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Affective and cognitive correlates of PTSD: Electrocortical processing of threat and perseverative errors on the WCST in combat-related PTSD

Julia A. DiGangi [a,b,*], Autumn Kujawa [c], Darrin M. Aase [a,b,d], Joseph M. Babione [a], Christopher Schroth [a,b], David M. Levy [a], Amy E. Kennedy [a,b], Justin E. Greenstein [a,b], Eric Proescher [a,b], Robert Walters [a], Holly Passi [a], Scott A. Langenecker [b], K. Luan Phan [a,b,e]

[a] Mental Health Service Line, Jesse Brown VA Medical Center, 820 S. Damen Ave., Chicago, IL 60612, USA
[b] Department of Psychiatry, University of Illinois at Chicago, 1747 Roosevelt Road, Chicago, IL 60608, USA
[c] Department of Psychiatry, Pennsylvania State University, College of Medicine, 500 University Dr, Hershey, PA 17033, USA
[d] College of Health & Human Services, Governors State University, 1 University Parkway, University Park, IL 60484, USA
[e] Departments of Psychology, Anatomy and Cell Biology, University of Illinois at Chicago, 808 S. Wood St., Chicago, IL 60612, USA

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ABSTRACT

PTSD is characterized by both affective and cognitive dysfunction. Affectively, PTSD is associated with both heightened emotional reactivity and disengagement. Cognitively, perseverative thinking is a core feature of the disorder. In order to assess the interactive effects of affective and cognitive correlates of PTSD symptoms, 47 OEF/OIF/OND veterans completed an emotional faces matching task while EEG (i.e., late positive potential; LPP) was recorded, and separately completed the Wisconsin Card Sorting Test (WCST) to assess perseverative errors. There was no relationship between PTSD symptoms and either perseverative errors or EEG reactivity to faces. However, an interaction was found such that high perseverative errors on the WCST and a relatively enhanced LPP to angry faces was associated with greater PTSD symptoms, while low errors on the WCST and a relatively blunted LPP to angry faces also related to greater PTSD symptoms. These findings suggest that emotion-cognition interactions are important for understanding PTSD, and that distinct emotion-cognition constellations interact with symptoms.

1. Introduction

Of the >2 million U.S. soldiers that have been deployed to Afghanistan and Iraq, 14–16% have developed posttraumatic stress disorder (PTSD; Tanielian et al., 2008). Consequently, PTSD represents one of the most prevalent injuries incurred during Operations Enduring Freedom (OEF), Iraqi Freedom (OIF), and New Dawn (OND). A heterogeneous disorder, PTSD is characterized by both affective and cognitive dysfunction. In recent years, substantial evidence from functional neuroimaging has indicated that disruptions in prefrontal, limbic and interactive brain function may underlie the disorder. While much work has pointed to the hyperresponsivity of the amygdala in concert with hyporesponsivity of the medial prefrontal cortex (mPFC) as core neural features of the disorder, findings are not entirely consistent or disorder specific. For example, ample evidence from functional magnetic resonance (fMRI) studies have questioned amygdalar hyperreactivity as a pathognomonic marker of the disorder (Etkin and Wager, 2007; Hayes, Hayes & Mikedis, 2012; Lanius et al., 2006; Simmons and Matthews, 2012). While the precise neurophysiology of the disorder has not been fully elucidated, it is clear that broad dysregulation is a hallmark feature of PTSD and, consequently, substantial deficits in affect regulation and neuropsychological functioning have been observed (American Psychiatric Association, 2013; Scott et al., 2015).

Affectively, PTSD is characterized by both heightened emotional reactivity (i.e., intrusive and hyperarousal symptoms) and emotional disengagement (i.e., avoidance and numbing). In addition to the aforementioned fMRI studies, prior work with electroencephalography (EEG) and, more specifically, event related potentials (ERPs) have been used to identify neural biomarkers of the disorder (Lobo et al., 2015).

A complementary method of neural measurement, ERPs offer superior temporal resolution, thereby providing information that cannot be ascertained by fMRI alone. One ERP component that is particularly relevant to examining PTSD is the late positive potential (LPP). The LPP is a centro-parietal, positive-going ERP component that appears approximately 400 ms after stimulus onset and is larger for emotional (e.g., threatening) stimuli than neutral stimuli (Foti et al., 2009; Schupp et al., 2000). Specifically, the LPP is considered to be a means of tracking

* Corresponding author at: Department of Psychiatry, University of Illinois at Chicago, Chicago, IL, USA.
E-mail address: jdigangi@psych.uic.edu (J.A. DiGangi).

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motivated attention toward emotional stimuli (Hajcak et al., 2013). Because of its relation to emotional processing, the LPP offers important potential as a putative neural measure of PTSD, but, to date, has been used relatively infrequently. The small body of literature available on PTSD and the LPP paints an inconclusive picture, with some research indicating the disorder is associated with increased reactivity to threat (Lobo et al., 2014) while other studies suggest emotional disengagement to threat (Fitzgerald et al., 2016; MacNamara et al., 2013). The reason for these discrepant findings is unclear. It is plausible that the discrepancies may be attributable to individual differences. It also may be that dysregulation leads to either over- or under-responsiveness to threat in specific subsets of those with PTSD. Another plausible explanation in the heterogeneity of findings may be due to methodological differences. While both studies used emotionally provocative stimuli, the former used disturbing images of mutilated bodies and the latter used emotional faces (i.e., happy, fearful, angry).

Cognitively, PTSD has been linked to broad neuropsychological deficits across multiple domains (Scott et al., 2015). For example, several prospective, longitudinal studies of PTSD have found that lower premorbid cognitive ability is a risk factor for the subsequent development of the disorder (DiGangi et al., 2013). In the context of neuropsychological domains, executive functioning (EF) abilities are of particular salience. Broadly, EF is defined as control of complex goal-directed behavior (Royall et al., 2002; Alvarez and Emory, 2006; McCabe et al., 2010). Within the broad domain of EF, perseverative behaviors are a common clinical indicator of EF dysfunction. In particular, earlier research suggests an interaction between PTSD symptoms and perseverative thinking. Perseveration about aspects of the trauma(s) is a critical contributing factor in the development and maintenance of PTSD (Ehlers and Clark, 2000; Ehlers and Steil, 1995; Joseph et al., 1995; Wells, 2000). Moreover, substantial research has demonstrated that perseverative thinking is related to PTSD symptom severity (Ehlers et al., 1998; Ehring et al., 2008; Kleim et al., 2007; Michael et al., 2007; Murray et al., 2002). Perseverative thinking is thought to be attributable to deficits in cognitive control systems (Luria, 1966; Stuss et al., 1986), and it is this inability to regulate the content of cognition that is a putative mechanism in the emotional dysregulation inherent to PTSD (Bomyea and Lang, 2016; Levy and Anderson, 2008).

A psychometric analogue to perseverative thinking is perseverative errors (PEs) on the Wisconsin Card Sorting Task (WCST). PEs are demonstrative of inflexibility in thinking and an inability to relinquish maladaptive strategies in favor of more adaptive strategies after receiving negative feedback. Earlier work with combat veterans found veterans with PTSD made more PEs on the WCST relative to their non-combat exposed counterparts (Gilbertson et al., 2001). Similarly, (Uddo et al., 1993) found increased perseveration in combat veterans relative to non-combat exposed controls, while (Sutker et al., 1995) found executive impairment to be significantly related to PTSD among prisoners of war. However, much like the work with the LPP, the neuropsychological findings are also mixed. Although the aforementioned studies indicate PE increases are associated with PTSD, other studies found no differences in PEs between individuals with PTSD and healthy controls (e.g., Rizo-Martínez et al., 2015; Vasterling et al., 2002).

Taken together, these mixed cognitive and affective findings indicate more research is warranted. As previously noted, one way to assess threat reactivity is through the use of the LPP. The LPP has commonly been used to measure emotion processing across a broad array of disorders, including PTSD (e.g., MacNamara et al., 2013). Perseverative thinking can be assessed through administration of the Wisconsin Card Sorting Test (WCST) as regions implicated in the pathophysiology of PTSD are also related to WCST performance. For example, earlier work has demonstrated both dorsolateral and ventrolateral prefrontal cortical engagement during the WCST (Monchi et al., 2001; Monchi et al., 2004).

As research in the field of psychopathology moves toward more dimensional investigations and greater integration of biologically-relevant data to inform our understanding of disorders, both EEG and neuropsychological assessment may serve as useful biomarkers, further elucidating the neuropathophysiology of PTSD (Insel et al., 2010). Although empirical understanding of emotion-cognitive interactions in PTSD has grown in recent years, more research is necessary to determine how different cognitive and affective constellations interact to affect the development and course of PTSD. To date, no study has examined how threat reactivity and perseverative errors interact in the context of PTSD. Thus, in the present study, we examined the main and interactive effects of PEs and heighted reactivity to threatening faces (i.e., angry and fearful) on PTSD symptoms.

We used a dimensional approach in our examination of PTSD and sought to include veterans with a range of PTSD severity. Many prior neuropsychological and EEG studies of veterans have used traditional diagnostic categories, thereby excluding many veterans experiencing subthreshold PTSD symptoms and limiting generalizability to the larger veteran population. Moreover, recent work has highlighted the pressing need to examine subthreshold PTSD due to the clinical and functional implications (e.g., heightened suicide risk, greater health problems) associated with subclinical symptoms (Eekhout et al., 2016; Jakupcak et al., 2011; Pietrzak et al., 2009). Examining PTSD symptom severity as a continuous predictor of LPP and neuropsychological outcomes will aid in our understanding of these variables for OEF/OIF/OND veterans. Therefore, in the current study, we hypothesized that both perseverative errors and heightened reactivity to threat (i.e., fear and angry faces) would be related to PTSD symptoms. As previously noted, although the current literature on emotional reactivity in PTSD is mixed, more evidence suggests that PTSD is associated with heightened threat responsivity. Moreover, we also predicted that there would be an interaction between PEs and reactivity to threat such that higher levels of both PEs and threat (i.e., anger and fear) reactivity would predict greater symptoms. Finally, we also examined reactivity to happy faces, predicting that heightened LPP would be specific only to threatening faces, and not to happy faces.

2. Methods

This study was approved by the Institutional Review Boards at Jesse Brown VA Medical Center, Chicago IL and its university affiliate, the University of Illinois at Chicago. Research was conducted in accordance with the Helsinki Declaration.

2.1. Participants

Forty-seven participants were included from a larger sample of OEF/OIF/OND veterans recruited at the Jesse Brown VA Medical Center and the University of Illinois Chicago. After completing informed consent procedures, participants completed the clinical assessment and ERP component of the study. Because completion of the clinical interview and ERP portion of the study took several hours, participants returned on another day to complete a neuropsychological assessment (NP). NP assessment was completed at a separate visit to avoid fatigue, and was typically completed within two weeks of the participants' initial visit. All veterans who were deployed as part of Operations Enduring Freedom, Iraqi Freedom or New Dawn and were between the ages of 18–45 were broadly eligible for participation; however, additional exclusionary criteria for participants included: presence of a clinically significant medical or neurological condition, presence of an organic mental syndrome, intellectual disability or pervasive developmental disorder, and current substance abuse or suicidal ideation at a level that would interfere with the study protocol. To assess general performance validity as it might apply to the WCST, the Forced Choice Recognition on the *California Verbal Learning Test – 2nd Edition* was used. Two participants did not have perfect performances (i.e., <16); however, their removal from subsequent analyses did not alter results and, due to our small sample size, they remained in analyses. Ages ranged from 21 to 49 years (mean: 33.2 SD: ± 6.2); 78.7% of the sample was male. Thirty-eight