THE EFFECT OF TRAUMATIC BRAIN INJURY ON EXPOSURE THERAPY IN VETERANS WITH COMBAT-RELATED POSTTRAUMATIC STRESS DISORDER

by

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ABSTRACT

Veterans of Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn are presenting for treatment with high rates of combat-related posttraumatic stress disorder (PTSD) and traumatic brain injury (TBI), spurring a need for clinical research on optimal treatment strategies. While exposure therapy has long been supported as an efficacious treatment for combat-related PTSD, some clinicians are hesitant to utilize this treatment for veterans with TBI history due to presumed cognitive deficits that may preclude successful engagement. The purpose of this study was to compare exposure therapy process variables in veterans with PTSD only and veterans with PTSD+TBI. Results suggest that individuals with PTSD+TBI engage successfully in exposure therapy, and do so no differently than individuals with PTSD only. Additional analyses indicated that regardless of TBI status, more severe PTSD was related to longer sessions, more sessions, and slower extinction rate during imaginal exposure. Finally, in a subset of participants, self-report of executive dysfunction did not impact exposure therapy process variables. Overall, findings indicate that exposure therapy should be the first-line treatment for combat-related PTSD regardless of presence of TBI history.

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CHAPTER ONE: INTRODUCTION

Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) present a unique and urgent healthcare challenge: the assessment and treatment of war related diseases and disorders. High rates of combat-related posttraumatic stress disorder (PTSD) and traumatic brain injury (TBI) have appeared in an unprecedented number of war fighters, spurring a need for clinical research and treatment. While advances in military protective gear and medical care have resulted in increasing rates of survival, these advances have also led to the development of higher rates of PTSD and mild traumatic brain injury (mTBI) (McNally & Frueh, 2013; Shively & Perl, 2012; Vasterling, Verfaellie, & Sullivan, 2009). In particular, a number of individuals have returned from these conflicts with both PTSD and a history of TBI, making it increasingly necessary to understand these clinical conditions and specifically, how their co-occurrence may impact symptom presentation and treatment outcome.

Posttraumatic Stress Disorder

PTSD represents a cluster of symptoms that occurs as a result of exposure to a traumatic event in which the person is exposed to actual or threatened death, serious injury, or threat to physical integrity of self or others (American Psychiatric Association [APA], 2013). Many different traumatic events can lead to the onset of PTSD (e.g., sexual assault, natural disasters, and physical attack) and the disorder occurs in both civilian and military populations. Ensuing symptoms are classified into four symptom clusters which include intrusion (e.g., flashbacks and intrusive memories), avoidance (e.g., avoidance of thoughts and feelings associated with the traumatic event), negative alterations in cognitions and mood (e.g., restricted range of affect), and alterations in arousal and reactivity (e.g., irritability and hypervigilance). Although the

community-based lifetime prevalence for PTSD in United States adults is approximately 6% (Pietrzak, Goldstein, Southwick, & Grant, 2011), rates vary considerably by sample (APA, 2013). Military combat populations yield some of the highest rates of PTSD (APA, 2013), likely due in part to exposure to traumatic events encountered in the combat arena. Since 2002, nearly 312,000 veterans have received diagnoses of PTSD through the Department of Veterans Affairs (VA; Veterans Affairs, 2014). However, this sample may be conservatively biased as it consists of honorably discharged veterans seeking healthcare at the VA and does not include active duty military personnel, VA Vet Center veterans, individuals initially diagnosed with other disorders (e.g., acute stress disorder), or those not enrolled or entitled to VA health care. Thus, the prevalence of PTSD in OEF/OIF/OND service members varies widely due to discrepant assessment measures and military populations, with estimates ranging from 2.2 to 17.3% (Hermann, Shiner, & Friedman, 2012). However, best estimates are closer to 8% (Richardson, Frueh, & Acierno, 2010; Smith et al., 2008).

Combat-related PTSD can lead to significant impairment in functioning and considerable distress. In a recent review, PTSD in OEF/OIF veterans was related to homelessness, unemployment, lower work functioning, higher levels of self-reported impairment in work, home, and interpersonal relationships, poorer role functioning due to physical and emotional problems, increased psychosocial difficulties, reduced marital satisfaction, and reduced overall life satisfaction (Schnurr, Lunney, Bovin, & Marx, 2009). Combat-related PTSD not only accrues significant personal cost, but also represents a significant healthcare cost. Among nearly 250,000 OIF/OEF veterans accessing VA healthcare between 2001 and 2007, utilization of both inpatient and outpatient medical care was higher for veterans with PTSD compared to veterans with other psychiatric diagnoses, with rates twice as high for veterans with PTSD compared to

veterans with no psychiatric diagnosis (Cohen et al., 2010). Clearly, combat-related PTSD results in significant personal, societal, and healthcare costs, thereby emphasizing the need for efficacious treatments.

Treatment for Posttraumatic Stress Disorder

Cognitive-behavioral therapy (CBT) is a well-accepted and empirically supported treatment for anxiety disorders (Chambless & Ollendick, 2001; Deacon & Abramowitz, 2004; Norton & Price, 2007) including PTSD (Bradley, Greene, Russ, Dutra, & Westen, 2005; Sherman, 1998; Van Etten & Taylor, 1998). A recent review of randomized controlled trials suggests that trauma-focused CBT, or repeated exposure and/or cognitive restructuring, is an efficacious and specific treatment for PTSD (Ponniah & Hollon, 2009). Exposure therapy is a procedure whereby the individual is placed in contact (either through imagination or real life) with the anxiety provoking stimuli in a controlled, clinician assisted manner. The goal of exposure is habituation, or a consistent decline in behavioral, physiological, and psychological responses, and thus extinction of anxiety. In contrast, cognitive restructuring focuses more specifically on challenging and modifying maladaptive cognitions associated with the trauma. The addition of cognitive restructuring does not appear to enhance treatment outcome over and above the exposure component alone (Foa et al., 2005; Marks, Lovell, Noshirvani, Livanous, & Threasher, 1998; Paunovic & Öst, 2001).

The theory behind the mechanism of action for exposure therapy is that exposure weakens the conditioned fear response associated with the trauma, thus allowing new learning (i.e., extinction learning) to occur (Foa, 2011; Foa, Steketee, & Rothbaum, 1989). This learning is achieved through systematic, controlled exposure to the trauma cues associated with the original traumatic event, which activates the fear complex (Foa & Kozak, 1986). As the patient

engages in exposure to the traumatic cues without the subsequent negative event, habituation occurs and new neural associations are formed. In in-vivo (real life) exposures, similar habituation and new learning occurs in response to associated stimuli. Simply, repeated presentation of traumatic cues without the traumatic outcome allows habituation and learning to occur, which leads to extinction of the anxiety/fear response.

Extant literature has also provided support for efficacious treatment for combat-related PTSD specifically (Frueh, Turner, & Beidel, 1995), with exposure based treatments proving to be the most effective (Goodson et al., 2011). In fact, the Institute of Medicine (IOM) reported exposure therapy was the only treatment with sufficient evidence to conclude its efficacy for combat-related PTSD treatment (IOM, 2007). One such treatment developed specifically for combat-related PTSD is Trauma Management Therapy (TMT), a multicomponent behavioral treatment utilizing exposure therapy (Frueh, Turner, Beidel, Mirabella, & Jones, 1996; Turner, Beidel, & Frueh, 2005). In fact, a recent randomized controlled trial of TMT demonstrated its efficacy for Vietnam-era combat veterans with chronic PTSD (Beidel, Frueh, Uhde, Wong, & Mentrikoski, 2011), and a similar trial with OEF/OIF veterans is underway, which provided the treatment sample examined in the current study.

Traumatic Brain Injury

Although combat-related PTSD is a significant healthcare concern, TBI has been coined the "signature injury" of the Afghanistan and Iraq wars. TBI is defined by either a penetrating or closed head injury that results in temporary or permanent neurological dysfunction (Marshall et al., 2012) and may result from a foreign object penetrating the brain (i.e., penetrating head injury), blunt force trauma, acceleration or deceleration of the brain, or blast injury (Department of Veterans Affairs and Department of Defense, 2009). Immediate resulting neurological

dysfunction can include loss or decreased level of consciousness, memory loss before or after the injury, alteration in mental status (e.g., slowed thinking, confusion, or disorientation), neurological deficits (e.g., weakness, change in vision, loss of balance), and/or brain lesions (Department of Veterans Affairs and Department of Defense, 2009).

TBI severity classifications range from mild to severe based on the length of time of the resulting dysfunction. According to the Department of Defense (2014), mTBI is defined by confusion or disorientation for less than 24 hours, loss of consciousness for up to 30 minutes, memory loss for less than 24 hours, and normal structural brain imaging. Moderate TBI is defined by confusion or disorientation for more than 24 hours, loss of consciousness for more than 30 minutes, memory loss greater than 24 hours but not more than seven days, and normal or abnormal structural brain imaging. Severe TBI is defined by confusion or disorientation for more than 24 hours, loss of consciousness for more than 24 hours, memory loss for more than seven days, and normal or abnormal structural brain imaging. Approximately 75% of all TBI cases are mild (Lu, Gary, Neimeier, Ward, & Lapane, 2012), with a similar prevalence rate found for the United States military population (77%; Marshall et al., 2012).

It is important to note that TBI is a historical event defined by the injury sustained. The resulting postconcussive symptoms (PCS) are defined as self-reported somatic, cognitive, and affective symptoms occurring post injury (Morissette et al., 2011) and can significantly vary between individuals (Hoge et al., 2008; Riggio & Wong, 2009). PCS of mTBI can include headaches, poor sleep, dizziness, balance problems, irritability, and concentration, and memory difficulties (Hoge et al., 2008; Shively & Perl, 2012).

A review of meta-analytic studies supports the presence of impaired cognitive abilities during the acute phase of an mTBI (i.e., within three months of the injury); however, a debate

exists regarding permanent or chronic effects (Ruff, 2011). Nonetheless, a portion of individuals with mTBI do experience symptom persistence three months post injury (Belanger, Curtiss, Demery, Lebowitz, & Vanderploeg, 2005). Further, research indicates that individuals with TBI present with more severe PTSD symptoms than individuals without a history of TBI (Barnes, Walter, & Chard, 2012; Davis, Walter, Chard, Parkinson, & Houston, 2013; Ragsdale, Neer, Beidel, Frueh, & Stout, 2013), suggesting that the historical event of the brain injury alone may in fact influence psychological functioning long term.

Treatment for Traumatic Brain Injury

Once patients are medically stabilized, treatment of TBI transitions to restoration of functioning (Lu et al., 2012), which may include psychological, educational, supportive, and pharmacological interventions. Systematic reviews of psychological (e.g., education and cognitive rehabilitation) treatments for mTBI suggest that educational interventions may be somewhat helpful if provided early; however, authors emphasize poor research methodology of available studies and a general lack of methodological rigor (Borg et al., 2004; Comper, Bisschop, Carnide, & Tricco, 2005; Snell, Surgenor, Hay-Smith, & Siegert, 2009). Within the military, treatment of mTBI is centered on symptom management, patient education, rest, and recovery (Marshall et al., 2012), with a focus on treatment of symptoms regardless of their etiology (Brenner, Vanderploeg, & Terrio, 2009).

Posttraumatic Stress Disorder with a History of TBI

Veterans with a history of TBI have higher rates of PTSD compared to veterans without a history of TBI (Carlson et al., 2010; Carlson et al., 2011; Hoge et al., 2008; Morissette et al., 2011; Walker, Clark, & Sanders, 2010). Comorbidity rates of probable PTSD and probable mTBI among Iraq and Afghanistan veterans range from 33% to 39% (Carlson et al., 2011). In

addition, veterans suffering from PTSD who have a history of mTBI endorse significantly more severe PTSD symptoms than those with PTSD alone (Barnes et al., 2012; Davis et al., 2013; Ragsdale at al., 2013), and the increased PTSD severity appears to negatively affect the clinical presentation, leading to higher overall anxiety and more functional limitations (Ragsdale et al., 2013). Finally, although the presence of TBI quadruples the median annual medical cost for veterans, the addition of PTSD results in even further increases in the cost medical care (Taylor et al., 2012).

Treatment for Posttraumatic Stress Disorder with a History Traumatic Brain Injury

Clearly, veterans of OIF/OEF/OND are presenting with high rates of PTSD with a history of TBI, forcing treatment of this complex condition to the forefront of clinical practice. Although well supported for the treatment of PTSD, some clinicians are hesitant to use exposure therapy with individuals who report a history of TBI due to concerns of cognitive impairment (Sripada et al., 2013). Indeed, the ability to recall and cognitively process the traumatic event is central to exposure therapy, as its repeated presentation allows for habituation, new learning, and extinction of the anxiety/fear response. As such, factors associated with TBI that could impede fear activation, such as memory difficulties (i.e., difficulty retrieving and/or holding and processing the memory), poor concentration (i.e., difficulty sustaining attention to imaginal aspects of the exposure), and/or damage to brain structures involved in the process of extinction learning could theoretically inhibit effective implementation, which could consequently reduce efficacy.

The amygdala, hippocampus, and ventromedial prefrontal cortex (vmPFC) are involved in both fear conditioning and extinction (Moustafa et al., 2013). If damaged by TBI, any impaired functioning could negatively impact treatment success. For example, both lesions and

compromised functions in these brain structures impair fear extinction in animals (Moustafa et al., 2013). Particularly, lesioning intercalated amygdala neurons (Likhtik, Popa, Apergis-Schoute, Fidacardo, & Paré, 2008), inactivation of the dorsal hippocampus (Corcoran & Maren, 2001), and lesioning of the ventral prelimbic cortex and the infralimbic cortex of the vmPFC in rats (Quirk, Russo, Barron, & Lebron, 2000) impair extinction learning, which in turn could attenuate the impact of exposure therapy.

Unfortunately, brain injuries sustained as a result of TBI are heterogeneous in nature due to the various locations and mechanisms of injury (e.g., penetrating head injury, blunt force trauma, acceleration or deceleration of the brain, and blast injury; Department of Veterans Affairs and Department of Defense, 2009), which makes it difficult to precisely locate brain injury or disruption. Further, mTBI is defined by normal structural brain imaging (Department of Defense, 2014), precluding study of potentially affected brain regions. Therefore, examining the extinction process that occurs during exposure therapy (through measures of fear activation and habituation) may be one of the few means by which to elucidate how mTBI may affect the process of extinction learning.

Recent research has begun to investigate the feasibility and outcome of cognitive behavioral therapies (e.g., prolonged exposure [PE] and cognitive processing therapy [CPT]) in samples of veterans suffering from PTSD with a history of TBI (Chard, Schumm, McIlvain, Bailey, & Parkinson, 2011; Sripada et al., 2013; Walter, Barnes, & Chard, 2012; Walter, Kiefer, & Chard, 2012; Wolf, Strom, Kehle, & Eftekhari, 2012). Several studies (Chard et al., 2011; Walter et al., 2012a, 2012b) have examined seven and eight week Veterans Administration PTSD/TBI residential programs incorporating modified CPT (CPT-C; Resick, Nishith, Weaver, Astin & Feuer, 2002) via manualized group and individual treatment (Chard, Resick, Monson, &

Kattar, 2008). These residential treatment programs also incorporated various individual speech and cognitive therapies, attention training, and psychoeducational groups (e.g., distress tolerance, cognitive enhancement, and anger management). Unfortunately, various methodological limitations in these studies preclude conclusions that would inform the current study. Samples were heterogeneous in nature (e.g., various wars and combat arenas [e.g., Vietnam]) (Chard et al., 2011; Sripada et al., 2013; Walter et al., 2012a; Walter et al., 2012b) and included non-combat related psychological and physical traumas [e.g., sports injuries] (Chard et al., 2011), which preclude conclusion or generalization specific to combat TBIs and combat PTSD. Additionally, and arguably most importantly, conclusions cannot be drawn regarding the effectiveness of CBT for individuals with TBI, as the multifaceted treatment programs (Chard et al., 2011; Walter et al., 2012a, 2012b) obscured the ability to examine the efficacy of any individual treatment component.

With specific regard to prolonged exposure therapy, two studies have investigated its feasibility for individuals with PTSD and a history of TBI; however, studies again suffer from methodological limitations. First, Wolf and colleagues (2012) examined an open trial of PE treatment in OEF/OIF veterans with chronic PTSD and a history of mild to moderate TBI; however, sample size was small (N = 10) and no control group was used. Similarly, Sripada and colleagues (2013) examined PE in 40 veterans with PTSD only and 11 veterans with PTSD and history of TBI. Unfortunately, the heterogeneous sample (only 32% of the sample served in Afghanistan or Iraq) and the few participants with TBI blunted the statistical power necessary to detect group differences.

To summarize, the small body of literature examining CBT for individuals with PTSD and history of TBI suffers from serious methodological limitations including limited power,

small sample size, lack of control groups, and treatment confounds. In particular, extant literature is currently lacking a large homogenous sample of OEF/OIF/OND veterans with combat-related PTSD and a history of combat-related TBI. Therefore, examination of the feasibility and impact of exposure therapy in a carefully diagnosed sample of OEF/OIF/OND veterans suffering from combat-related PTSD with and without history of TBI is warranted.

Given that veterans with PTSD and a history of mTBI endorse significantly more severe PTSD symptoms than those with PTSD alone (Barnes et al., 2012; Davis et al., 2013; Ragsdale et al., 2013), it is crucial to ensure that this population can successfully engage in exposure therapy. The purpose of this study was to examine the potential impact of TBI history on exposure therapy for combat-related PTSD using a carefully diagnosed sample of OEF/OIF veterans. The following hypotheses were tested:

1. Individuals with PTSD and history of TBI will demonstrate significantly higher fear activation compared to individuals with PTSD only.
2. Individuals with PTSD and history of TBI will show significantly longer session times compared to individuals with PTSD only, as individuals experiencing higher fear activation will likely require longer times to habituate within a treatment session.
3. Individuals with PTSD and history of TBI will require more exposure sessions compared to individuals with PTSD only, as higher fear activation and longer session times will likely require a greater number of sessions to achieve overall extinction.
4. Individuals with PTSD and history of TBI will be less likely to achieve overall extinction within a 14-session treatment protocol. Although between-session habituation is considered the indication of positive treatment outcome, some individuals may not achieve overall habituation after a prescribed number of sessions.

5. Individuals with PTSD and history of TBI will evidence slower extinction rate, or change in slope of peak subjective distress, across sessions when compared to individuals with PTSD only.

CHAPTER TWO: METHOD

The treatment study from which these data were extracted is an ongoing randomized controlled trial comparing individual exposure therapy to individual exposure therapy plus group therapy for combat-related PTSD. The study is located at two sites: the University of Central Florida and the Medical University of South Carolina/Ralph Johnson Veterans Affairs Medical Center. All procedures were approved by the Institutional Review Boards at UCF or MUSC, as well as the United States Army Institutional Review Board.

Participants

Participant recruitment consisted of advertising through clinician referral, radio, various websites, and public events, and in the case of MUSC, through the PTSD clinic at the Ralph Johnson VAMC in Charleston, South Carolina. The sample consisted of treatment seeking individuals with combat-related PTSD who had served in Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF). All participants included in the current study completed the individual exposure therapy component of the clinical trial. Ninety-three participants (90.3% male) with a mean age of 36.27 (*SD* = 9.60; range = 23–63) were included (UCF; N = 84; MUSC; N = 9). There were no differences on any demographic variable between the two sites.

The sample was 61.3% Caucasian, 21.5% Hispanic/Latino, 11.8% African American, 2.2% Asian/Pacific Islander, 1.1% Indian subcontinent, and 2.2% “other”. With regard to marital status, 47.3% were married, 28% were single, 15.1% were divorced, and 9.7% were separated. With regard to education, 17.2% of participants completed high school only, 57% completed some college, 20.4% had earned a Bachelor’s degree, and 5.4% had earned a Master’s degree.

The majority of the sample served in the Army (69.9%), followed by the Marine Corps (18.3%), Air Force (7.5%), Navy (3.2%) and as a Civilian Contractor (1.1%).

All participants met the Diagnostic and Statistical Manual of Mental Disorders (4th ed., Rev.; DSM-IV-TR; American Psychiatric Association, 2000) criteria for PTSD as assessed by the Clinician Administered PTSD Scale (CAPS; Blake et al., 1995). Symptom scores for the three DSM-IV criterion clusters (Criterion B: Reexperiencing, Criterion C: Avoidance and Numbing, and Criterion D: Hyperarousal) are derived by summing the frequency and intensity scores for relevant individual items. Summing the subscale scores provides overall frequency, intensity, and total PTSD scores. The CAPS has excellent reliability, convergent and discriminant validity, diagnostic utility, and sensitivity to clinical change (Weathers, Keane, & Davidson, 2001). The CAPS was administered by licensed clinical psychologists, post-doctoral fellows, masters level clinicians or supervised senior doctoral students. Ten percent of interviews were randomly selected and scored by a blinded clinician for inter-relater reliability (total score ICC = .969; PTSD diagnosis $\kappa = 1.00$).

Traumatic Brain Injury Validation Procedure

During the initial diagnostic interview for the treatment study, TBI status was determined by simple self-report (i.e., "Were you ever diagnosed with a TBI?"). To strengthen the validity of TBI status for the current investigation, we attempted to re-contact previously treated participants in order to conduct a more thorough assessment. Each participant was contacted a maximum of three times by telephone. Participants who were successfully contacted were interviewed using current TBI status criteria (listed below) (Department of Defense, 2014; Department of Veterans Affairs and Department of Defense, 2009).

1. Have you experienced a blow or jolt to the head such as the head being struck by, or striking, an object; acceleration or deceleration of the brain; blast or explosion injury; or object penetration of the brain? If so, following the head injury:
2. Did you experience any alteration in mental state at the time of the injury, such as confusion, disorientation, or slowed thinking?

    Note. Observed signs of neurological or neuropsychological dysfunction (e.g., headache, dizziness, or poor concentration) is not sufficient to make a diagnosis of TBI (i.e., these do not indicate a change in mental state) when loss of or altered consciousness is not present (Department of Veterans Affairs and Department of Defense, 2009).

3. Did you experience loss of or a decreased level of consciousness?
4. Did you experience memory loss for events immediately before or after the injury?

Participants who answered affirmatively to question one and at least one additional question are considered by these criteria to have experienced a TBI.

Of the 93 participants included in the current study, 46 (49%) completed the TBI validation. The other 47 participants were unable to be reached for a variety of reasons (e.g., they did not answer the phone or return the calls, had changed their phone number, or their voicemail was full or not set up). Of the 46 participants who completed the TBI validation protocol, 44 (96%) remained the same TBI status as determined by their original assessment, whereas two (4%) changed from a negative to a positive TBI status. These two participants reported being diagnosed with a concussion during the military, which, perhaps unknown to the participants, is synonymous with mTBI (Department of Veterans Affairs and Department of Defense, 2009).

Although unable to contact the entire sample, it appeared that the participants' initial self-reports of TBI history were valid, and that the re-querying did not add significant incremental validity. Therefore, with the exception of the two participants whose TBI status changed from negative to positive, participants' initial TBI statuses were utilized for all analyses.

Across the entire sample, 47% (N= 44) had a history of TBI. There were no significant TBI group differences on any demographic characteristics with the exception of age. Military personal with PTSD+TBI (M = 33.77, SD = 10.52) were significantly younger than those with PTSD only (M = 38.51, SD = 7.84), $t(88.08) = 2.48$, $p = .02$, a consistent finding in the literature (Carlson et al., 2010; Hoge et al., 2008; Ragsdale et al., 2013; Taylor et al., 2012).

Measures

Subjective Units of Distress Scale (SUDS)

Fear activation was determined using the Subjective Units of Distress Scale (SUDS), a self-report rating of the participant's subjective fear and anxiety. The scale ranged from 0 (none) to 8 (extreme) and were assessed every five minutes during exposure therapy. SUDS ratings are used to determine when within- and between-session habituation occurs. Specific treatment process variables examined in this study include initial fear activation, overall fear activation, within-session habituation, overall extinction (or between-session habituation), and extinction rate. Operational definitions are largely based on prior conceptualizations of these variables (Turner, Beidel, Long, & Greenhouse, 1992; Craske et al., 2008) and are presented below.

Initial fear activation was operationally defined as the change from the baseline SUDS to the peak SUDS during the first treatment session.

Overall fear activation was operationally defined as the change from the lowest SUDS to the peak SUDS (peak SUDS – lowest SUDS) across all sessions, which captured each individual's maximum increase in anxiety or fear as a result of the exposure.

Within-session habituation was operationally defined as a return to baseline SUDS, or at least a 50% reduction of fear activation (change from baseline SUDS to peak SUDS, during each individual session), and therefore was a dichotomous variable for each session.

Overall within-session habituation, the within-session habituation variable used for analysis purposes, was the percentage of sessions during which habituation occurred (total number of sessions which achieved habituation/total number of imaginal exposure sessions).

Overall extinction (or between-session habituation) was operationally defined by at least a 50% reduction from the first session peak SUDS to the final session peak SUDS (e.g., an initial peak SUDS of 8 and final peak SUDS of 4), and therefore, was a dichotomous variable.

Extinction rate was calculated by determining the slope of peak SUDS over time for each participant.

Finally, **total number of exposure sessions** and **average length of time of sessions** were examined.

Procedure

Following assessment, eligible participants initiated imaginal exposure therapy. The imaginal scene used for exposure was constructed during session 1 and was based on the individual's most severe trauma. At session 2, the clinician assisted the participant to imagine the traumatic event by reading the scene, inquiring about SUDS every five minutes. The exposure continued until the participant evidenced within-session habituation. During subsequent sessions, the participant verbalized the scene him or herself, which was again continued until the

participant evidenced within-session habitation. Throughout all exposures, the clinician continuously observed the participant's behaviors and inquired about physiological responses and cognitions to corroborate SUDS. The clinician's goal was to assist the participant in remaining in contact with the feared stimuli (i.e., the traumatic memory) until habituation occurred. Imaginal exposure was conducted for up to 14 sessions, but was terminated once the participant evidenced between-session habituation.

CHAPTER THREE: RESULTS

Preliminary Analyses

Continuous dependent variables were first examined for violations of normality. The Kolmogorov-Smirnov test indicated that extinction rate ($D = .18$, $p < .001$), overall fear activation ($D = .17$, $p < .001$), initial fear activation ($D = .15$, $p < .001$), and total number of sessions ($D = .18$, $p < .001$) deviated significantly from a normal distribution, whereas average session time ($D = .06$, $p = .20$) and pre-CAPS total score ($D = .06$, $p = .20$) did not. Attempts to normalize the relevant data using various transformations (e.g., log transformations) were unsuccessful. However, given the central limit theorem and the robustness of *t*-tests, groups were compared with both parametric (*t*-tests) and non-parametric (Mann-Whitney U) tests.

Analysis of univariate outliers revealed three statistical outliers. In each case, a participant's score on one standardized z-score exceeded three standard deviations from the mean of the dependent variable. Analysis of multivariate outliers revealed one statistical outlier (i.e., Mahalonobis distance value of 28.93 exceeded the critical value of 20.52) who was previously identified during analysis of univariate outliers. The three participants identified in these analyses were excluded from all future analyses, leading to a final sample size of 90 (PTSD only = 48, PTSD+TBI = 42).

Impact of TBI on Process of Exposure Therapy

Following preliminary analyses, groups were compared on exposure therapy process variables (initial and overall fear activation, average session time, total number of exposures sessions, extinction rate, and overall extinction). See Table 1 for results of all *t*- and Mann-Whitney U tests, interpreted below.

Initial Fear Activation

The implementation of imaginal exposure therapy requires participants to imagine and hold the traumatic event in memory. By doing so, fear associated with the traumatic event is elicited and perceived by the participant, suggesting the presence of fear activation. Fear activation during the initial treatment session (peak SUDS—lowest SUDS) was compared using an independent samples *t*-test. Results indicated that participants with PTSD+TBI (M = 2.55, SD = 1.53) experienced less fear activation than participants with PTSD only (M = 3.44, SD = 1.96, $t(88) = -2.38$, $p = .02$), which was supported by a Mann-Whitney U test ($p = .04$). It should be noted, however, that examination of peak and baseline SUDS revealed that participants with PTSD+TBI had significantly higher SUDS at baseline (M = 4.71, SD = 1.76) compared to participants with PTSD only (M = 3.90, SD = 1.92, $t(88) = 2.10$, $p = .04$ [Mann-Whitney-U p =.03]). Thus, the lesser activation in participants with PTSD+TBI most likely resulted from a ceiling effect, as SUDS contain a finite number of points. When controlling for baseline differences, a one-way analysis of covariance (ANCOVA) revealed that the two groups did not differ on initial fear activation, $F(1,87) = 1.16$, $p = .28$.

In contrast, the groups did not significantly differ on their peak SUDS rating in the first treatment session (PTSD+TBI [M = 7.26, SD = 0.91] versus PTSD only [M = 7.33, SD = 0.86], $t(88) = -0.38$, $p = .70$, [Mann-Whitney-U p =.70]), suggesting that individuals in both groups experienced a high level of distress when imagining the situation.

Overall Fear Activation

Because high levels of anticipatory anxiety are common in the first treatment sessions, fear activation can sometimes be attenuated. Another way to determine fear activation is to examine the baseline and peak SUDS regardless of the session in which it occurred. The results

of a *t*-test comparing differences in overall fear activation (overall peak SUDS – overall lowest SUDS) revealed no difference between participants with PTSD+TBI (M = 6.29, SD = 1.40) and participants with PTSD only (M = 6.50, SD = 1.27, $t(88) = -0.76$, $p = .45$), a finding supported by a Mann-Whitney U test ($p = .54$).

Length of Exposure Sessions

A *t*-test comparing the average treatment session time (in minutes) indicated that the groups were not significantly different, PTSD+TBI (M = 60.19, SD = 10.97) versus PTSD only (M = 63.10, SD = 9.67, $t(88) = -1.34$, $p = .18$). This finding was supported by a Mann-Whitney U test ($p = .17$).

Number of Sessions

The groups were not significantly different on the number of exposure sessions necessary for extinction (between-session habituation) to occur, PTSD+TBI (M = 10.64, SD = 2.95) versus PTSD only (M = 10.54, SD = 3.14, $t(88) = 0.16$, $p = .88$), a finding supported by a Mann-Whitney U test ($p = .87$).

Extinction Rate

To determine if participants with PTSD+TBI experienced a slower decline in anxiety during exposure sessions, the extinction rate (slope of peak SUDS) across sessions was compared using a *t*-test. There was no significant difference in extinction rate between participants with PTSD+TBI (M = -0.43, SD = 0.34) and participants with PTSD only (M = -0.49, SD = 0.31; $t(88) = 0.80$, $p = .43$). This finding was supported by a Mann-Whitney U test ($p = .30$). The average peak SUDS across all 14 sessions for both groups is depicted in Figure 1.

The treatment protocol dictated that achievement of between-session habituation via imaginal exposure should be followed by a change to in vivo exposure to address behavioral

avoidance. Thus, as some individuals did not require 14 exposure therapy sessions to achieve between-session habituation, the SUDS for the latter sessions depicted in Figure 1 may be inflated by the reduced number of participants remaining in the sample. As such, average peak SUDS were re-examined using each participant's peak SUDS reported during their initial, middle, and final imaginal exposure session (see Figure 2). Results indicated that the groups did not differ on initial peak SUDS (PTSD+TBI [M = 7.27, SD = 0.90] versus PTSD only [M = 7.33, SD = 0.86], $t(88) = -0.32$, $p = .75$), middle peak SUDS (PTSD+TBI [M = 5.98, SD = 1.48] versus PTSD only [M = 5.66, SD = 1.52], $t(88) = 1.03$, $p = .31$), or final peak SUDS (PTSD+TBI [M = 3.83, SD = 1.95] versus PTSD only [M = 3.17, SD = 1.81], $t(88) = 1.68$, $p = .10$)

Overall Extinction

Overall, 64.4% of all participants achieved overall extinction (N = 58); 35.6% did not (N = 32). A Chi-square analysis for independence (with Yate Continuity Correction) was used to determine if participants with PTSD+TBI achieved overall extinction comparable to participants with PTSD only. Results indicated no significant association between TBI status and overall extinction, $\chi^2(1, n = 90) = .06$, $p = .80$. Specifically, 67% of PTSD only and 62% of PTSD+TBI achieved overall extinction.

Exploratory Analyses

Although not part of formal hypothesis testing, the results above suggested additional data analysis that might inform future investigations. Exploratory analyses are presented here.

Overall within-session habituation

The treatment protocol required within-session habituation for session termination; however, post hoc analyses revealed that some sessions were terminated prior to the required criterion for extinction. Some sessions were terminated early for various reasons (e.g., unique or

unforeseen time constraints or sudden patient illness). Descriptive analyses revealed that 73.3% of participants (N = 66) habituated to all imaginal exposure sessions (i.e., achieved within-session habituation to every session). Remaining participants (N = 24) habituated to 57.1% - 92.86% of sessions.

Restricting the sample to participants who did not achieve within-session habituation across all sessions, participants with PTSD+TBI (M = 84.02, SD = 10.54) and participants with PTSD only (M = 77.49, SD = 10.16) did not differ on percentage of individual sessions during which within-session habituation occurred, $t(22) = 1.51$, $p = .15$.

Impact of Poor Executive Functioning on Process of Exposure Therapy

Inasmuch as the results above suggest that a diagnosis of TBI per se does not attenuate exposure therapy, exploratory analyses examined whether cognitive impairment (i.e., PCS which might result after a TBI) affected the treatment process. The Behavior Rating Inventory of Executive Function –Adult Version (BRIEF-A; Roth, Isquith, & Gioia, 2005) was available on a subset of participants and could be used as an assessment of executive functioning. The BRIEF-A assesses an individual's perception of their executive functions in nine areas and provides an overall summary score, the Global Executive Composite (GEC). A *t*-score of 65 or greater is considered clinically significant. The BRIEF-A adequately assesses patients with TBI and evidences strong reliability in this particular population (0.94 to 0.96; Waid-Ebbs, Wen, Heaton, Donovan, & Velozo, 2012).

While only a small percentage of the total sample completed a pre-treatment BRIEF (N = 26), two groups were defined based on GEC *t*-scores (regardless of TBI status). Individuals who scored a *t*-score of 65 or higher (N = 14; M = 74.71; SD = 7.44) and individuals who scored a *t*-score of 64 or below (N = 12; M = 57.41; SD = 4.14) were compared on treatment process

variables. Results indicated that self-reported executive function difficulty did not impact any of the exposure therapy process variables described above. See Table 2 for descriptive statistics and results of *t*-tests.

Pre-treatment PTSD Severity

Consistent with prior investigations (Barnes et al., 2012; Davis et al., 2013), participants with PTSD+TBI reported significantly higher PTSD symptoms (as measured by the CAPS total score at pre-treatment) (M = 94.33, SD = 16.88) than participants with PTSD only (M = 86.40, SD = 17.62, $t(87) = 2.16$, $p = .03$). Therefore, a one-way between-groups multivariate analysis of covariance (MANCOVA) examined group differences on treatment process variables when controlling for PTSD severity. Overall extinction was converted from a dichotomous to a continuous variable by calculating the decrease from initial session peak SUDS to final session peak SUDS. See Table 3 for MANCOVA results, interpreted below.

When controlling for PTSD severity, the overall MANCOVA was statistically significant, $F(6, 81) = 2.44$, $p = .03$; Wilks' Lambda = .85; $\eta_p^2 = .15$. Examination of simple effects revealed that groups significantly differed on initial fear activation, $F(1, 86) = 6.06$, $p = .02$, and average session length, $F(1, 86) = 4.12$, $p = .046$. Results again indicated that participants with PTSD+TBI experienced less fear activation during the initial treatment session (M = 2.55, SD = 1.53) compared to participants with PTSD only (M = 3.49, SD = 1.94), which held true even when controlling for session baseline SUDS, $F(1, 86) = 4.80$, $p = .03$. While this finding suggests that individuals with TBI might experience less fear activation during their initial treatment session, examination of the mean SUDS revealed that the groups differed by only one point, a difference that may be statistically, but not clinically, significant. Similarly, with regard to average session length, participants with PTSD only had longer sessions (in minutes) (M = 63.26,

SD = 9.71) than participants with PTSD+TBI (*M* = 60.19, SD = 10.97). However, the average difference was three minutes, which, while statistically significant, is not clinically significant. There were no group differences on overall fear activation, average number of sessions, extinction rate, or overall extinction while controlling for PTSD severity.

In contrast, the MANCOVA results revealed significant relationships between PTSD severity and average session length, $F(1, 86) = 7.44$, $p = .01$, average number of sessions, $F(1, 86) = 6.29$, $p = .01$, and extinction rate, $F(1, 86) = 4.27$, $p = .04$. In each case, follow-up Pearson correlations revealed that longer sessions, $r(89) = .29$, p = .03, more sessions, $r(89) = .26$, p = .01, and a slower extinction rates, $r(89) = .23$, p = .03, were associated with higher PTSD severity. There were no significant relationships between PTSD severity and initial fear activation, overall fear activation, and overall extinction. See Figures 3-7 for scatterplots of PTSD severity and each dependent variable for both groups.

CHAPTER FOUR: DISCUSSION

Although prior investigations suggested that the presence of TBI does not impact CBT treatment outcome, treatment confounds and limitations in sample size and composition preclude application of those findings to substantiate the feasibility of exposure therapy for OEF/OIF/OND combat veterans with combat-related PTSD+TBI. This study represents the first time process variables crucial for successful outcome using exposure therapy were examined in a carefully controlled and diagnosed sample of OEF/OIF/OND combat-veterans with combat-related PTSD and TBI. The results of this study indicate that TBI history does not impact overall fear activation, session length, number of sessions, within-session habituation, overall extinction, or rate of extinction. Individuals with PTSD and a history of TBI do not engage in exposure differently, or less effectively, than individuals with PTSD only, with one exception. Individuals with PTSD+TBI experienced less fear activation during their first exposure session, a difference that was accounted for by higher baseline SUDS. This suggests that the PTSD+TBI group may experience greater anticipatory anxiety or overall higher general anxiety. The lack of group differences is actually good news for clinicians as it means that, regardless of TBI status, exposure therapy for PTSD remains the treatment of choice.

One reason for the reluctance to use exposure therapy when participants report a history of TBI may be the often misunderstood fact that TBI is an event, and not a disorder. It is unclear whether individuals, at least with mTBI, continue to experience cognitive difficulties three months post injury (Ruff, 2011). In fact, research suggests that the majority of these individuals will fully recover from their head injury within 90-days (Karr, Areshenkoff, & Garcia-Barrera, 2014). As such, TBI status may not influence the exposure therapy process when therapy is

initiated after ninety-days. Conversely, a percentage of individuals with mTBI continue to experience cognitive difficulties three months post injury (Belanger et al., 2005), and chronic neurocognitive deficits are typical for moderate and severe TBI (Dikmen et al., 2009). Future investigations may need to specifically identify the subset of individuals with chronic cognitive difficulties (assessed via more comprehensive neuropsychological examinations) to determine their ability to fully engage in exposure therapy.

Further complicating the matter, however, is the significant overlap of TBI, PCS, and PTSD symptoms (Morissette et al., 2011), which suggests that the negative long term effects may in fact be related to PTSD, and not TBI. For example, extant literature suggests that PCS is not unique to TBI (Meares et al., 2008; Meares et al., 2011), and that PCS are actually better predicted by PTSD (Schneiderman, Braver, & Kang, 2008). Given the significant overlap between PTSD symptoms and PCS (e.g., irritability, sleep difficulty, and impaired concentration), psychological symptoms occurring post-combat should be treated with evidenced-based treatments regardless of their presumed etiology (Brenner et al., 2009).

Additionally, TBI status may have had no impact on the exposure therapy process due to the physiological nature of habituation; that is, exposure therapy does not require higher order cognitive functions to successfully extinguish fear. Specifically, fear activation and habituation are the active ingredients of exposure therapy. Given that fear conditioning can occur outside one's level of awareness (i.e., some individuals with severe TBI and no memory of traumatic events develop PTSD) (Bryant, Marosszeky, Crooks, & Gurka, 2000; Bryant, Marosszeky, Crooks, & Gurka, 2004), it is likely that extinction can as well. These findings suggests that regardless of the potential long-term cognitive effects of a TBI, individuals who retain basic

attentional processes (e.g., ability to pay and to visualize the traumatic event as described by the therapist) should still be capable of achieving extinction via exposure therapy.

Higher PTSD severity scores are often found in individuals with comorbid mTBI, as occurred in this sample. After controlling for PTSD severity, participants with PTSD+TBI had longer treatment sessions than participants with PTSD only; however, session length differed by approximately three minutes, which is not likely clinically significant. Second, participants with a history of TBI continued to endorse greater fear activation (one-point higher on a nine-point SUDS scale) during the initial exposure session, but again, this minimal difference in fear activation is unlikely to be clinically significant. Overall, findings indicate that TBI status has no clinically significant effect on the exposure therapy process, even when pre-treatment PTSD severity is taken into account.

Interestingly, examining the relationship between PTSD severity and exposure therapy process variables (without regard for TBI history) revealed that severity of the disorder may impact the length of treatment. More severe PTSD at pre-treatment was related to longer sessions, more sessions, and slower extinction. These data suggest that consideration of PTSD symptom severity is necessary for optimal treatment planning and the treatment process, whereas TBI status does not offer such insights. The findings of this study are similar to prior research suggesting that TBI and PCS have no effect on functional outcomes (e.g., general health or missed work days) when PTSD severity is taken into account (Hoge et al., 2008; Polusny et al., 2011; Schneiderman et al., 2008; Wilk, Herrell, Wynn, Riviere, & Hoge, 2012). Furthermore, the data from this investigation add a novel understanding of how pre-treatment PTSD severity influences the process of exposure therapy. Individuals with more severe symptom presentation may require more sessions, and/or longer sessions, to achieve extinction. Treatment sessions may

need to extend beyond 60-minutes to assure sufficient exposure time for patients with the most severe symptoms. Extending the exposure session until within-session habituation occurs is clinically important given that some research suggest superior treatment gains when within-session habituation occurs (see Bluett, Zoellner, & Feeny, 2014 for review).

Limitations and Future Directions

The principle limitation of the current study was the need to rely on patient self-report of TBI status, particularly when there is no penetrating wound or evidence of injury via brain imaging. While a patient report of TBI history may initially appear problematic, 96% of participants who completed the TBI validation process two- to three-years later retained their initial status. This agreement demonstrates the consistency of the Department of Defense (2014), Department of Veterans Affairs and Department of Defense (2009) criteria for the TBI, but is based, as noted above, on the occurrence of an event and not a specific constellation of symptoms. Our data do indicate that self-report of prior TBI diagnosis may be sufficient to classify individuals based on the current diagnostic criteria, which supports existing literature suggesting similar TBI frequency rates for varied assessment methods (Carlson et al., 2011). What remains for future investigations is the validity of the diagnostic label, whether there can be a discrete constellation of symptoms identified (unique to TBI), and whether there exists a subset of individuals with specific cognitive impairments that are contraindicated for exposure therapy.

Further, neither severity nor total number of TBIs was determined for this sample, variables not yet known to affect PTSD severity and/or the exposure therapy process. During the TBI screening, the clinician attempted to obtain these clinical markers, but participants had difficulty reporting the specifics necessary to determine severity. However, none of the participants in this sample presented with history of penetrating head wounds or other types of

injuries more likely to be labeled as moderate or severe TBIs. Nonetheless, future research would benefit from determining how severity and total number of TBIs affect engagement in exposure therapy.

This study sheds light on the procedure currently used to determine the presence of a TBI. Given that individuals only need to experience "a blow or jolt to the head" accompanied by a single neurological symptom (e.g., alteration in mental state, change in consciousness or memory loss) (Department of Defense, 2014; Department of Veterans Affairs and Department of Defense, 2009), this diagnosis may be overly inclusive. There are vast differences in the neurological status between an individual who accidently bumped their head and felt disoriented, compared to an individual whose brain was penetrated with mortar shrapnel, resulting in days of unconsciousness. Given this, it is extremely important that clinicians and medical providers are aware of a specific caveat present in the diagnostic criteria. Specifically, observed signs of neurological or neuropsychological dysfunction (such as headache, dizziness, or poor concentration) as a marker for the criterion of alteration of mental state are not sufficient to make a diagnosis of TBI (i.e., they do not indicate a change in mental state) when loss of or altered consciousness is not present (Department of Veterans Affairs and Department of Defense, 2009). This caveat should ameliorate the overpathogizing of minor head injuries and reduce false positives.

After the results indicated that TBI status did not affect the process of exposure therapy, we attempted to determine if cognitive impairment might affect engagement in the process. Unfortunately, the BRIEF-A was only administered to a subsample of participants, and lack of significant findings may be due to lack of statistical power. More importantly, the BRIEF-A assesses for perceived difficulty with executive functioning, and is not an objective

neuropsychological measure of actual cognitive dysfunction. As such, future investigations would benefit from examination of neuropsychological dysfunction, both with and without consideration to TBI status, in order to understand how these factors may play a role in the exposure therapy process.

Conclusion

Overall, results of this study suggest that individuals with PTSD and a history of TBI can successfully engage in exposure therapy, and do so no differently than individuals with PTSD only. Given that exposure based treatments are deemed efficacious for combat-related PTSD (Goodson et al., 2011; IOM, 2007), a history of TBI should not preclude individuals from receiving this treatment. In fact, results of this study, coupled with the extant literature, suggests that exposure therapy should be the first-line treatment for combat-related PTSD regardless of TBI history. Secondarily, clinicians and medical providers should ensure patients understand that TBIs are events, and not disorders, and that its prior occurrence does not preclude treatment with exposure therapy. Adoption of exposure therapy as clinical practice by all clinicians should ensure that we provide our veterans with the most efficacious and appropriate treatment for their difficulties post-combat.

APPENDIX A: TABLES

Table 1: TBI Group Differences on Treatment Process Variables (N = 90)

Treatment Variable	PTSD only	PTSD+TBI	*t*	*p*	Mann-Whitney U *p*
Initial Fear Activation	3.44 (1.96)	2.55 (1.53)	-2.38	.020*	.035*
Overall Fear Activation	6.50 (1.27)	6.29 (1.40)	-0.76	.449	.538
Average Session Length	63.10 (9.67)	60.19 (10.97)	-1.34	.184	.170
Average Number of Sessions	10.54 (3.14)	10.64 (2.95)	0.16	.876	.866
Peak SUDS Extinction Rate	-0.49 (0.31)	-0.43 (0.34)	0.80	.425	.302

Note. *$p < 0.05$.

Table 2: BRIEF Group Differences on Treatment Process Variables (N = 24)

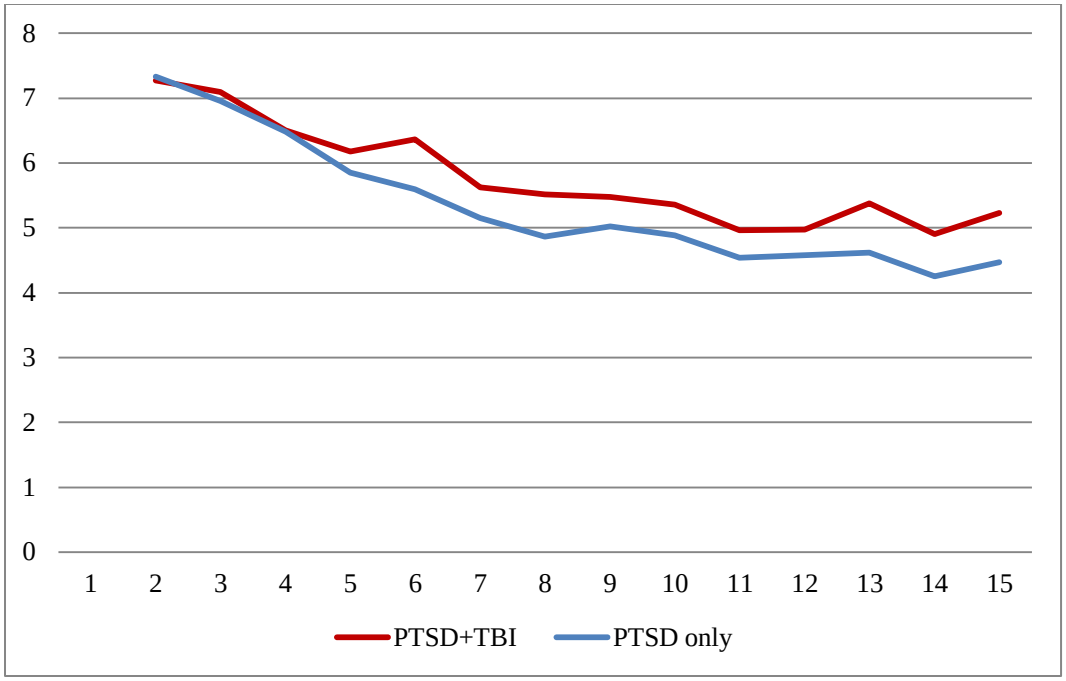
Treatment Variable	*t*-score ≥ 65 (N = 14)	*t*-score ≤ 64 (N = 12)	*t*	*p*
Initial Fear Activation	3.14 (1.61)	3.33 (1.67)	-.296	.770
Overall Fear Activation	6.21 (1.53)	6.58 (1.28)	-.642	.527
Average Session Length	63.25 (10.29)	65.09 (10.62)	-.444	.661
Average Number of Sessions	9.57 (2.59)	11.00 (3.54)	-1.19	.248
Peak SUDS Extinction Rate	-0.60 (0.27)	-0.46 (0.30)	-1.26	.221

Table 3: Group Difference Controlling for PTSD Severity (N = 89)

Treatment Variable	F (1, 86)	p	η^2
Overall Fear Activation			
TBI Status	1.07	.304	.012
PTSD Severity	1.36	.247	.016
Initial Fear Activation			
TBI Status	6.06	.016*	.066
PTSD Severity	0.01	.914	.000
Average Session Length			
TBI Status	4.12	.046*	.046
PTSD Severity	7.44	.008**	.080
Average Number of Sessions			
TBI Status	0.09	.769	.001
PTSD Severity	6.29	.014*	.068
Peak SUDS Extinction Rate			
TBI Status	0.13	.719	.002
PTSD Severity	4.27	.042*	.047
Overall Extinction			
TBI Status	2.55	.114	.029
PTSD Severity	0.67	.417	.008

Note. *$p < 0.05$, *$p < 0.01$.

APPENDIX B: FIGURES



Note. Ns from session 2 to session 15 are as follows: 90, 90, 90, 90, 87, 87, 83, 73, 61, 55, 45, 38, 36, 28.

Figure 1: Average Peak SUDS across Sessions

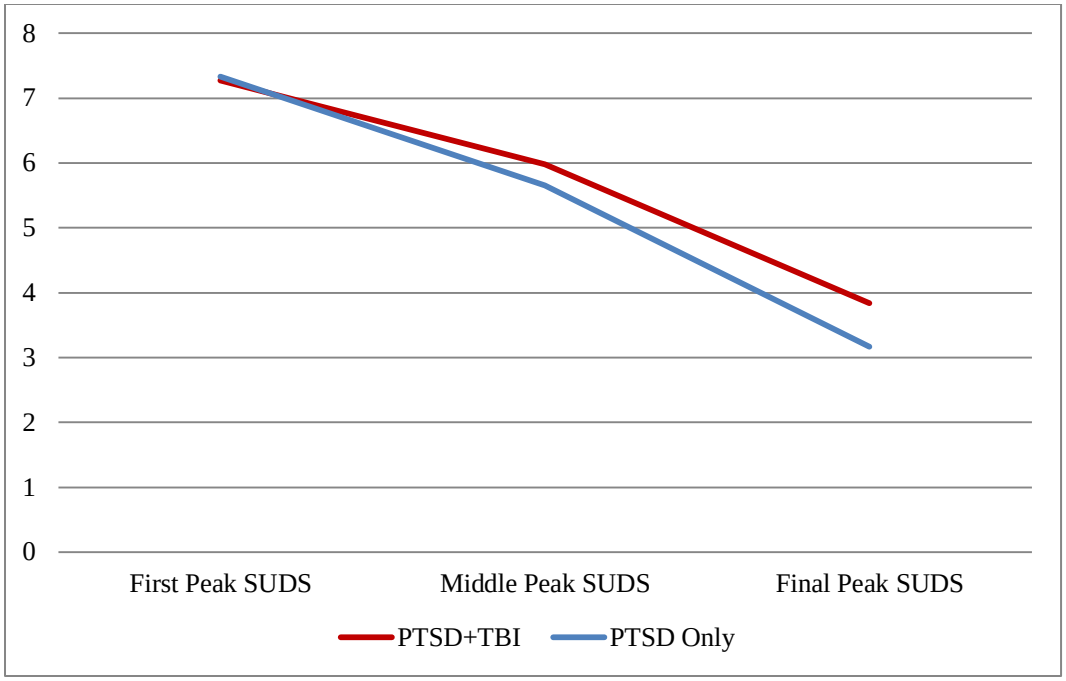


Figure 2: Average First, Middle, and Final Peak SUDS

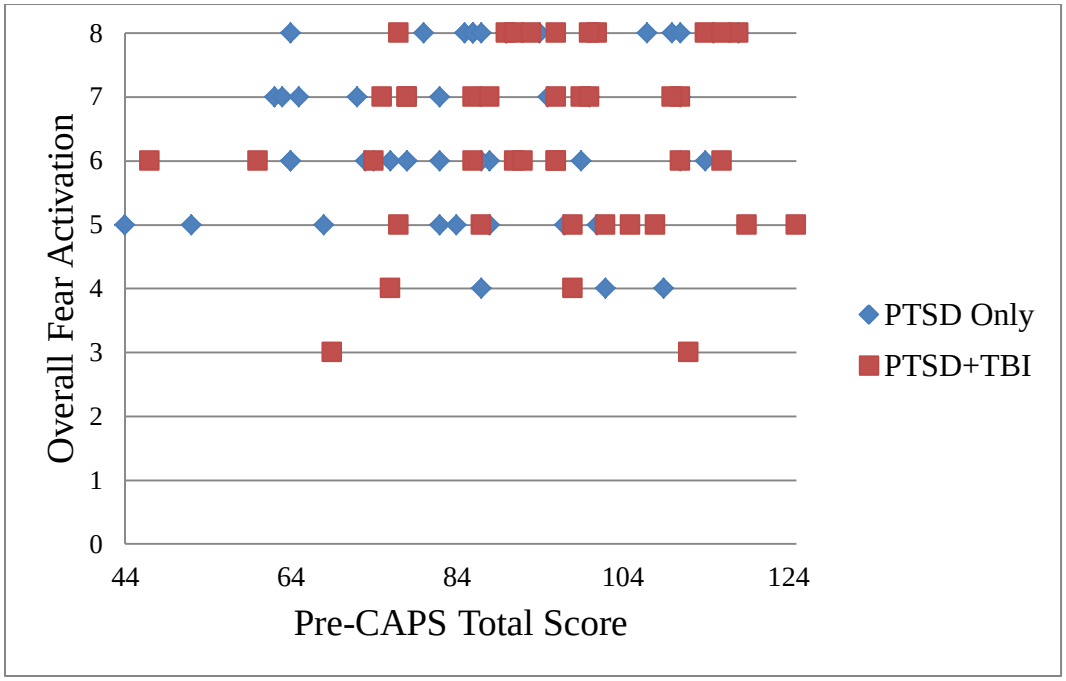


Figure 3: Scatterplot of PTSD Severity and Overall Fear Activation

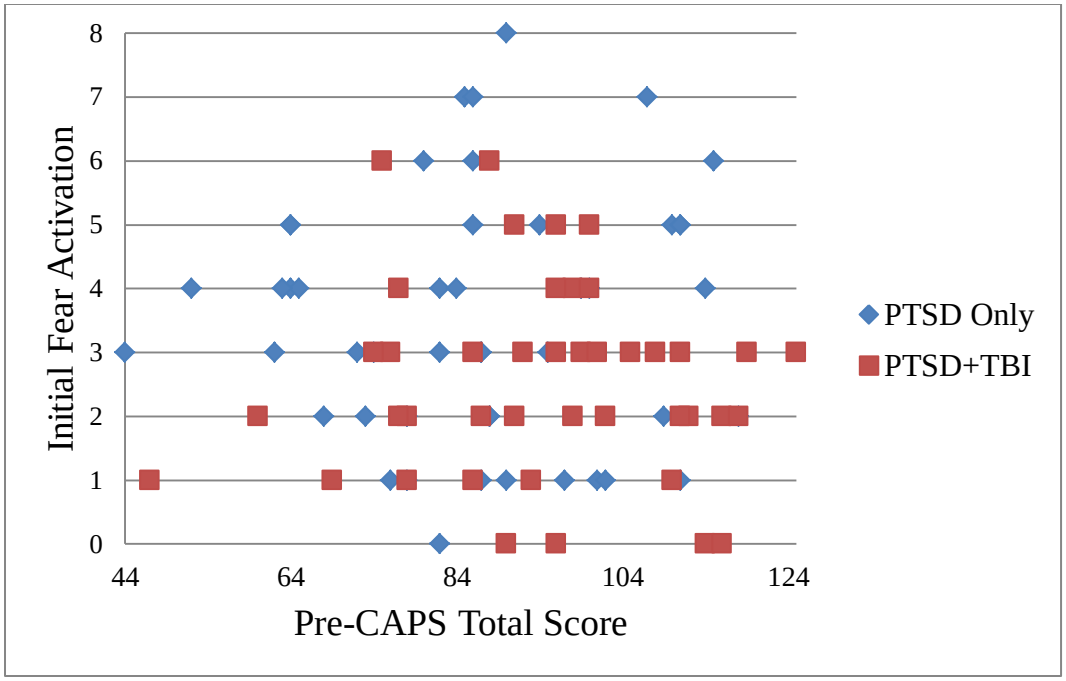


Figure 4: Scatterplot of PTSD Severity and Initial Fear Activation

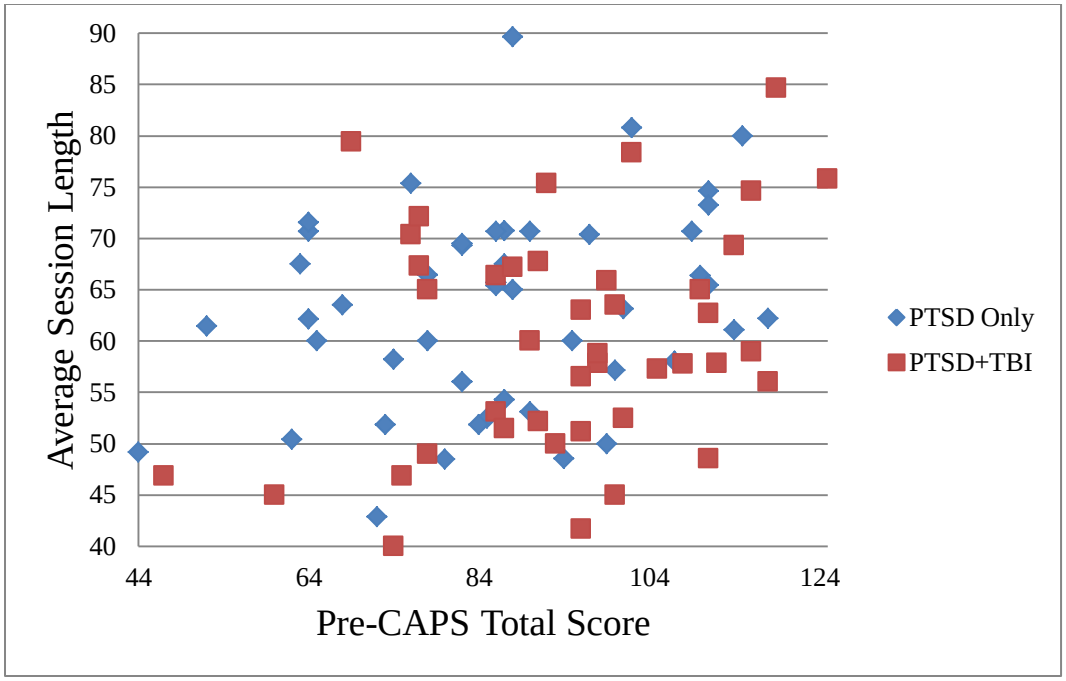


Figure 5: Scatterplot of PTSD Severity and Average Session Length

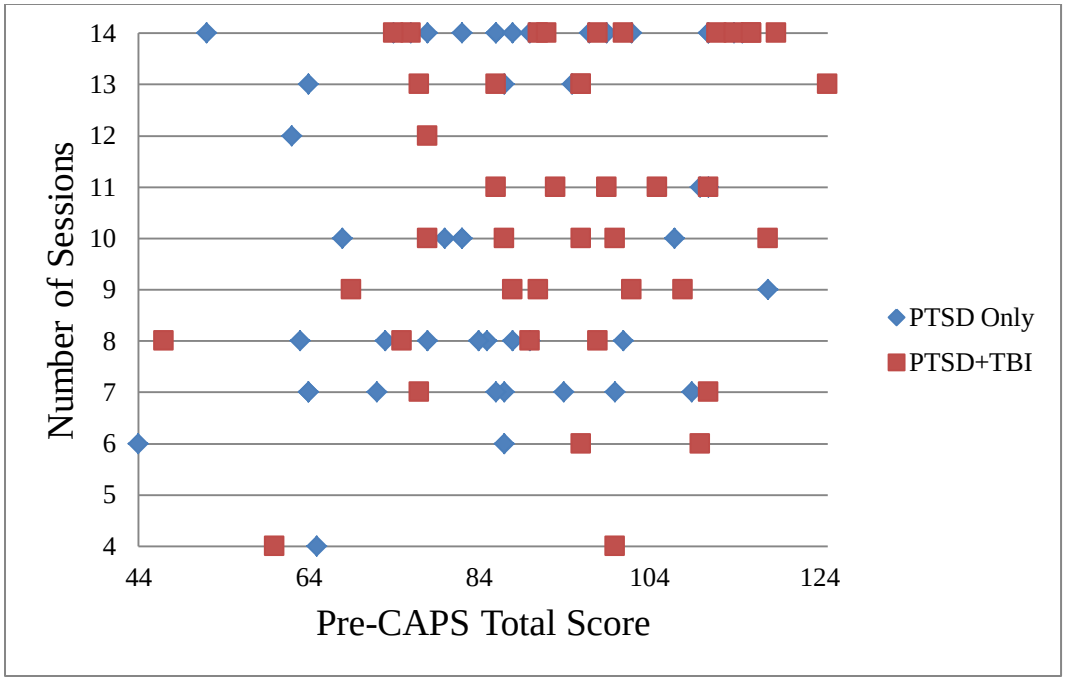


Figure 6: Scatterplot of PTSD Severity and Number of Sessions

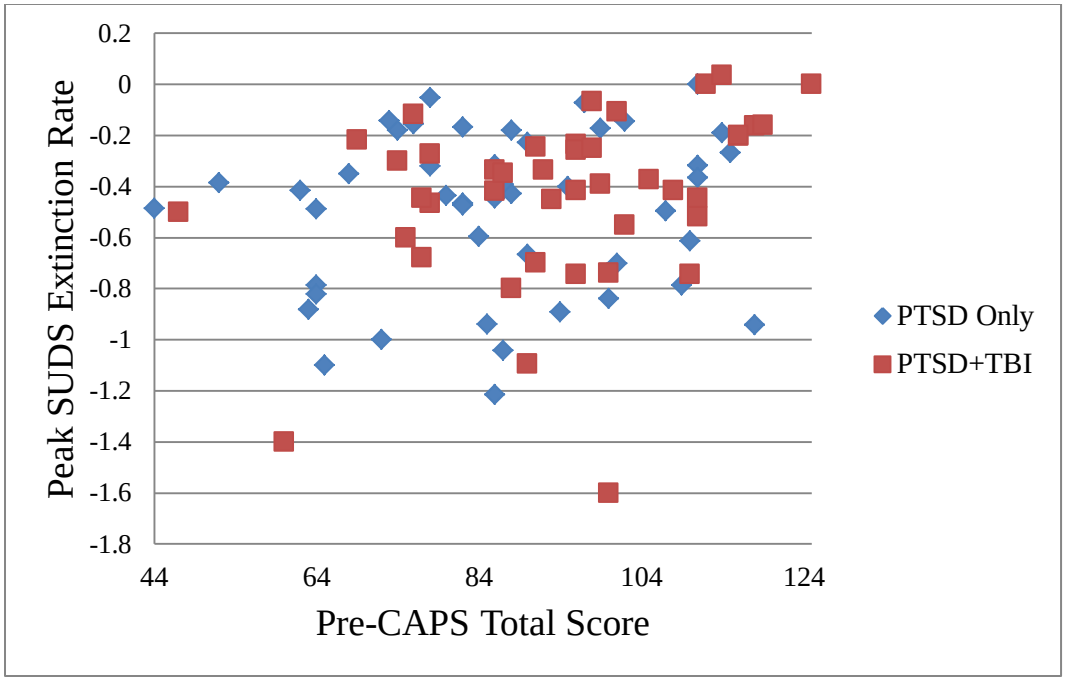


Figure 7: Scatterplot of PTSD Severity and Extinction Rate

APPENDIX C: IRB APPROVAL LETTER

University of Central Florida Institutional Review Board
Office of Research & Commercialization
12201 Research Parkway, Suite 501
Orlando, Florida 32826-3246
Telephone: 407-823-2901 or 407-882-2276
www.research.ucf.edu/compliance/irb.html

Approval of Human Research

From: **UCF Institutional Review Board #1**
FWA00000351, IRB00001138

To: **Deborah Casamassa Beidel**

Date: **November 23, 2010**

Dear Researcher:

On 11/23/2010, the IRB approved the following human participant research until 11/16/2011 inclusive:

Type of Review:	UCF Initial Review Submission Form
Project Title:	Trauma Management Therapy for OEF and OIF Combat Veterans
Investigator:	Deborah Casamassa Beidel
IRB Number:	SBE-10-07066
Funding Agency:	DOD/Army
Grant Title:	Trauma Management Therapy for OEF and OIF Combat Veterans
Research ID:	1048785

The Continuing Review Application must be submitted 30days prior to the expiration date for studies that were previously expedited, and 60 days prior to the expiration date for research that was previously reviewed at a convened meeting. Do not make changes to the study (i.e., protocol, methodology, consent form, personnel, site, etc.) before obtaining IRB approval. A Modification Form **cannot** be used to extend the approval period of a study. All forms may be completed and submitted online at https://iris.research.ucf.edu .

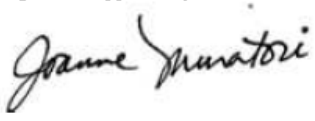
If continuing review approval is not granted before the expiration date of 11/16/2011, approval of this research expires on that date. When you have completed your research, please submit a Study Closure request in iRIS so that IRB records will be accurate.

Use of the approved, stamped consent document(s) is required. The new form supersedes all previous versions, which are now invalid for further use. Only approved investigators (or other approved key study personnel) may solicit consent for research participation. Participants or their representatives must receive a signed and dated copy of the consent form(s).

In the conduct of this research, you are responsible to follow the requirements of the Investigator Manual.

On behalf of Joseph Bielitzki, DVM, UCF IRB Chair, this letter is signed by:

Signature applied by Joanne Muratori on 11/23/2010 10:45:01 AM EST



IRB Coordinator

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