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Intact error monitoring in combat Veterans with post-traumatic stress disorder

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ABSTRACT

The error-related negativity (ERN) is a neuroelectric signature of performance monitoring during speeded response time tasks. Previous studies indicate that individuals with anxiety disorders show ERN enhancements that correlate with the degree of clinical symptomology. Less is known about the error monitoring system in post-traumatic stress disorder (PTSD). PTSD is characterized by impairments in the regulation of fear and other emotional responses, as well as deficits in maintaining cognitive control. Here, combat Veterans with PTSD were compared to control Veterans in two different versions of the flanker task ($n=13$ or 14 per group). Replicating and extending previous findings, PTSD patients showed an intact ERN in both experiments. In addition, task performance and error compensation behavior were intact. Finally, ERN amplitude showed no relationship with self-reported PTSD, depression, or post-concussive symptoms. These results suggest that error monitoring represents a relative strength in PTSD that can dissociate from cognitive control functions that are impaired, such as response inhibition and sustained attention. A healthy awareness of errors in external actions could be leveraged to improve interoceptive awareness of emotional state. The results could have positive implications for PTSD treatments that rely on self-monitoring abilities, such as neurofeedback and mindfulness training.

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1. Introduction

The capacity for self-monitoring is critical for effective performance in everyday tasks. If we make mistakes, the ability to detect and correct our errors helps us stay on track. Altered self-monitoring is a core feature of many psychiatric disorders, with deficient monitoring seen in schizophrenia (Frith and Done, 1989; Turken et al., 2003), and excessive monitoring in obsessive compulsive disorder (OCD) (Salkovskis, 1999; Gehring et al., 2000). Numerous studies have implicated the medial frontal cortex (MFC), especially the anterior cingulate cortex (ACC), in this crucial executive control function (Carter et al., 2001; Rushworth et al. 2004; Posner et al. 2007; Ridderinkhof et al. 2007; Ullsperger et al., 2014).

A key brain indicator of performance monitoring is the error-related negativity (ERN), a prominent electrophysiological response that occurs around the time an error is made (Falkenstein et al., 1991; Gehring et al., 1993). This event-related potential (ERP) component peaks about 50–100 ms after an erroneous response, showing maximal amplitude at fronto-central midline scalp electrodes (reviewed in Gehring et al., 2012). It is generally larger when accuracy is emphasized over speed, and when errors carry greater motivational significance. Lesion and dipole modeling studies suggest that the dorsal ACC is a major neural generator of the ERN (Dehaene et al., 1994; Holroyd et al., 1998; Swick and Turken, 2002; Stemmer et al., 2004), with contributions from lateral prefrontal cortex (Gehring and Knight, 2000; Ullsperger et al., 2002) and orbitofrontal cortex (Turken and Swick, 2008; Solbakk et al., 2014) as well.

Parallel to the alterations in self-monitoring behavior, clinical populations can exhibit changes in ERN amplitude. Individuals with schizophrenia show reductions in the ERN (Alain et al., 2002; Mathalon et al., 2002), whereas those with generalized anxiety disorder (GAD) and OCD show increases (Gehring et al., 2000; Endrass and Ullsperger, 2014; Xiao et al., 2011). The findings in major depressive disorder are mixed, with some studies showing increases in ERN amplitude (Chiu and Deldin, 2007; Holmes and Pizzagalli, 2008; Aarts et al., 2013) and others decreases (Ruchsow et al., 2006) or no difference (Compton et al., 2008; Schrijvers et al., 2009). Co-morbid conditions that occur with depression may

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account for some of the mixed results. For instance, Weinberg et al. (2012) replicated the typical finding of ERN enhancement in GAD, but found that patients with co-morbid anxiety and depression did not differ from controls.

Post-traumatic stress disorder (PTSD) has traditionally been classified as an anxiety disorder that can develop after a traumatic event (DSM-TR-IV: American Psychiatric Association, 2000). According to those criteria, PTSD is characterized by three symptom clusters: (1) re-experiencing of intrusive memories, such as flashbacks and nightmares; (2) avoidance of stimuli associated with the trauma and feelings of emotional numbing; and (3) hyperarousal symptoms such as hypervigilance to surroundings, increased startle, and insomnia.[1] Because of the serious hyperarousal symptoms in particular, one might predict that PTSD would be associated with larger ERNs and an exaggerated sensitivity to errors, accompanied by maladaptive signs of hypervigilance in everyday life. Thus, an important line of inquiry is whether individuals with PTSD show changes in ERN amplitude. This is particularly salient in light of the structural and functional alterations in MFC observed in this disorder (Hamner et al., 1999; Shin et al., 2001; Rauch et al., 2003; Kim et al., 2005).

Two previous studies have addressed whether the electrophysiological indices of error monitoring are altered in PTSD (Clemans et al., 2012; Rabinak et al., 2013). The first paper focused on time-frequency analysis but informally reported an intact ERN in civilians with PTSD (Clemans et al., 2012). The second study found comparable ERNs in healthy civilian controls and combat Veterans with PTSD, strongly suggesting that PTSD does not affect ERN amplitude (Rabinak et al., 2013). In contrast, combat-exposed Veterans without PTSD showed a drastic reduction in ERN relative to both the PTSD and the civilian control groups (Rabinak et al., 2013). However, the paper did not report whether the Veterans had sustained traumatic brain injuries (TBIs) during their service in Iraq or Afghanistan. Approximately 20% of Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) Veterans have sustained TBIs, the majority of which are mild in severity (Tanielian and Jaycox, 2008; Fischer, 2014). TBI can be associated with reductions in ERN (Larson et al. 2007, 2009), so one cannot exclude the possibility that the combat-exposed control Veterans experienced more severe brain injuries than the Veterans with PTSD.

Three recent studies have looked at the effects of mTBI (or concussion) on the ERN in young athletes, with mixed results (Pontifex et al., 2009; Larson et al., 2012; De Beaumont et al., 2013). Pontifex et al. (2009) tested athletes with self-reported mTBI(s) and observed a reduction in ERN peak amplitude at the FCz electrode site. In contrast, Larson et al. (2012) tested a somewhat similar population of young adults with self-reported mTBI (s) due to sports injuries (69%) and other causes. No difference in ERN amplitude was found, even when measured in the same way as in the Pontifex et al. (2009) study. Finally, De Beaumont et al. (2013) tested athletes with two or more mTBIs, who showed ERN reductions in two separate experiments. It's unclear why the results were discrepant in these studies, but differences in the populations tested (including age at injury and time post-injury) and the EEG recording and analysis methods may have contributed.

To our knowledge, no studies have specifically examined the effects of mTBI on the ERN in OEF/OIF Veterans. Deployment-related changes in self-monitoring could hinder optimal transition to civilian life, particularly in military personnel exposed to blasts and other traumatic events. The brain injuries caused by blast waves may alter brain structure and function differently than impact-related injuries (Fischer et al., 2014), so the effects on the ERN are unknown.

Our previous results indicated this group is impaired on a number of cognitive control tasks, showing more errors of commission in a Go/NoGo task (Swick et al., 2012), more variable RTs (Swick et al., 2013), greater interference in an emotional Stroop task using trauma-related words (Ashley et al., 2013), and decreases in working memory performance and ERPs in a dual-task condition (Honzel et al., 2014). More pronounced deficits in these tasks were associated with greater PTSD symptom severity. Thus, one line of reasoning suggests that PTSD would be associated with impaired error monitoring and decreased ERNs, another sign of difficulties with cognitive control.

Our original prediction for the present study was that Veterans with PTSD would show increased ERNs, due to elevated vigilance and hyperarousal. This would agree with findings in other anxiety disorders. However, the majority of patients seen clinically and recruited into the study had both PTSD and mTBI, which is consistent with the observations of other investigators (Carlson et al., 2011; Taylor et al., 2012). Thus, the question is whether combat Veterans with PTSD (most with mTBI as well, but some with PTSD-only) will show deficits in error monitoring as indexed by the ERN.

Another error-related component, the error positivity (Pe), occurs after the ERN (Overbeek et al., 2005). The Pe is observed between 200–400 ms following an error, with a central–parietal scalp topography. The Pe reflects post-error processing of some sort, although the exact nature of the psychological processes is unclear (Falkenstein et al., 2000). The existing literature suggests that neither PTSD nor mTBI affect the Pe component. Rabinak et al. (2013) did not find a difference in Pe among the combat-exposed PTSD, combat-exposed control, and civilian control groups. Likewise, three separate studies failed to find a difference between mTBI patients and controls (Pontifex et al., 2009; Larson et al., 2012; De Beaumont et al., 2013).

The current study administered two different versions of the Eriksen flanker task (Eriksen and Eriksen, 1974) to Veterans with PTSD $\pm$ mTBI and Veterans without PTSD or mTBI. We initially predicted that PTSD would be associated with an exaggerated sensitivity to errors, as indicated by larger ERNs and maladaptive signs of hypervigilance in everyday life. The co-existence of mTBI could result in either a dampening of the hyperactive ERN (i.e., no net effect) or even a reduction in ERN relative to controls. The recent results of Rabinak et al. (2013) align more with the former prediction: that the ERN would be unchanged in the present population of combat Veterans with PTSD. Given the previous null findings for the Pe (Rabinak et al., 2013), we did not expect to see a difference between groups for this component.

2. Methods

2.1. Participants

2.1.1. Experiment 1

Participants were 18 Iraq and Afghanistan combat Veterans were diagnosed with combat-related PTSD (17 male, 1 female) and 16 control Veterans matched in age and gender (15 male, 1 female). None of the enrolled participants reported significant substance abuse or a history of other psychological disorders, excluding depression. Six participants (four in the patient group and two in the control group) were excluded due to incorrect task performance that resulted in an average of 247 errors. These six participants mistakenly responded to the arrow in the center of the flanker array (the relative center) and not to the arrow in the center of the screen, and were therefore excluded. The final analysis yielded $n=14$ for each group.

[1] We note, however, that PTSD is no longer classified as an anxiety disorder in DSM-5 (American Psychiatric Association, 2013), which was released after we conducted these experiments.

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