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Understanding Posttraumatic Stress Disorder in Military Populations for Designing Research Protocols

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14. ABSTRACT The US Army Combat Capabilities Development Command (DEVCOM) Army Research Laboratory has a long-term effort toward enhancing our understanding of the physiological and behavioral components of Warfighter-relevant tasks, such as situational awareness (SA) acquisition and maintenance. A critical component of this effort is to understand the effects of stress on Warfighter state to predict and enhance performance during operational missions, especially in high-stress environments, and how individual differences (resiliency, mental health, etc.) impact performance. While we can often induce only a limited amount of stress in traditional laboratory settings, we can induce elevated stress responses by utilizing immersive environments (e.g., virtual environments or virtual reality) and by leveraging certain military personnel and veteran populations to better understand performance effects. In particular, those with posttraumatic stress disorder (PTSD) demonstrate altered physiological and behavioral processes that support SA. This report provides a basic overview of PTSD, its prevalence in the military, and how it is related to individual differences, behavior, and physiology. We hope that this review will provide an insightful and ethical lens to other DEVCOM Army Research Laboratory researchers considering leveraging this population for research.					
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Contents

List of Figures	v
1. Introduction	1
2. Posttraumatic Stress Disorder in the Military	2
2.1 Trauma	2
2.2 Military as an At-Risk Population for Developing PTSD	3
3. PTSD and Individual Differences	4
3.1 Military Experience	4
3.2 Sex Differences	6
3.3 Comorbid Diagnosis	6
3.4 Personality	6
3.5 Stress Response to Trauma	8
3.6 Interpersonal Functioning	8
4. PTSD and Cognitive Deficiencies Related to Memory and Attention	9
5. PTSD and Physiological Markers	10
6. Special Considerations for Experimental Protocols	12
7. References	15
Appendix A. Example Measures to Include in a Study Including a Posttraumatic Stress Disorder (PTSD) Population	25
Appendix B. Example Demographics Questions	27
Appendix C. Diagnostic Criteria for Posttraumatic Stress Disorder (PTSD)	32
Appendix D. Example Informed Consent Potential Risk Section	35

Appendix E. Distress Log	37
List of Symbols, Abbreviations, and Acronyms	40
Distribution List	41

List of Figures

Fig. 1	Prevalence of PTSD in veterans as reported by the US Department of Veterans Affairs National Center for PTSD 2018	5
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1. Introduction

The US Army Combat Capabilities Development Command (DEVCOM) Army Research Laboratory (ARL) has a long-term focus toward enhancing our understanding of the physiological and behavioral components of Warfighter-relevant tasks, such as situational awareness (SA) acquisition and maintenance. A critical component of this effort is to understand the effects of stress on Warfighter state to predict and enhance performance during operational missions, especially in high-stress environments, and how individual differences (resiliency, mental health, etc.) impact performance. While we can often induce only a limited amount of stress in traditional laboratory settings, we can induce elevated stress responses by utilizing immersive environments (e.g., virtual environments or virtual reality) and by leveraging certain military personnel and veteran populations. This allows us as researchers to better understand how stress responses vary depending on individual differences, behavior, and physiology and allows us to test how well advancing algorithms understand and predict behavior across individuals.

One population that could be leveraged to study stress response and individual differences are Warfighters affected by posttraumatic stress disorder (PTSD). According to a comparison of the prevalence of PTSD among veterans across different conflicts, PTSD among military personnel can be as high as 30% (Reisman 2016). PTSD is unlike most other mental health disorders through the requirement of a distinct etiologic event outside of the person, such as those experienced during deployments to hostile environments. PTSD is further distinguishable from other anxiety-related disorders by memory disruptions and dysfunctional threat processing. In particular, those with PTSD demonstrate altered physiological and behavioral processes that support SA. For example, those with PTSD are at a constant heightened state of arousal, showing an increased resting heart rate (Bedi and Arora 2007). We can utilize this baseline heightened state of arousal to investigate how stress may affect performance, as this population would produce a wide variation in performance responses to stress when included as a comparison to those without PTSD. This may provide us with a better understanding of the effects of high stress beyond what we could induce in a healthy population in traditional laboratory manipulations.

In preparation for ARL 21-104, a study focused on identifying behavioral and physiological markers of SA and their dependence on cognitive states between those with military experience with and without PTSD, we conducted an extensive literature review. This report is a compilation of that review and provides a basic overview of PTSD, its prevalence in the military, and how it is related to individual differences (e.g., personality), behavior, and physiology. We hope that this review

will provide an insightful lens to other DEVCOM Army Research Laboratory researchers who are considering leveraging this population for research. We conclude with special considerations for designing experimental protocols (e.g., coping with triggers). Examples of related measures that may be relevant in a study including this population are described in Appendix A.

2. Posttraumatic Stress Disorder in the Military

Over the centuries, terms like shell-shock, Soldier's heart, battle fatigue, fright/combat neurosis, and gross stress reaction have been used to describe the psychological effects of trauma (Zohar et al. 2000; Friedman et al. 2007), and to foreshadow the developing diagnosis of PTSD. PTSD is a psychobiological phenomenon resulting from a maladaptive and pathological response to trauma that can be severely incapacitating, affecting multiple domains of an individual's life (Everly 1995; American Psychological Association [APA] 2000; Zohar et al. 2000). Although PTSD can occur in noncombatant populations, it has long been associated with the horror and trauma of human warfare (Everly 1995).

2.1 Trauma

A key component of PTSD is the requirement of a distinct etiologic event outside of the person, often the result of a traumatic event. Trauma is pervasive and takes many forms. The American Psychological Association (APA) generally defines a traumatic event as one involving, experiencing, or witnessing an event(s) involving "actual or threatened death or serious injury" to one's self or others, causing "intense fear, helplessness, or horror" (APA 2000). Traumatic events encompass a wide variety of experiences (Southwick et al. 1995); for example, some of those identified in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR) include military combat, violent assault, kidnapping, terrorist attack, torture, automobile accidents, and natural disasters (APA 2000). Type of trauma has also been found to be relevant regarding lifetime prevalence of trauma exposure, with the prevalence of some trauma types occurring more often than others (Kessler et al. 1995). The three types of trauma with the highest prevalence of lifetime trauma exposure include witnessing another person being killed or injured, or experiencing a natural disaster or life-threatening accident (Kessler et al. 1995). Furthermore, at-risk populations for developing PTSD have been identified by the DSM-IV-TR as those experiencing "rape, military combat and captivity, and ethnically or politically motivated internment and genocide," and estimates that anywhere from one-third to more than half of those exposed to these types of traumatic events develop PTSD.

2.2 Military as an At-Risk Population for Developing PTSD

As noted previously, the military population is especially at an increased risk for exposure to many types of traumas that could lead to the development of PTSD. War exposes individuals to a tremendous amount of physical and psychological stress, such as harsh environments, foreign cultures, and terrain, and placing military personnel in a position where they are at an increased risk of experiencing or witnessing death or serious bodily injury (Shay 1994). Furthermore, military personnel are often distanced from their primary support groups and often form close familial-like bonds with their comrades; therefore, witnessing the death of such a close companion can have detrimental emotional effects (Shay 1994).

Much of the initial PTSD research focused on war related to Vietnam veterans. Data collected from the National Vietnam Veterans Readjustment Study demonstrated a lifetime prevalence of PTSD for Vietnam veterans was estimated as 30% with 13%–17% actively suffering from PTSD at the time of the study (Kulka et al. 1990). Increased prevalence rates of PTSD were associated with war-zone exposure for both men and women, estimating that 35.8% of men and 17.5% of women that had war-zone exposure and were included in the study met the criteria for PTSD (Kulka et al. 1990). More recently, data collected from Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) provide insights into the prevalence of PTSD occurring in relation to military deployments to modern hostile operational environments. The costs for OEF and OIF operations have been incredibly high in terms of finances, lives, and both physical and psychological trauma.

The modern hostile operational environments of OEF/OIF exposed military personnel to unprecedented combat and logistic scenarios that could have unique and long-lasting impacts on mental health. Conflict during OEF/OIF has been characterized as involving counterinsurgency operations occurring within an irregular and asymmetric warfare environment that is dramatically different than the conventional war environments once considered standard (Hoge et al. 2004; Planning Committee on Unifying Social Frameworks and National Research Council 2011). Irregular warfare was defined for OEF/OIF as involving two opposing forces possessing unequal military capabilities and tactics (Research and Development Corporation n.d.). Conflict increasingly occurred in urban areas devoid of distinct boundaries and lacking traditional front lines (Planning Committee on Unifying Social Frameworks & National Research Council 2011). Enemy insurgencies composed of irregular forces were not associated with having identifiable uniforms and were frequently dispersed throughout the civilian population, intensifying the difficulty of discerning civilian from combatant

(Shaver 2006; Planning Committee on Unifying Social Frameworks & National Research Council 2011). Moreover, the initial goal of overcoming an armed enemy in OEF/OIF was expanded to incorporate goodwill missions where military personnel interacted with local citizens to provide aide, enhanced living conditions, and increased local support for US operations (Planning Committee on Unifying Social Frameworks & National Research Council 2011). Military personnel were thus required to leave their bases and venture into communities to conduct missions. When there is little to differentiate enemy combatants from the civilians that military personnel are tasked to help, the possibility for combative encounters and the potential for contributing to civilian casualties rises. Combat exposure significantly impacts post-deployment mental health (King et al. 2006), and added pressures of modern warfare could further the negative effects of such exposure on military personnel's mental health and recovery post-deployment (Wrobel 2016). In fact, the most common diagnoses for veterans of modern conflicts involve mental health, with one in three post 9/11 to 2016 veterans seeking treatment having experienced PTSD (Wrobel 2016).

3. PTSD and Individual Differences

Given the complexities of PTSD, it is important to also consider the effects of individual differences. These may be explored through collecting demographic information (see Appendix B for an example demographics questionnaire). It may be especially relevant to solicit specific information from participants to understand differences that may exist between military experience, comorbid diagnoses, and personality.

3.1 Military Experience

Studies have revealed OEF/OIF rates of PTSD differ according to military branch of service: Marines, Army, Navy, and Air Force (Shen et al. 2009). In addition to considering branch of military, there is the potential for many variants of military experience (e.g., time in service, service era, deployments) to influence the rate of PTSD. The National Center for PTSD (2018) reported how common PTSD is in veterans, highlighting differences across service era (Fig. 1).

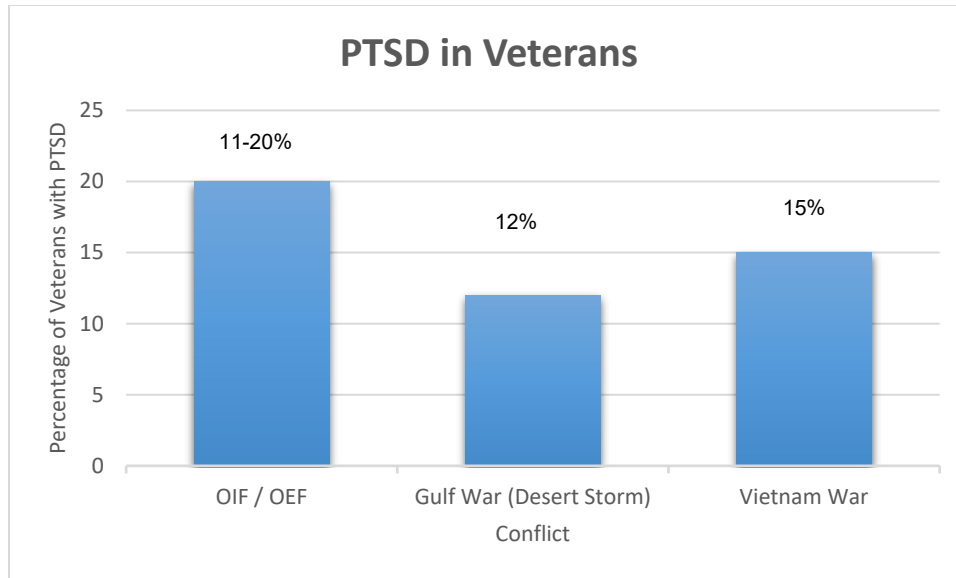


Fig. 1 Prevalence of PTSD in veterans as reported by the US Department of Veterans Affairs National Center for PTSD 2018

Considering deployments, the largest and smallest effect for deployments longer than 180 days were reported for the Navy (increased odds by 9.06 times) and Air Force (increased odds only by 1.25 times), respectively (Shen et al. 2009). Longer deployments to OEF/OIF have been shown to increase the risk for developing PTSD for the Army and Navy (Shen et al. 2009). Compared to other worldwide deployment locations, deployments to Afghanistan and Iraq (such as OEF and OIF, respectively) are associated with increased odds of developing PTSD (Shen et al. 2009). Without accounting for differences in gender, a study found that in a sample of 88,000 Soldiers serving in OIF, 67% to 70% reported exposure to at least one combat experience (Milliken et al. 2007). Deployments during OEF/OIF are longer and more frequent compared to prior conflicts (Eisenhower Study Group 2011). Compared to deployments lasting under 120 days, deployments lasting over 180 days have been found to increase the odds of developing PTSD by 1.1 to 2.48 times (Shen et al. 2009). The Army and Marines are most likely to have deployments lasting 180 days, while deployments for those in the Air Force are more likely to last less than 120 days (Shen et al. 2009). The greatest number of enlisted deployed to Iraq and Afghanistan are from the Marines and the Army, with more enlisted in the Navy and Air Force having been deployed to other locations in support of OEF/OIF missions (Shen et al. 2009). The greater numbers of enlisted Army and Marines in addition to the longer deployments for these groups may suggest an increased risk for developing PTSD compared to military personnel in the Navy and Air Force.

3.2 Sex Differences

The majority of studies investigating combat trauma and PTSD have historically focused on men (Shay 1994; Street et al. 2009). Only recently has research begun to examine the issue within the female military population (Clark et al. 2006; Hoge et al. 2007; Vogt et al. 2011). The recent modern war environments of OEF/OIF, coupled with the changing roles of women serving therein, have led to unprecedented levels of combat exposure for women serving in the US military (La Bash et al. 2008; Geppert 2009; Street et al. 2009; Vogt et al. 2011). Recent research suggests with the increasing role women play in combat, the prevalence of women now exposed to combat may be closer to that experienced by men (Jacobson et al. 2008).

In addition to trauma associated with combat, sexual trauma can be another cause of PTSD in the military (National Center for PTSD 2018). The National Center for PTSD (2018) reports that sexual harassment and/or assault may lead to developing PTSD in the military, with 23% of female veterans who use Veterans Affairs health care reporting a sexual assault, and 55% of women and 38% of men reporting having experienced sexual harassment. While military sexual trauma is more commonly reported in female veterans, because there are more male than female veterans, over half of all veterans with military sexual trauma are men (National Center for PTSD 2018).

3.3 Comorbid Diagnosis

Several other psychiatric disorders commonly co-occur with PTSD. Data from epidemiologic studies indicate that the majority of individuals with PTSD meet criteria for at least one other disorder, with a substantial portion having three or more (Brady 2000). The most common comorbid diagnoses include depressive disorders, substance use disorders, other anxiety disorders, and attention-deficit hyperactivity disorder. Additionally, traumatic brain injury (TBI) is associated with PTSD, especially for those diagnosed in the military given the increased potential of exposure to blast-related injuries (Hoge et al. 2008; Phipps et al. 2020). With just under half of post 9/11 veterans seeking treatment receiving TBI diagnoses, TBI has been described as the signature wound of modern warfare (Wrobel 2016). In order to control for these in a study, it is important to collect information related to these conditions.

3.4 Personality

The makeup of an individual's personality influences how they perceive and interpret the world around them. Previous research has examined the relationship

between personality, emotional processing, and PTSD in some detail (e.g., McDevitt-Murphy et al. 2012). One example of this can be seen in facial dot probe tasks, where individuals with bipolar personality disorder and PTSD have shown slower reaction times to incongruent, angry targets (Kaiser et al. 2020). This suggests an attentional bias toward the negatively charged emotion and an overall difficulty disengaging from threat-related stimuli. In one meta-analysis that focused on the relationship between PTSD and personality, it was concluded that different types of personality traits are consistent with both positive and negative PTSD (Jakšić et al. 2012). Specifically, symptoms of PTSD have a positive relationship with negative emotionality (Kunst 2011), neuroticism, harm avoidance (Gil 2005), novelty-seeking (Wang et al. 1997; Evren et al. 2010), self-transcendence (Evren et al. 2010), trait hostility/anger (Zuiden et al. 2011), and trait anxiety (Collimore et al. 2008). Additionally, symptoms of PTSD are negatively correlated with extraversion (Campbell-Sills et al. 2006), conscientiousness (Campbell-Sills et al. 2006), self-directedness (North et al. 2012), a combination of high positive and low negative emotionality (Kunst 2011), hardiness (Bartone 1999), and optimism (Thomas et al. 2011). Given the relationships found between not only PTSD and personality, but also personality traits and their biological bases, it may be helpful to measure constructs of personality when gathering data from a PTSD population.

The five-factor model of personality (Costa and McCrae 1992) is one of the most popular structural personality models and has been confirmed across almost all cultures and is fairly stable over time (McCrae and Costa 2003). This model describes personality across the following five dimensions: neuroticism, extraversion, openness, agreeableness, and conscientiousness. The Big Five Inventory (BFI) is one of the most widely used self-report inventories to measure personality across these five dimensions. Research has found evidence suggesting that these traits have a physiological and biological basis and that the heritability of its dimensions are substantial (Bouchard and McGue 2003; Ožura et al. 2012). From these five traits it is conceivable that one can further understand and describe a person's personality and predicted level of behavior (Fleeson and Jayawickreme 2015).

Caska and Renshaw (2013) utilized the BFI to assess the impact of personality traits on responses to traumatic events for OEF/OIF deployed National Guard/Reserve military personnel. Results suggested personality traits are an important risk/resiliency factor contributing to an individual's responses to trauma. For instance, extraversion was found to moderate the associations between combat and battle aftermath experiences with PTSD such that the association lessened with increased levels of extraversion. The association between battle aftermath and PTSD was further moderated, with the relation lessening, with higher levels of

agreeableness, conscientiousness, and openness, and lower levels of neuroticism. A more recent study (Mattson et al. 2018) found that coping style among OIF/OEF veterans mediated (explained or partially explained) the relationship between personality and posttraumatic growth and PTSD. While adaptive coping partially mediated the relationship between openness and posttraumatic growth (positive changes following trauma), maladaptive coping partially mediated the relationship between neuroticism and PTSD symptoms. Including measures of personality such as the BFI in a study with PTSD can help gain a greater understanding of individual variability as it relates to factors related to risk and resiliency.

3.5 Stress Response to Trauma

Individuals can experience a range of reactions following exposure to a traumatic event. Common reactions may be emotional (e.g., feeling helpless, fearful, numb, agitated, guilt or shame) or physical (e.g., sweating, headache, changes in appetite or sleep) and can impact different dimensions of a person's life (Department of Veteran Affairs 2011). Despite the numerous reactions one may experience post-trauma, the majority of individuals exposed to a traumatic event will recover and maintain their ability to function (Zohar et al. 2000; Price 2007). However, some may go on to develop more serious disorders such as substance abuse, depression, acute stress disorder, or PTSD. As reported earlier, prevalence of PTSD among military personnel can be as high as 30% (Reisman 2016). One important individual difference to consider that may affect why only a portion of those exposed to trauma go on to develop PTSD is resiliency. Whereas trauma increases the chances of developing PTSD, higher resiliency as a trait is positively associated with growth and negatively associated with the development of PTSD (Bensimon 2012).

3.6 Interpersonal Functioning

Intrapersonal biases toward threat and negative cues bleed into maladaptive behaviors that can have adverse effects on relationship functioning. The following section highlights differences in social effects and orientations between individuals with and without PTSD, and how they may manifest in their close social interactions.

From interactions, individuals with PTSD experience heightened levels of ostracism as compared to those without PTSD in tasks manipulated to induce social exclusion (Nietlisbach and Maercker 2009a; Nietlisbach and Maercker 2009b). This may have important implications for critical social life events such as attending college or romantic relationships. Elliott et al. (2011) found that student veterans exposed to higher levels of combat had more symptoms of PTSD and

experienced greater alienation on college campuses compared to other student veterans. Sippel and Marshall (2011) found through the administration of an emotional Stroop task that shame-sensitivity experienced in individuals with PTSD may facilitate aggressive behavior toward romantic partners, which was measured using a self-report scale. PTSD is also associated with increased personal distress and expressing lower levels of empathy (Nietlisbach and Maercker 2010), as demonstrated by a decreased ability to describe and perceive emotional experiences in others (Mazza et al. 2012), to identify the social cognitive perspective of others (Parlar et al. 2014), and to recognize displays of mental states (Schmidt and Zachariae 2008), in addition to reporting lower scores in scales measuring empathy (Parlar et al. 2014) as compared to those without PTSD. When interacting with others, disclosure attitudes toward close others (Mueller et al. 2008) and perceived social support (mediated by posttraumatic thoughts) influence PTSD symptom severity (Woodward et al. 2015).

PTSD symptomology was found to be associated with insecure orientations of attachment (i.e., avoidant and anxious) in intimate relationships (Renaud 2008; Solomon et al. 2008; Woodhouse et al. 2015). When observing these relationships in greater detail, individuals with PTSD show more frequent displays of hostility and aggression as well as fewer expressions of acceptance as compared to those without PTSD (Miller et al. 2013; Taft et al. 2011). A longitudinal study that looked at PTSD individuals in romantic relationships suggests that these markers can have unfavorable effects on relationship functioning over time (Meis et al. 2017).

Notably, a majority of the studies have examined these effects of PTSD in the context of romantic relationships and childhood trauma. However, it is crucial to expand on these findings in different social environments and within different contexts of trauma including that which may be experienced in the military. Nevertheless, these findings can serve as theoretical considerations that pave a window into how PTSD interferes with relationship functioning, and can guide researchers to find ways individuals with PTSD can adapt interpersonally.

4. PTSD and Cognitive Deficiencies Related to Memory and Attention

The requirement of a distinct etiologic event outside of the person, such as the trauma associated with war, differentiates PTSD from most other mental diagnoses. PTSD is further distinguishable from other anxiety-related disorders by memory disruptions and dysfunctional threat processing. Specifically, PTSD has been characterized by dysregulated emotional networks, memory deficits, and a hyper-attentive response to stimuli that is perceived as threatening (DeLaRosa et al. 2020).

Studies focusing on the cognitive memory deficits associated with PTSD have demonstrated a general inferior working memory compared to healthy individuals for both emotional and non-emotional stimuli (Nejati et al. 2018). Evidence suggests memory retrieval deficits in PTSD may result from hyper-responsive limbic systems and a failure of top-down cortical inhibition (Pitman et al. 2012).

A large area of interest within PTSD research has been focused on the attentional bias toward threats. Previous studies have indicated a significant attentional bias toward threat-related cues (Fani et al. 2012) with priority often being awarded to the most significant perceived threat (Ohman and Mineka 2001). Studies using virtual search tasks and eye-tracking concluded that attentional bias in PTSD is characterized by interference (difficulty disengaging from threat) rather than facilitation or enhanced threat detection (Pineles et al. 2009). The effects of PTSD on attention are often assessed by modified dot probe (Fani et al. 2012) or Stroop tasks (Constans et al. 2004). Regarding the Stroop paradigm, findings consistently associate disorder-related words with the largest degree of processing interference (Williams et al. 1996; Pineles et al. 2009; Felmingham et al. 2011). Pineles et al. (2007, 2009) further demonstrated those higher in PTSD showed increased interference to trauma-related words compared to those lower in PTSD. Impaired target detection among veterans with PTSD following combat-related threat distractors further suggests an increased attentional capture by threatening stimuli and difficulty disengaging from those cues (Olatunji et al. 2013).

5. PTSD and Physiological Markers

Tasks involving the perpetual search for and detection of threatening targets have been proposed to increase arousal and anxiety for those with PTSD (Mathews and MacLeod 2002; MacLeod et al. 2002; Eysenck et al. 2007; Vythilingam et al. 2007). Results from studies including eye-tracking corroborate earlier findings that those with PTSD maintain attention longer on negative stimuli (Kimble et al. 2010; Armstrong et al. 2013). Kimble et al. (2010) noted those with higher PTSD showed larger pupils when looking at negatively valenced images and had a tendency to view combat- or trauma context-related images first. Additionally, significantly greater fixations and skin conductance responses indicating autonomic arousal to initial fixations to trauma-related stimuli have been observed (Felmingham et al. 2011). In a study using nonthreatening stimuli, those with PTSD rated scenes as more threatening, and those reporting more severe hypervigilance made more saccades and fixations of shorter durations (Stewart et al. 2013). Hypervigilance conditions are also associated with significantly more fixations, fixations spread out over a greater percentage of the scene, and larger pupil size suggesting increased visual scanning and arousal even to neutral stimuli (Kimble et al. 2014).

These findings suggest that the hypervigilance associated with PTSD may have measurable physiological responses, such as those observed through eye-tracking.

While the threat processing bias associated with PTSD has often been characterized behaviorally, little is known about the neurophysiological underpinning of this bias (DeLaRosa et al. 2020). DeLaRosa et al. (2020) state that while there have been several imaging studies that have identified structural and functional abnormalities associated with PTSD, there have been few studies utilizing electroencephalogram (EEG). To begin to address this gap, DeLaRosa et al. (2020) administered an implicit visual threat semantic memory recognition task to veterans with and without PTSD. Results revealed veterans with PTSD had slower reaction times for threatening stimuli. Trauma-specific effects were observed in the frontal regions, with theta band EEG power reductions for the threatening combat scenes in the PTSD group. A moderate negative correlation was found between trauma-specific frontal theta power and hyperarousal symptoms measured by the Clinician-Administered PTSD Scale (CAPS). An earlier study, using a sentence completion design, revealed those with PTSD were more likely to endorse threat responses as sensible and demonstrated event-related potential (ERP) responses consistent with expecting threat endings to the sentences (Kimble et al. 2012). Similar to DeLaRosa et al. (2020), this study reported a moderate negative correlation between trauma-specific frontal theta power and hyperarousal symptoms measured by the CAPS.

In addition to physiological differences being associated with eye gaze behavior and brain activity, several studies have shown cardiovascular manifestations of PTSD as well. Specifically, it has been reported that those with PTSD have increased resting heart rate, increased startle reaction, and increased heart rate and blood pressure in response to traumatic stimuli such as slides, sounds, or scripts (Bedi and Arora 2007; Paulus et al. 2013). When exposed to an orthostatic stressor, diastolic blood pressure was shown to increase over time in the non-PTSD veterans, suggesting a reduced autonomic response in those with PTSD (Orr et al. 1998). Heart rate variability (HRV), a measure of the autonomic nervous system's functioning, reflects an individual's ability to adaptively cope with stress. Veterans with combat-related PTSD have shown significantly depressed HRV compared to those without PTSD (Tan et al. 2010).

Another avenue for physiological markers of PTSD may be found through auditory processing. When considering auditory processing in the PTSD population, it has been common to use ERP paradigms to investigate differences compared to a control population. There are generally three different ERP waveforms that are studied: the P50, the P200, and the P300. With the P50, previous research has found that individuals with PTSD exhibit decreased habituation to auditory stimuli (Gillette et al. 1997; Ghisolfi et al. 2004; Hunter et al. 2011). In particular,

correlations between the P50 component and arousal scores in PTSD have been observed (Hunter et al. 2011). Alongside ERP research, it is common to correlate ERP components with subscales of PTSD measures (e.g., CAPS-DX), including hyperarousal. However, correlational results of PTSD subcomponents, like arousal, and ERP components have been mixed (Gillette et al. 1997; Metzger et al. 2002; Karl et al. 2006; Hunter et al. 2011). By including multiple physiological measures in our study, we hope to create a stronger and more integrated model of behavior and physiology related to PTSD and state changes induced by our manipulations.

6. Special Considerations for Experimental Protocols

Part of the criteria for a PTSD diagnosis is that a person persistently re-experiences the traumatic event in at least one way, such as through persistent and distressing recollections or dreams, behaving or feeling as though the trauma were recurring, intense psychological distress, or physical reactivity upon exposure to internal or external stimuli reminiscent of the traumatic event. Exposure to these types of stimuli may then trigger a psychological reaction reminiscent of the trauma. While some of these triggers may be obvious (e.g., loud explosions), some may be very specific to the individual's traumatic experience (e.g., a song that was playing at the time of the trauma). Also included in the PTSD diagnostic criteria is that the person not only experiences these triggers but that they actively avoid them. To be diagnosed with PTSD, a person must show that they persistently avoid stimuli associated with the trauma (see Appendix C for full diagnostic criteria). Therefore, when we design experiments that may expose individuals with PTSD to possible triggers (e.g., combat related images), it is critical that we incorporate appropriate supports and risk mitigations into our protocols.

It is important to be as transparent as possible about your design and manipulations when it comes to potential triggers. For example, clear language should be included in any consent forms that describe the types of stimuli participants may be exposed to should they choose to participate. Furthermore, as with any informed consent, it should declare that participants may withdraw at any time without penalty. Researchers should be especially conscientious with checking in with participants and unobtrusively monitoring participants throughout the study to ensure their comfort, as military personnel may be especially reticent to share their feelings of distress. Participants should be reminded throughout the experiment, and not just at the initial consent, that they may withdraw from the study at any point and without penalty.

In order to be considerate of triggers, it would be helpful to provide participants a sample of any high-stress or possibly triggering stimuli used in the study prior to

participants starting the experimental task. This initial exposure will help participants to decide whether the experiment may be triggering for them beyond their coping ability. Researchers should then check in with participants on their state following this early exposure and again inquire as to whether the participants would like to continue to the task.

Researchers should include in their protocol relevant supports that will be available should the participants become overwhelmed at any point. This may include having a trained and licensed psychologist on site and available to intervene or access to mental health supports. For example, if participants become overwhelmed at any point during the study, they may be referred to local and accessible clinics where they would have access to mental health experts. Researchers including this population in their studies and without a clinician on staff can reach out to local clinics to seek guidance on their particular protocols. One suggestion is to compile an information sheet to share with all the participants in the study. This information sheet should provide a list of local clinics including key information related to each (e.g., phone, who is eligible for services, what types of services are offered, location, hours, and a website). Researchers without a clinician on their study may not be qualified to discuss PTSD scores (e.g., from the PTSD Checklist [PCL]) with participants and therefore should plan to distribute the information sheet to all participants rather than single out those identified as possibly having PTSD through the study.

It is possible that experiencing a trigger may lead to a strong response. If at any point during the course of a study researchers perceive or witness any form of physical, mental, or psychological harm, or threat of harm among participants, the study should immediately be halted and the participant in question should be offered access to emergency medical and/or mental health providers. In the event that a participant reports wishing to harm themselves or others, or is observed experiencing any severe signs of stress (e.g., respiratory or cardiac), the research staff should immediately call 911. Appendix D provides an example of how researchers might provide transparency regarding potential triggers and details available supports that are in place.

Per guidance on planning for respondent distress from the Public Responsibility in Medicine and Research (PRIM&R) 2020 Advancing Ethical Research Conference, researchers should include a distress log to document any distress events. In the event that a participant experiences elevated levels of distress, the Institutional Review Board (IRB) should be notified immediately. An example distress log is provided in Appendix E.

In addition to the supports and expertise, having a clinician on your research staff enables the ability to include more rigorous assessments of PTSD, such as the CAPS. CAPS, the gold standard for diagnosing PTSD, is a 30-item structured interview that can be used to make current or lifetime diagnoses of PTSD as well as assess symptoms. Without a clinician on your staff or access to CAPS scores or medical records, you may be limited to self-report of diagnoses and/or the use of a PTSD assessment scale such as the PCL. The PCL, while not generally a diagnostic tool by itself, may be scored to provide a presumptive diagnosis. This differentiation is important to note as individuals who self-report as being diagnosed with PTSD or present as having PTSD symptoms on the PCL or similar scale, versus individuals who are classified as being medically diagnosed with PTSD, may have differential effects when compared. When using measures to indicate a likely PTSD diagnosis (binary) or classify PTSD symptom severity (continuous), it is important to consider different thresholds or definitive classifications and how they might differ per sample. For example, the PCL-5 currently has five different ways to classify an individual with PTSD, with one of them choosing a cutoff score that is dependent on the characteristics of the population (National Center for PTSD n.d.). There are also PCL versions that are specific to military (PCL-M) and civilian (PCL-C) populations. These two versions are similar, yet have instructions and phrasing referring to the traumatic events that are specific to each group. This makes the PCL a versatile tool when designing and recruiting for a study involving a potential PTSD population. It may be beneficial to use more than one reliable measure to classify PTSD symptomology and severity and to report justifications for classifications used in your analysis. This is especially true if you are not using a medical diagnosis.

Perhaps the best consideration researchers should take when leveraging a PTSD population is to be considerate and thoughtful in their experimental design. As with any study, researchers should carefully consider whether the benefits from conducting this research outweigh the risks that may be associated with it (e.g., participants potentially experiencing a negatively triggering event). Along with conducting a well-informed literature review to form a solid basis for their study, researchers should consider consulting with subject matter experts (SMEs) related to this field (clinicians, experienced researchers in this area, etc.) and/or members of the population of interest to gain key insights that may better inform their research design. Researchers should work closely with these SMEs and their Human Research Protection Program's IRB to ensure they are building proper supports into their protocol and maintaining all human safety considerations to the highest standard. This population should only be leveraged when it will clearly further scientific gain and ideally in a way that may benefit this population directly.

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**Appendix A. Example Measures to Include in a Study Including a
Posttraumatic Stress Disorder (PTSD) Population**

Demographic Questionnaire: Researchers should ask participants to provide general demographic information (e.g., sex and age) as well as military-specific demographics (Military Occupational Specialty, years in service). See Appendix B for an example.

PTSD Checklist for DSM-IV Military (PCL-M): The PCL-M was developed specifically for a military population and asks about symptoms in response to “stressful military experiences.” The PCL-M is often used with both active duty military personnel and veterans. The suggested cut-off for PTSD at specialized medical clinics or Veterans Affairs primary care is a total score of 36 or above.¹ The PCL generally has high internal consistency (alpha = 0.75–0.80; Wilkens et al., 2011).²

Combat Exposure Scale (CES): The CES is a seven-item self-report measure that assesses wartime stressors experienced by combatants along a five-point Likert scale. The CES was developed for both research and clinical settings and classifies participants into one of five categories of combat exposure ranging from “light” to “heavy.” Reliability for this scale was reported as alpha = 0.85 (Keane et al., 1989).³

Adult Attention-Deficit Hyperactivity Disorder (ADHD) Self-Report Scale (ASRS-v1.1) Symptom Checklist: This measure consists of 18 DSM-IV-TR criteria. Part A of the questionnaire consists of the six questions found to be the most predictive of symptoms consistent with ADHD.

Big Five Inventory (BFI): The BFI is a self-report personality inventory designed to measure the big five personality dimensions (openness, conscientiousness, extraversion, agreeableness, and neuroticism). The BFI consists of 44 items of short phrases that participants are asked to indicate how much they identify with these statements on a five-point Likert scale.

¹ National Center for PTSD. Using the PTSD checklist for DSM-IV (PCL). US Department of Veterans Affairs; n.d. https://www.ptsd.va.gov/professional/assessment/documents/PCL_handoutDSM4.pdf.

² Wilkens KC, Lang AJ, Norman SB. Synthesis of the psychometric properties of the PTSD checklist (PCL) military, civilian, and specific versions. *Depression and Anxiety*. 2011;28(7):596–606. <https://doi.org/10.1002/da.20837>

³ Keane TM, Fairbank JA, Caddell JM, Zimering RT, Taylor KL, Mora CA. (1989). Clinical evaluation of a measure to assess combat exposure. *Psychological Assessment: A Journal of Consulting and Clinical Psychology*. 1989;1(1):53–55. <https://doi.org/10.1037/1040-3590.1.1.53>

Appendix B. Example Demographics Questions

During the study, we will be collecting physiological data, and accurate health history information is important for correctly interpreting physiological data. A very brief medical history must be obtained as part of the experimental protocol. It is very important that you be completely honest. This information will be kept strictly confidential.

Eligibility Verification:

Are you fluent in English? Y/N

Do you have normal or corrected to normal vision? Y / N

Are you color blind? Y / N

Have you experienced any significant brain trauma or brain injuries in the last three months? Y / N

Do you have any heart problems? Y / N

Can you hear most environmental sounds? Y / N

General Demographics:

Sex: ___ M ___ F

Age: _____ years

Education level:

- Less than high school
- High school graduate
- Associate's degree
- Bachelor's degree
- Master's degree
- Ph.D./Professional degree

Ethnicity:

- Hispanic or Latino
- Not Hispanic or Latino
- No Response

Race:

- American Indian or Alaska Native
- Asian
- Black or African American
- Native Hawaiian or Other Pacific Islander
- White
- Two or More Races

- No Response

What is your handedness preference?: right, left, ambidextrous

Military status: Active Duty, Reserve, National Guard, Veteran

What military branches do/did you serve in? Army, Marines, Air Force, Navy, National Guard

What is/was your time in service? _____ years

MOS _____ Military _____ Occupational
Specialty: _____

What is/was your rank?: _____

How many deployments have you been sent on? _____

Please list the locations and dates of your deployments:

Location	Date (mm/yyyy – mm/yyyy)

Do you have combat experience? ___ Yes ___ No

Please list the locations and dates of being exposed in harms way (combat):

Location	Date (mm/yyyy – mm/yyyy)

Do you have normal hearing? ___ Yes ___ No

If No, briefly explain:

Have you ever experienced a concussion or lost consciousness for greater than 30 minutes?

Yes No

If Yes, briefly explain:

Have you been diagnosed with any significant brain trauma or brain injuries such as mild Traumatic Brain Injury (mTBI)?

Yes No

If Yes, briefly explain:

Have you ever been diagnosed with Posttraumatic Stress Disorder (PTSD)?

Yes No

If Yes, briefly explain:

Please indicate time of onset: childhood adult both

Was this diagnosis combat related? Yes No

Have you ever been diagnosed as having:

Depressive Disorder Yes No

Substance Use Yes No

Anxiety Disorder Yes No

Panic Attacks Yes No

Attention Deficit Disorder Yes No

Attention deficit hyperactivity disorder Yes No

Are you currently using drugs or medications of any kind? Yes No

If Yes, please list here:

Do you use tobacco products of any kind?

Yes No

If Yes, describe what kind how often/much:

What is your average daily caffeine consumption (approximate number of cups of coffee, tea, or caffeinated soda)?

_____ cups of caffeinated beverages per day

What is your average weekly alcohol consumption (approximate number of alcoholic beverages)?

_____ number of alcoholic beverages per week

How many hours of sleep do you average per night?

_____ hours

**Appendix C. Diagnostic Criteria for Posttraumatic Stress Disorder
(PTSD)**

PTSD was first formally included as an official diagnosis in 1980, in the third revision of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III) as an anxiety disorder.^{1,2} Since the first inclusion of PTSD as an official diagnosis in the DSM,¹ later editions and text revision have refined the diagnostic criteria for PTSD, the most current being the DSM-V.³ The current DSM-V uses eight primary diagnostic criteria (A through H) to determine a diagnosis of PTSD.

Criterion A necessitates a person experiencing or witnessing a traumatic event that is characterized by an “actual or threatened death, serious injury, or sexual violence” (p. 271), to oneself or others. If the event is not directly experienced, it may be witnessed, or in the event that the trauma occurred to a close family member of friend, learning that the trauma occurred. In addition to meeting requirements for Criterion A, to receive a diagnosis of PTSD, an individual must also experience the required symptoms from across the criteria, as specified below, for a period greater than one month as stipulated by Criterion F.

Criterion B requires the presence of one or more intrusive symptoms associated with the traumatic event and beginning after the event occurred. These intrusive symptoms may present as persistent and distressing recollections or dreams, behaving or feeling as though the trauma were recurring, intense psychological distress or physical reactivity upon exposure to internal or external stimuli reminiscent of the traumatic event.

Criterion C requires the persistent avoidance of internal (e.g., memories, thoughts, or feelings) or external (e.g., people, places, situations) stimuli associated with the trauma (p. 271).

To meet the requirements for Criterion D, a person must experience negative alterations in cognition and mood associated with the trauma and beginning or worsening after the event occurred. This must be evidenced in at least two ways, such as through the inability to recall a critical aspect of the traumatic event, persistent and exaggerated negative beliefs or expectations about themselves, others, or the world, persistent distorted cognition about the cause or consequences of the trauma leading to blaming themselves or others, persistent negative emotional state, decreased interest or participation in important activities, feelings

¹ American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 3rd ed. American Psychiatric Association; 1980.

² Friedman MJ, Keane TM, Resick PA. *Handbook of PTSD: science and practice*. Guilford Press; 2007.

³ American Psychiatric Association. *Diagnostic and statistical manual of mental disorders: DSM-5*. 5th ed. American Psychiatric Association; 2013.

of detachment/estrangement from others, or a persistent inability to experience positive emotions.

Criterion E requires an individual to experience marked changes in arousal and reactivity associated with the trauma, as evidenced by at least two symptoms. This may include irritable or angry behavior, reckless or self-destructive behavior, hypervigilance, exaggerated startle response, or difficulties with concentrating or sleeping.

Criterion F specifies the duration of the disturbance—as defined through criteria B, C, D, and E—is greater than one month.

According to Criterion G, the individual must also experience “clinically significant distress or impairment in social, occupational, or other important areas of functioning” (p. 272).

Additionally, Criterion H requires the disturbance experienced is not attributable to the physiological effects of a substance or other medical condition.

It is also not atypical for individuals to experience a delay in the onset of symptoms; if at least six months have gone by after the traumatic event before the occurrence of symptoms or all diagnostic criteria being met, the specifier “with delayed expression” (p. 271), is added to the diagnosis. It may also be specified whether a person meets criteria for PTSD with depersonalization (persistent or recurrent feeling of being detached) or derealization (persistent or recurrent feeling of unreality).

Appendix D. Example Informed Consent Potential Risk Section

The following excerpt is a sample taken directly from the approved Informed Consent for ARL 21-104, thus all aspects of this example may not apply directly to your study (e.g., study location and available resources). It may also help to include additional pieces of information not provided here, like whether there is a cost associated with accessing available resources. You can also provide more specific content, such as an information sheet. For instance, in ARL 21-104 we provided all participants with an information sheet that contained details on four local mental health clinics available to them including the contact information (e.g., phone and website), who was eligible for care, what type of care was provided, and hours of operation.

Reading negative words that describe people, places, and things could be uncomfortable, or trigger you to recall or remember emotional events that may also cause unwarranted stress. Similarly, viewing stressful stimuli such as those associated with combat or hearing loud noises may be triggering. You will be provided a sample of the high stress features of the environment before completing the visual search task. You will be allowed to take your time completing any assessments that require more time. If for any reason you feel overwhelmed, you can stop, rest, and/or speak to one of the researchers. If you feel you may need medical assistance then you will have access to on-post care.

If, for any reason, you feel overwhelmed at any point during the study, you may be referred to one of four mental health clinic locations on JBSA where you will have access to post mental health experts. Additionally, if at any point during the course of the study, the research staff perceive or witness you engaging in any form of physical, mental, psychological harm, or threat of harm, the study will be halted and you will be offered access to emergency medical and/or mental health providers at Fort Sam Houston.

Appendix E. Distress Log

PROTOCOL: Title

DISTRESS LOG

Seq.	Date	PID#	Description of Event	Participant Distress level (0-10)	Distress level (Low/Mod or High)	IRB notified	Resources provided
1			Date Started: _____ Date Stopped: _____			Yes <input type="checkbox"/> No <input type="checkbox"/> Date: _____	
2			Date Started: _____ Date Stopped: _____			Yes <input type="checkbox"/> No <input type="checkbox"/> Date: _____	
3			Date Started: _____ Date Stopped: _____			Yes <input type="checkbox"/> No <input type="checkbox"/> Date: _____	
4			Date Started: _____ Date Stopped: _____			Yes <input type="checkbox"/> No <input type="checkbox"/> Date: _____	
5			Date Started: _____ Date Stopped: _____			Yes <input type="checkbox"/> No <input type="checkbox"/> Date: _____	

Term Index: Sequence (SEQ)- order in which events are recorded; Date- refers to date of reported incidence; Participant ID- number issued to participant at study entry; Description of event- describe in detail the event, nature of the event, and when it started and stopped; Participant Distress Level- indicate the participant self-reported level of distress of the event-(0=no stress to 10=Extremely stressed); Distress Level – refer to Distress Log Reference page to indicate level of signs of distress (low/moderate or high); IRB notified- Indicate whether event is considered an adverse event (AE) report to IRB as appropriated; Resources provided- indicate specific referrals or support information given to participant.

Principal Investigator Signature _____ Date _____

Date Submitted to IRB _____ Researcher initials _____

DISTRESS LOG REFERENCE PAGE¹

Levels of Signs of Distress:

Low/Moderate	High
<ul style="list-style-type: none">• Changes in tone of voice• Being easily distracted• Sudden quietness	<ul style="list-style-type: none">• Crying• Overly emotional• Angry• Disassociated

Course of Action:

Level of Distress	Course of Action
Low to Moderate	Pause or stop
High without threat of harm	Stop, offer resources including referring or connecting to a counselor to the SAMMC or Moreno Clinic
High with threat of harm	Immediately stop, connect with counselor at SAMMC or Moreno if available and Call 911.

***Immediate notification to the IRB if a respondent experiences elevated levels of distress.**

List of Reference Available:

- **The National Suicide Prevention Lifeline** – available 24 hours, 800-273-8255
- **List any local clinics or available resources here**

¹ Levin K, Zack S, Silva M. Planning for respondent distress [PowerPoint slides]. PRIMR 2020 Advancing Ethical Research Conference; 2020.

List of Symbols, Abbreviations, and Acronyms

ADHD	Attention-Deficit Hyperactivity Disorder
APA	American Psychological Association
ARL	Army Research Laboratory
BFI	Big Five Inventory
CAPS	Clinician-Administered PTSD Scale
DBP	diastolic blood pressure
DEVCOM	US Army Combat Capabilities Development Command
DSM	Diagnostic and Statistical Manual of Mental Disorders
EEG	electroencephalogram
ERP	event-related potential
HRV	heart rate variability
IRB	Institutional Review Board
NVVRS	National Vietnam Veterans Readjustment Study
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
PRIM&R	Public Responsibility in Medicine and Research
PTSD	posttraumatic stress disorder
PCL	PTSD Checklist
SA	situational awareness
SME	subject matter expert
TBI	traumatic brain injury

1 DEFENSE TECHNICAL
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TECH LIB

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BLDG 5400 RM C242
REDSTONE ARSENAL AL
35898-7290

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6662 GUNNER CIRCLE
ABERDEEN PROVING
GROUND MD
21005-5201

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875 N RANDOLPH STREET
BLDG 87
ARLINGTON VA 22203-1986

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NATICK MA 01760-2642

1 OSD OUSD ATL
(PDF) HPT&B B PETRO
4800 MARK CENTER DRIVE
SUITE 17E08
ALEXANDRIA VA 22350

ABERDEEN PROVING GROUND

13 DEVCOM ARL
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Y CHEN
P FRANASZCZUK
K MCDOWELL
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G BOYKIN
FCDD RLH FB
J GARCIA (A)
H ROY
FCDD RLH FC
J TOURYAN (A)
T ROHALY
FCDD RLH FD
A MARATHE