score of 0 indicates the patient has no functional disabilities within the domain assessed. A 1 signifies a mild impairment but, with appropriate assistance, the patient's functioning is generally normal. If a patient indicates a score of 2, then it is interpreted as a mild problem that interferes with the patient's life less than 25% of the time. A score of 3 specifies the patient is impaired 25% to 50% of the time with the particular item or activity. A 4 indicates impairment 75%, or most, of the time (Bellon et al., 2012). A total score of social functioning was obtained by summing the ratings for the Participation Index (items 22 through 29 on the full scale MPAI-4); with designated items reverse scored in accordance to the MPAI-4 manual scoring instructions (e.g. 27 and 28). The higher the sum of the scores, the more impairment the participant reported experiencing.

The MPAI-4 as a whole is a product of almost 20 years of research and development using item response and classic psychometric theory (Wilde et al., 2010; Kean et al., 2011) with well-established concurrent, construct, and predictive validity (e.g., Kean et al., 2011; Malec et al., 2003; Malec, 2004; Bohac, Malec, & Moessner, 1997; Malec & Thompson, 1994; Malec, 2001; Altman, Swick, Parrot, & Malec, 2010; Eicher, Murphy, Murphy, & Malec, 2012; Trexler et al., 2010). The Participation Index on the MPAI-4 has been shown to be a concise, psychometrically sound instrument capable of reliably assessing outcomes after brain injury and can be implemented as a stand-alone measure (Malec, 2004). Previous research has demonstrated satisfactory concurrent (Malec & Thompson, 1994) and predictive validity (Malec, 2001; Malec et al,

2000) as well as internal consistency and construct validity (Kean et al., 2011; Malec et al., 2003). The Participation Index showed high internal consistency in our sample (α = 0.77), consistent with previous research (α = 0.79; Malec et al., 2003).

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CHAPTER 3: RESULTS

STATISTICAL ANALYSIS

Aim 1

Aim 1 compared cognitive performance via the ANAM-4 TBI among three groups – service members with a TBI-only diagnosis, service members who were experiencing significant PTSD symptoms, and service members with both a TBI and significant PTSD symptoms. A one-way ANOVA revealed a significant effect of group on cognitive performance, $F(2, 208) = 6.356$, $p = .002$, $\omega = .14$. Homogeneity of variance was evaluated via Levene's Test, $F(2, 208) = .778$, $p = .460$. Least significant difference post hoc tests were performed to make pairwise comparisons and revealed significant differences between the comorbid group ($\overline{x} = -3.10$) and the PTSD-symptoms-only group ($\overline{x} = -2.08$, $p = .005$) as well as between the comorbid group and the TBI-only group ($\overline{x} = -1.90$, $p = .002$). However, there was no significant difference between the PTSD-symptoms-only group and the TBI-only group ($p = .674$). Notably, all three groups performed significantly below the norms for US service members matched for age and gender where the ACS score is reported in standard deviations with a mean of 0.

Aim 2

Aim 2 intended to determine whether cognitive performance, neurobehavioral symptoms, and emotional distress predicted social functioning among service members with TBI and/or PTSD symptoms. Correlations were computed among the four measures of interest, the ACS, NSI, PCL-C, and the Participation Index from the MPAI-4. Results indicated significant associations among all measures, with the exception of the ACS and the Participation Index ($p = .09$). Higher endorsement of emotional distress

and neurobehavioral symptoms were each associated with greater difficulties in areas of social functioning. The zero-order correlations are presented in Table 4.

A multiple linear regression was calculated to predict social functioning based on cognitive performance, neurobehavioral symptoms, and emotional distress. A significant regression equation was found, $F(3, 67) = 12.516$, $p = .000$, with an R of .599 and an R^2 of .359. Participants' social functioning is equal to .414 + .022(ACS) + .193 (NSI Total Score) + .038 (PCL-C Total Score). However, total score on the NSI was the only significant independent variable (t = 3.152, $p = .002$); ACS and total score on the PCL-C did not reach statistical significance (t = .100, $p = .921$ and t = .717, $p = .476$, respectively) in the multiple regression model.[1] A summary of results is provided in Table 5.

Aim 3

Aim 3 sought to determine whether neurobehavioral symptoms mediate the relation between emotional distress and social functioning as well as the relation between cognitive performance and social functioning. Mediation analyses were conducted using the PROCESS MACRO (Hayes, 2017) plug-in for SPSS. Generally, bootstrapping is recommended when testing indirect effects in order to generate confidence intervals and to ensure the assumption of normality (Preacher, Rucker, & Hayes, 2007). Therefore, bootstrap analyses were conducted with 5,000 samples in order to compute bias corrected and accelerated confidence intervals.

There was a significant indirect effect of emotional distress on social functioning through neurobehavioral symptoms, $b = .139$, 95% CI [.011, .256]. Neurobehavioral

[1] These and other results were re-run using only participants with a TBI classified as mild and no substantive differences were found. In other words, even when excluding participants with moderate and severe levels of TBI, interpretation of results remained the same.

symptoms completely mediated the relationship between emotional distress and social functioning (a path: *b* = .696, SE = .066, t = 10.469, *p* = .000; b path: *b* = .191, SE = 0.059, t = 3.239, *p* = .002; c path: *b* = .171, SE = .35, t = 4.926, *p* = .000; c' path: *b* = .038, SE = .052, t = 7.285, *p* =.468, 95% CI [-.066, .147]. . There was no significant mediating effect of neurobehavioral symptoms on the relationship between cognitive performance and social functioning (a path: *b* = -1.675, SE = 0.650, t = -2.578, *p* = .012; b path: *b* = .226, SE = .039, t = 5.873, *p* = .000; c path: *b* = -.349, SE = . 254, t = -1.375, *p* = .174; c' path: *b* = .031, SE = .2178, t = .1402, *p* = .889, 95% CI [-0.404, -.465]). These results are illustrated in Figure 2.

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CHAPTER 4: GENERAL DISCUSSION

Overall, the results of this study supported initial hypotheses. Service members with comorbid TBI and PTSD-symptoms performed worse on the cognitive performance task than those with either condition alone. However, contrary to what was hypothesized, cognitive performance of individuals with PTSD-symptoms-only did not significantly differ from those with TBI-only. Notably, all three groups had overall cognitive performance scores significantly below the norms for US military personnel, i.e., two standard deviations below the mean for the TBI-only and PTSD-symptoms-only groups and three standard deviations below the mean for the comorbid group. It is important to emphasize that the overall performance score on the ANAM is a composite score reported in standard deviations. Although it is not uncommon for a small number of individuals without diagnosed cognitive impairment to perform at lower levels than expected on a battery of neuropsychological tests (Heaton, Ryan, Grant & Matthews, 1996; Schretlen, Testa, Winicki, Peralson & Gordon, 2008), it is rare for healthy, non-treatment seeking service members to obtain a score in the impaired range on the ANAM (Vincent et al., 2012). In a study that established normative data for healthy, non-treatment seeking active duty service members (Vincent et al., 2012), a "Clearly Below Average" score, defined as more than two standard deviations below the mean, on at least one subtest occurred in only 8.3% of individuals and only 1.3% scored below this range on two or more subtests. In the present study, all three groups scored in the "Clearly Below Average" range. This is not completely unexpected due to the fact that the present sample consisted of treatment-seeking patients and included individuals with a history of

moderate/severe TBI and therefore was not part the population assessed by Vincent and colleagues.

These results also differ from those obtained in two previously conducted studies examining ANAM performance in non-treatment-seeking service members with a history of TBI and PTSD symptoms. In a sample of active duty Army soldiers who had recently returned from deployment to Iraq, Vasterling and colleagues (2006) found those with higher levels of PTSD symptoms performed worse on several ANAM subtests (cognitive functioning), but a history of TBI was not associated with cognitive performance. In 2012, Vasterling and colleagues examined the effects of TBI and PTSD on cognitive performance post-deployment in another sample of active duty Army soldiers who recently returned from Iraq. Here, they found a similar pattern – TBI was not associated with performance on the ANAM, but PTSD scores were associated with worse performance on several of the ANAM's subtests.

In contrast to the findings of Vasterling and colleagues, a study conducted by Betthauser and colleagues (2018) in a non-clinical sample of soldiers who recently returned from either Iraq or Afghanistan found results similar to the present study. Our results from treatment seeking service members in the present study suggest TBI can negatively impact cognitive performance for some, similar to the impact of PTSD symptoms (both groups performing significantly worse). In other words, the results found by Betthauser and colleagues in a more general sample mirrored our results using a clinical, treatment-seeking sample.

Future research should continue to examine the interactions and impacts of these variables in both clinical and non-clinical samples to provide the field some clarity about

the impact of TBI on cognitive performance across the spectrum of functionality. Researchers should also consider including variables to assess the chronicity of TBI symptoms and time elapsed since injury.

The present results extended existing literature by examining a sample of treatment-seeking active duty service members who identified as having cognitive difficulties. Previous research had only assessed service members as part of the post-deployment health assessment (PHA) process, which because of the context may lead to some individuals under-reporting symptoms in order to return home as quickly as possible (Hourani, Bender, Weimer, & Larson, 2012; Warner eta l., 2011). This could, in part, explain the results obtained by Vasterling and colleagues (2006; 2012).

Additionally, our study adds to the literature in that our sample not only included service members from all branches of the military, but also included women, individuals who had diagnoses of moderate or severe TBI, and service members who were reporting a history of TBI not limited to only their most recent deployment. In future studies, branch, gender, and TBI severity differences should be explored in addition to examining various moderators of performance on individual subtests on the ANAM. Furthermore, the sample in the present study and the substantially low scores on the ANAM suggest that the cognitive impact of comorbid TBI and PTSD results in potentially clinically significant cognitive difficulties and perhaps even deficits.

To our knowledge, this is the first study to find a significant difference in cognitive performance among a treatment-seeking sample of a diverse group of active duty service members. Results suggest there may be something particularly impactful about the combination of TBI and PTSD and their subsequent influence on cognitive

performance. Years of research has found overlapping symptoms among TBI and PTSD, including memory and concentration difficulties. In our study, the combination of these two conditions, and perhaps their additive effects, led to worse cognitive performance than either condition alone. Although awareness of the individual effects of TBI and PTSD on cognitive functioning has greatly increased over the recent years, the impact of the comorbid presentation of the two conditions has received less attention, albeit focus on such comorbid patient groups is beginning to increase. The present results highlight the importance of attending to the clinical impact of comorbid PTSD and TBI and the need for further research of this population.

Results examining the correlates of social functioning demonstrated three main findings: (1) a higher endorsement of neurobehavioral symptoms is associated with poorer social functioning; (2) a higher endorsement of emotional distress is associated with poorer social functioning; and (3) cognitive performance was not significantly associated with social functioning. Notably, only neurobehavioral symptoms explained a significant amount of the variance in a model evaluating all three predictors simultaneously, suggesting that neurobehavioral symptoms might mediate the relationship between emotional distress and social functioning, but not the relationship between cognitive performance and social functioning.

Additional analyses helped fine-tune the interpretation of the mediation model suggested by the results of the regression analysis. Findings supported the view that neurobehavioral symptoms did indeed completely mediate the relation between emotional distress and social functioning. The results involving emotional distress and social functioning align with those of a study conducted by Samuelson and colleagues

(2017) in which perceived cognitive difficulties mediated the relationship between PTSD diagnosis and social functioning. Findings suggest one mechanism underlying the relation between emotional distress and social functioning is self-reported neurobehavioral symptoms. In other words, individuals with more perceived difficulties characterized as neurobehavioral complaints (dizziness, headaches, concentration difficulties, etc.) will report more difficulty in day-to-day areas of functioning, such as social engagement, initiation, and self-care. This is particularly important as current treatments for both PTSD and TBI largely ignore these symptoms and instead aim to address emotional complaints separately through various psychotherapies. However, findings from the present study indicate the importance of attending to neurobehavioral symptoms in conjunction with treating symptoms related to emotional distress to improve social functioning across a multitude of domains. Perhaps through addressing neurobehavioral complaints in addition to emotional, clinicians can help patients achieve greater functional outcomes.

Future research should also examine specific symptoms characterized as neurobehavioral complaints to better understand the relations among cognitive performance, emotional distress, and social functioning. An examination of the NSI's particular symptom clusters should be explored in an effort to address the question of which types of symptoms are more influential in mediating the relation between emotional distress and social functioning. Specifically, the cognitive and affective subscales of the NSI should be examined. Based on the results of the present study, symptoms identified by the cognitive subscale on the NSI could be related to both cognitive performance as well as social functioning. Additionally, symptoms on the

affective subscale will likely be associated with both emotional distress measures and social functioning. On the cognitive subscale, service members with TBI and comorbid TBI will likely report more symptoms than those with PTSD-symptoms-only whereas on the affective subscale, service members with PTSD-symptoms-only and comorbid TBI and PTSD will likely endorse more symptoms than those with TBI alone.

IMPLICATIONS

Our results draw attention to the complex comorbidity of TBI and PTSD and indicate there is something particularly impactful regarding the combination of these often co-occurring conditions on both cognitive performance and social functioning. The present study additionally highlights the idea that self-reported neurobehavioral symptoms are key to understanding functional outcomes of service members with clinically significant levels of TBI and/or PTSD symptoms.

There are several broad implications for our findings. As clinicians and policy makers debate the best healthcare strategies for active duty service members with TBI and PTSD, attention to the management of the co-occurring symptoms as well as the perceived experience of more severe neurobehavioral symptoms is important. From a clinical perspective, understanding the complexity of this relationship is of utmost significance. In working with active duty military personnel who endorse symptoms of TBI and PTSD, providers should take into account individuals may have more cognitive difficulties and should consider how these difficulties might affect the planned course of treatment. It will also be important for mental health clinicians to recognize and emphasize the overlap between PTSD and TBI in order to help patients better understand their difficulties. Furthermore, prioritizing concurrent, collaborative care that allows for

consultation among various disciplines (e.g. polytrauma, neurology, mental health) will lead to better coordinated and more robust care strategies.

Additionally, patients exposed to trauma often present to their providers with cognitive complaints, yet providers may find interpreting patient self-reports challenging due to concerns of biases and irregularities (Samuelson et al., 2017). Patients with comorbid TBI and PTSD may also know of the effects their injury or condition can have on the brain and its functioning and so they may be particularly aware of any perceived subsequent difficulties. However, results of the present study indicate neurobehavioral symptoms are an important mechanism that influences social functioning and thus attending to these complaints and self-reports are indeed an important aspect of treatment. It is especially pertinent that providers also remain cognizant of the significant influence subjective complaints can have on a patient's social functioning, in addition to reports of emotional distress.

There may be a tendency of patients with comorbid TBI and PTSD to attribute their cognitive complaints, or other somatic difficulties, to TBI rather than PTSD due to both societal and self-stigma surrounding psychological illnesses. Some research has examined the stigma stemming from psychological illness versus a physical illness and have noted a diagnosis of a physical condition carries with it less stigma (Britt, 2000). Typically, individuals with psychological disorders are viewed as more responsible for their difficulties than are those with physical illnesses. With this responsibility comes a perception of controllability (Corrigan et al., 2001; Weiner, Perry, & Magnusson, 1988). Thus, individuals with physical illnesses are viewed by others with more empathy or pity and less anger than those with psychological disorders (Corrigan, 2000). It has further

been suggested that individuals who assign their symptoms to a physical, medical, or biological etiology have more satisfaction in their interpersonal relationships and overall quality of life compared to those who attribute symptoms to a psychological condition. These individuals may not only believe they should have more control over their symptoms than those with a physical condition, but also may be the recipient of more social stigma (Mechanic, McAlpince, Rosenfield, & Davis, 1994). In the context of the results of the current study, it could be that initially targeting neurobehavioral complaints, rather than emotional symptoms, may offer a "way in" to treating individuals who are hesitant to engage in mental health treatment. In other words, treating subjective complaints that could be attributed to a physical cause, such as dizziness or nausea, could offer a less-stigmatized way for individuals to engage with mental health treatment. However, while it is important to keep this presentation in mind when assessing and treating individuals with comorbid TBI and PTSD, it is imperative to note it has been suggested that clinicians who incorrectly attributing PTSD symptoms to TBI can stymie patients' progress by decreasing expectation for recovery (Bryant, 2011). Because of the complexity of the comorbidity of TBI and PTSD, maintaining caution when concluding certain symptoms stem from brain injury versus other causes is encouraged (Howe, 2009).

The present results may also have important therapeutic considerations. Findings highlight the potential importance of challenging certain cognitions and specifically helping patients with TBI and PTSD assess and examine the validity of self-reported neurobehavioral symptoms. In the way that clinicians focus on challenging negative cognitions about the self and the world in treating patients with depression, clinicians

should intentionally target negative self-appraisals about cognitive functioning in treating patients with TBI and PTSD. This may be a valuable part of achieving better social functioning - the goal of most therapeutic interventions. Treatment for TBI and PTSD focused on managing subjective neurobehavioral difficulties could have broad effects on patients' perceived functioning in social/community domains.

The present results also have several important theoretical implications to our understanding of TBI and PTSD. First, these findings provide support for the idea that emotional distress could be particularly influential in regards to the long-term impact of TBI among military personnel. Our results indicate that service members who sustained a TBI and were also reporting PTSD symptoms perform worse cognitively than either condition alone. It could be reasoned that the combination of emotional distress and physical symptoms may increase cognitive difficulties.

Additionally, our results may add to the theory of why military-related TBIs appear to be different from sports-related concussions and why service members may have a more difficult recovery. TBI and PTSD both stem from trauma exposure, whether that be a physical assault to the brain or psychological. However, in the case of military-related TBI, which are often sustained in combat or through blast exposure, the event is not only physically traumatic, but also psychologically traumatic. These events can be overlapping or coexisting. Of course, this does not mean that PTSD symptoms in a military population are always related to the same event that led to a TBI - it is well known that most service members have experienced multiple traumas during deployments before and after the TBI-causing event (Belanger, Uomoto, & Vanderploeg, 2009). However, we do know PTSD and TBI both impact (and likely interact) symptom

presentation and social functioning. If TBIs among service members are most often incurred during traumatic events, then emotional distress may exacerbate symptoms and lead to a more challenging recovery.

LIMITATIONS

Several limitations in the present study should be discussed. First, the study was a retrospective case review that examined data previously collected as part of a larger clinical assessment project. Thus, we faced certain constraints, such as using pre-selected measures for our variables. This also created a reliance on primarily self-report measures, which may be particularly vulnerable to under- or over-reporting, self-serving biases, or lack of agreement between different raters (Warnecke et al., 1997).

Second, it is important to note that the sample used in this study was not representative of the general population. This sample was composed of treatment-seeking patients who appear to have more emotional, cognitive, and neurobehavioral complaints than the general or larger military population. Additionally, we intentionally sought to study active duty service members who were receiving treatment for cognitive difficulties and therefore results may be difficult to generalize accurately to civilians, veterans, reservists, or National Guardsmen. The sample also consisted of primarily members of the Army (over 50% of the sample for all three aims) and thus may not be completely generalizable across branches. However, the majority of military TBI patients are soldiers (Defense Veterans and Brain Injury, 2018b) due to both the higher number of individuals deployed as well as the higher rate of exposure to combat and other hazardous settings (Jaffee, 2009). In fact, between January 2000 and April 2018 soldiers comprised nearly

60% of the total TBI cases in the MHS (Defense and Veterans Brain Injury Center, 2018a).

Finally, we used cut-off scores for PTSD symptoms rather than a clinical diagnosis of PTSD made by a healthcare provider. As previously discussed, we specifically employed a cut score of 35 or greater on the PCL-C to indicate significant levels of PTSD symptoms. While in line with previous research and the VA National Center for PTSD guidelines, other research studies have used and recommended various other cut-off scores to indicate a probable diagnosis of PTSD (e.g. Weathers et al., 1993; Forbes, Creamer, & Biddle, 2001; Yeager, Magruder, Knapp, Nicholas, & Frueh, 2007). Thus, we cannot conclusively say that participants in our sample had a diagnosis of PTSD as the PCL-C does not yield clinical diagnoses

STRENGTHS

Despite its limitations, the present study represents a significant addition to the growing literature on TBI and PTSD. To our knowledge, this is the first study to use a diverse sample of treatment-seeking active duty service members to examine how the comorbid effects of TBI and PTSD in the postacute *and* chronic phases impact cognitive performance. The only other study to examine the specific effect of comorbid TBI and PTSD on cognitive performance employed a sample of only male US Army soldiers who recently returned from deployment and were not necessarily experiencing cognitive difficulties (Betthauser et al., 2018) and were not treatment-seeking patients. Different than previous studies, we included 60 women in Aim 1 and 26 women in Aims 2 and 3. We also included service members who may or may not have physical or behavioral health problems that could preclude them from normal duty status. Additionally,

participants in the study did not necessarily recently return from a deployment and were not excluded if they had deployed to GWOT-related locations other than Iraq and Afghanistan. The sample was not limited to injuries directly related to a deployment or military service in general.

Of the service members with TBI in our sample, the majority of them had a diagnosis of mTBI. We believe that including mild, moderate, and severe levels of TBI diagnoses represents a strength of our study as much of the existing research has only examined mTBIs, and as such have excluded a significant minority of individuals. Although we were not able to analyze the effect of TBI severity due to the small number of participants with moderate and severe levels of TBI severity, we believe their inclusion in our study broadens the implications of our findings. The inclusion of these individuals also allows for the better generalization of the results to an actual population of active duty service members seeking care.

Finally, the study employed several well-validated and commonly used measures of cognitive performance, PTSD symptoms, neurobehavioral symptoms, and social functioning. The use of self-reports is also directly relatable to clinical care as many clinicians employ these in treatment plans and assessments. However, in addition to these self-reports, we used an objective measure to assess cognitive performance specifically designed to assess TBI-related cognitive changes and has been routinely utilized by the military and MHS.

CONCLUSION

The current study contributes to the growing literature on the overlap between TBI and PTSD. These findings suggest that service members with comorbid TBI and

PTSD will have more difficulty with cognitive performance (e.g. memory, attention, concentration, etc.) than those with either condition alone. Additionally, subjective neurobehavioral symptoms appear to be especially pertinent in understanding how emotional distress decreases social functioning

Table 1. Aim 1 Sample Demographics

	TBI-Only (N = 55)	PTSD-Only (N = 66)	Comorbid (N = 90)	Total Sample (N = 211)
Mean Age (Years)	33.6	35.6	34.4	34.5
Gender				
Male	44	33	74	151 (71.6%)
Female	11	33	16	60 (28.4%)
Branch				
USA	27	35	53	115 (54.5%)
USN	10	18	14	42 (19.9%)
USMC	8	5	18	31 (14.7%)
USAF	9	7	4	20 (9.5%)
USPHS	0	1	1	2 (.9%)
USCG	1	0	0	1 (.5%)
Rank				
Enlisted	41	51	66	158 (74.8%)
WO or Officers	13	15	21	49 (23.2%)
Other	--	--	4	4 (.1%)

Table 2. Aims 2 and 3 Sample Demographics

	TBI-Only (N = 18)	PTSD-Only (N =21)	Comorbid (N = 32)	Total Sample (N = 71)
Mean Age (Years)	36.9	37.0	35.0	36.1
Gender				
Male	11	8	26	45 (63.4%)
Female	7	13	6	26 (36.6%)
Branch				
USA	10	11	21	42 (59.2%)
USN	4	5	5	14 (19.7%)
USMC	1	1	3	5 (7.0%)
USAF	3	4	2	9 (12.7%)
USPHS	0	0	1	1 (1.4%)
USCG	0	0	0	0 (0%)
Rank				
Enlisted	14	13	22	49 (69%)
WO or Officers	4	8	10	22 (31%)
Other	--	--	--	0 (0%)

Table 3. ANAM Subtests and Cognitive Functions Targeted

ANAM Subtest	Functions Targeted
Simple Reaction Time (SRT)	Attention and visuomotor response timing
Code Substitution – Learning (CDS)	Complex scanning, visual tracking, and attention
Procedural Reaction Time (PRO)	Reaction time and processing efficiency
Mathematical Processing (MTH)	Basic computational skills, concentration, and working memory
Matching to Sample (M2S)	Spatial processing and visuospatial working memory
Code Substitution – Delayed (CDD)	Learning and delayed visual recognition memory
Simple Reaction Time – Repeated (SR2)	Attention, visuomotor response timing, and fatigue

Table 4. Means, standard deviations, and zero-order correlation matrix (N = 71)

Variable	*M*	*SD*	Participation Index	PCL-C	NSI	ACS
Participation Index	8.86	5.93				
PCL-C	47.75	17.68	.510***			
NSI	34.79	15.70	.595***	.783***		
ACS	-2.74	2.78	-.163	-.199*	-.296**	

Note: M and *SD* are used to represent mean and standard deviation, respectively. Participation Index is the total score on the Participation Index of the Mayo-Portland Inventory, PCL-C is the total score on the Posttraumatic Stress Disorder Checklist-Civilian version, NSI is the total score on the Neurobehavioral Symptom Inventory, and ACS is the ANAM Composite Score.
* Indicates $p < .05$; ** indicates $p < .01$; *** indicates $p < .001$

Table 5. Summary of Multiple Regression Analysis for Social Functioning

Variable	*B*	*SE(B)*	*β*	*t*	*p*
(Constant)	.414	1.690	--	.245	.807
Total NSI Score	.193	.061	.510	2.152	.002
ACS	.022	.219	.010	.100	.921
Total PCL Score	.038	.053	.113	.717	.476

Note: N = 71; R^2 = .359

Criteria	Mild	Moderate	Severe
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of Consciousness (LOC)	0–30 min	> 30 min and < 24 hrs	> 24 hrs
Alteration of consciousness/mental state (AOC) *	a moment up to 24 hrs	> 24 hours. Severity based on other criteria	
Post-traumatic amnesia (PTA)	0–1 day	> 1 and < 7 days	> 7 days
Glasgow Coma Scale (best available score in first 24 hours)	13-15	9-12	< 9

Figure 1. VA and DoD Traumatic Brain Injury Severity Criteria. *Alteration of mental status must be immediately related to the trauma to the head. Typical symptoms would be: looking and feeling dazed and uncertain of what is happening, confusion, difficulty thinking clearly or responding appropriately to mental status questions, and being unable to describe events immediately before or after the trauma event. Adapted from "VA/DoD Clinical Practice Guideline for Management of Concussion/Mild Traumatic Brain Injury" by the Department of Veterans Affairs and the Department of Defense, 2016.

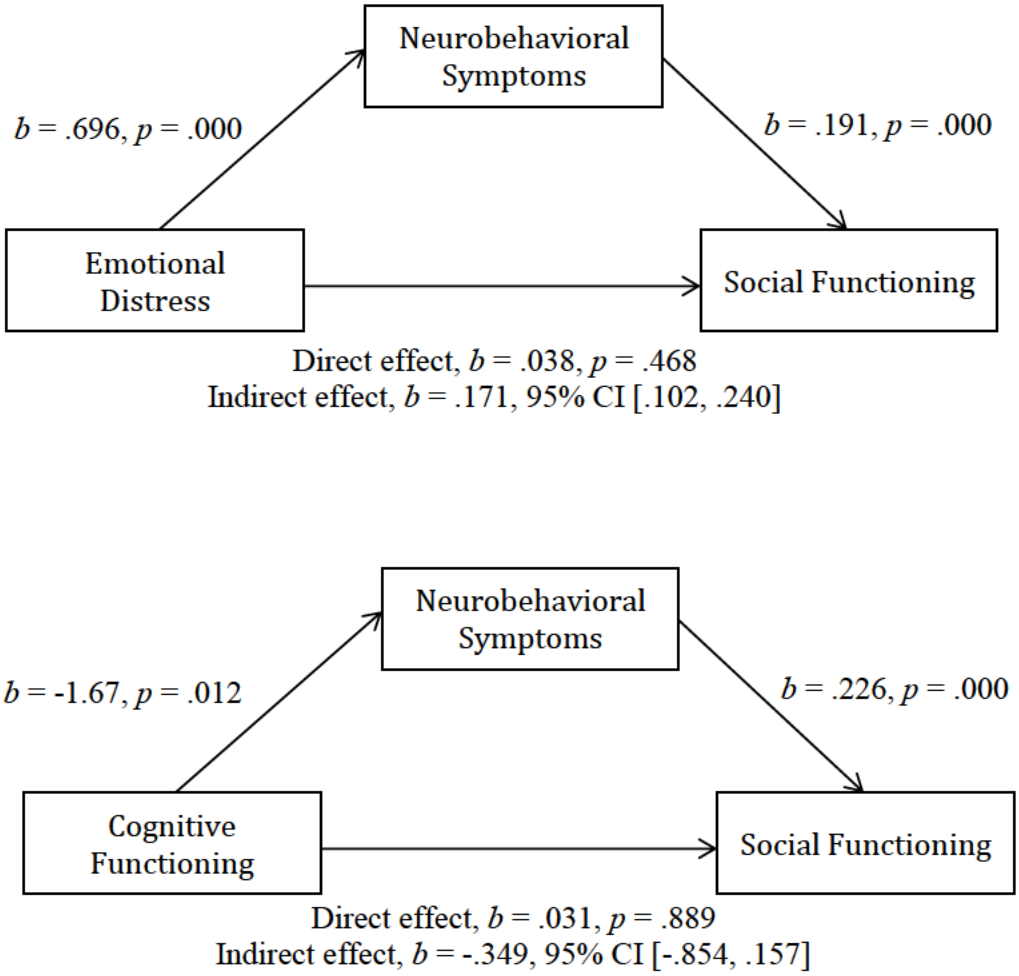

Figure 2. Mediation model results of Aim 3.

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