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Individual differences in combat experiences and error-related brain activity in OEF/OIF/OND veterans

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ABSTRACT

Increased error-related negativity (ERN) has been implicated in the pathophysiology of multiple forms of psychopathology. Although there is increasing evidence that the ERN can be shaped by environment and experience, no studies to date have examined this question in a clinical sample. In the current study, we examined the influence of combat exposure on the ERN using electroencephalogram (EEG) in a sample of military veterans with a high prevalence of psychopathology. Participants included sixty-seven U.S. military veterans from Operations Enduring Freedom, Iraqi Freedom, and New Dawn (OEF/OIF/OND). The degree of combat exposure was assessed using the Deployment Risk and Resilience Inventory-2 (DRRI-2) and Combat Exposure Scale (CES). A well-validated flanker task was used to elicit the ERN during continuous EEG recording. Results revealed that veterans who reported experiencing greater combat exposure exhibited a more enhanced ERN, even when adjusting for broad anxiety and posttraumatic stress disorder (PTSD) symptoms. The association between combat exposure and ERN was not moderated by PTSD symptom severity. The current study demonstrates that greater combat exposure is associated with a more enhanced ERN among OEF/OIF/OND veterans. This enhanced ERN may be one mechanism that places veterans at greater risk for developing psychiatric disorders following exposure to combat. Future longitudinal studies are needed to directly test whether the ERN mediates the relation between level of combat exposure and the development of internalizing disorders.

1. Introduction

Increased neural response to errors has been implicated in the pathophysiology of multiple forms of psychopathology, including anxiety disorders and alcohol use disorders (Gorka et al., 2016, 2017; Weinberg et al., 2012). To capture these effects at the psychophysiological level, researchers have utilized the error-related negativity (ERN), a negative-going deflection in the event-related potential (ERP) waveform that occurs approximately 50–100 ms following the commission of an error (e.g., Hajcak and Foti, 2008). The ERN is thought to be generated by the anterior cingulate cortex (ACC), a region associated with responding to negative emotional stimuli and cognitive conflict (Bush et al., 2000). Consistent with the notion that the ERN is a measure of defensive reactivity and threat responding, the ERN amplitude is positively associated with other indices of threat reactivity such as the magnitude of the startle reflex following the commission of an error (Meyer et al., 2017a).

Recent research suggests that negative environmental experiences can shape neural response to errors (e.g., Endrass et al., 2010; Meyer and Gawlowska, 2017; Riesel et al., 2012), albeit with mixed evidence (Moser et al., 2005). For example, the ERN has been shown to be potentiated when errors are made among highly anxious individuals, relative to less anxious individuals (Meyer and Gawlowska, 2017). In a separate study, larger increases in negative affect following a negative mood induction were associated with a more enhanced ERN (Olvet and Hajcak, 2011). However, not all studies have found that inducing negative affect potentiates the ERN, especially when the induction does not involve making mistakes. For instance, one study showed that adults with spider phobia did not exhibit a change in the ERN after being exposed to a tarantula while performing the task (Moser et al.,

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2005). A limitation to the majority of previous studies examining the relation between environmental experiences and ERN is the examination of negative experiences in the laboratory (i.e., exposure to negative images, scenes, and events) versus capturing exposure to stressful or threatening stimuli in the natural environment. Although no studies to date have examined whether exposure to negative experiences (i.e., trauma) influences the ERN, there is evidence from neuroimaging studies that trauma history can influence alterations in structure, function, and connectivity of several neural regions involved in cognitive and emotional processing, including the ACC (for a review, see Thomason and Marusak, 2017), the region in which the ERN is thought to be localized (Bush et al., 2000).

One population experiencing a high degree of trauma and stress is military service members exposed to combat during deployment. Due to the inherently dangerous nature of a war-zone, veterans in combat might be particularly reactive to the commission of an error, as these errors may threaten their safety. For example, a soldier may die by accidentally stepping on an improvised explosive device (IED), or may harm a fellow soldier by misfiring weapons. Veterans may therefore develop a learned sensitivity to the commission of errors, which could increase the ERN and facilitate survival during combat. However, this enhanced ERN may become problematic in the long term by making veterans exhibit overactive performance monitoring and excessive worry outside of dangerous environments. Thus, an enhanced ERN response might be one mechanism implicated in the high documented rates of psychopathology among veterans returning from combat (Hoge et al., 2006).

Although no studies to date have directly examined whether the degree of combat exposure is associated with the magnitude of the ERN, researchers have compared ERN amplitude between veterans and healthy controls participants. For examples, studies have failed to find a significant difference in the magnitude of ERN when comparing healthy controls to veterans with PTSD (Rabinak et al., 2013; Swick et al., 2015). However, one study showed that combat-exposed veterans with no history of psychopathology exhibited a smaller ERN relative to healthy controls and combat-exposed veterans with PTSD (Rabinak et al., 2013). Notably, none of these prior studies examined how individual differences in the degree of combat exposure may influence ERN amplitude. However, there is evidence from behavioral studies to suggest that attention to threat is directly impacted by the amount of exposure to war-related stressors in the laboratory (Bar-Haim et al., 2010).

In the current study, we therefore sought to examine the influence of combat exposure on ERN in a sample of military veterans post-deployment to Iraq or Afghanistan during Operations Enduring Freedom, Iraqi Freedom, and New Dawn (OEF/OIF/OND). To assess combat experiences, we utilized the widely-validated Deployment Risk and Resilience Inventory-2 (DRRI-2; Vogt et al., 2013) and Combat Exposure Scale (CES; Keane et al., 1989). Both of these measures include a series of questions regarding combat experiences (deployment factors), such as witnessing of civilians or combatants being killed or seriously injured, being exposed to fires, and other combat-related events. Consistent with the notion that ERN can be influenced by environmental experiences (Olvet and Hajcak, 2011; Meyer and Gawlowska, 2017; but see Moser et al., 2005), we predicted that there would be a relationship between the ERN and combat exposure, such that veterans with a greater number of combat experiences would exhibit a more enhanced ERN. Finally, to explore whether the current effects were specific to the degree of combat exposure (versus other forms of life stress), we also examined whether ERN amplitude was related to pre- and post-deployment stressors.

Table 1
Characteristics of sample.

	Mean (SD)
Age	32.75 (5.80)
CAPS	43.89 (29.40)
BAI	16.02 (12.94)
DRRI-2-CE	36.55 (19.43)
CES	16.27 (9.66)
ERN-Error (uV)	1.05 (6.26)
ERN-Correct (uV)	6.40 (5.10)
Error RT (ms)	335.70 (79.55)
Correct RT (ms)	428.43 (107.46)
Accuracy	0.89 (0.11)
	N (%)
Sex (Male)	55 (82.10)
Current PTSD	32 (47.80)
Current MDD	16 (23.90)
Current OCD	4 (6.0)
Current panic disorder	14 (20.90)
Current GAD	4 (6.0)
Current social anxiety	5 (7.50)
Current alcohol abuse	8 (11.90)
Current alcohol dependence	15 (22.4)
Current substance abuse	3 (4.50)
Current substance dependence	10 (14.19)

Note: CAPS = Clinician-Administered PTSD Scale; BAI = Beck Anxiety Inventory; DRRI-2-CE = Deployment Risk and Resiliency Inventory – Combat Experiences Scale; CES = Combat Exposure Scale; ERN = Error Related Negativity; RT = Response Time; PTSD = Post Traumatic Stress Disorder; OCD = Obsessive Compulsive Disorder; GAD = Generalized Anxiety Disorder; MDD = Major Depressive Disorder.

2. Methods

2.1. Participants

Sixty-seven participants were recruited from the Jesse Brown VA Medical Center with a wide range of PTSD symptoms. All participants were screened using M.I.N.I. (Mini International Neuropsychiatric Interview) to assess for psychiatric diagnoses and CAPS (Clinician-Administered PTSD Scale, CAPS-IV) to assess for PTSD symptoms. Table 1 displays a summary of the diagnostic data among the participants in the study. Exclusionary criteria in the current study included a history of schizophrenia, clinically significant neurological or medical condition, and alcohol or drug use that would interfere with completion of the study protocol.

2.2. Measures

2.2.1. Clinical measures

Diagnostic criteria were assessed according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and using the Mini-Interactional Neuropsychiatric Interview (MINI; Sheehan et al., 1998). The Clinician-Administered PTSD Scale (CAPS; Blake et al., 1995) was administered to all participants to determine PTSD symptom severity. Participants also completed the well-validated Beck Anxiety Inventory (BAI; Beck & Steer, 1990) to assess for symptoms of anxiety over the past week.

2.2.2. Combat exposure and stress

Participants were administered the DRRI-2 (Deployment Risk and Resilience Inventory-2; Vogt et al., 2013), a questionnaire with high validity and reliability designed to assess various aspects relating to deployment. The DRRI-2 includes 17 scales measuring pre-deployment (prior stressors and family functioning during childhood), deployment (including combat experiences and perceived threat) and post-deployment factors (stressors, social support, and family functioning). Each section comprises of a series of questions for which the participants