



## Reduced lateral prefrontal cortical volume is associated with performance on the modified Iowa Gambling Task: A surface based morphometric analysis of previously deployed veterans



Nicholas D. Fogleman<sup>a</sup>, Farah Naaz<sup>a</sup>, Lindsay K. Knight<sup>b</sup>, Teodora Stoica<sup>b</sup>, Samantha C. Patton<sup>a</sup>, Jennifer H. Olson-Madden<sup>c,d</sup>, Meghan C. Barnhart<sup>c,d</sup>, Trisha A. Hostetter<sup>c,d</sup>, Jeri Forster<sup>c,d</sup>, Lisa A. Brenner<sup>c,d</sup>, Marie T. Banich<sup>e,f</sup>, Brendan E. Depue<sup>a,b,g,\*</sup>

<sup>a</sup> Department of Psychological and Brain Sciences, University of Louisville, Louisville, KY, USA

<sup>b</sup> Interdisciplinary Program in Translational Neuroscience, University of Louisville, Louisville, KY, USA

<sup>c</sup> VISN 19 Mental Illness Research Education and Clinical Center, Denver, CO, USA

<sup>d</sup> University of Colorado Denver, Anschutz Medical Campus, Aurora, CO, USA

<sup>e</sup> Institute of Cognitive Science, University of Colorado at Boulder, Boulder, CO, USA

<sup>f</sup> Department of Psychology and Neuroscience, University of Colorado at Boulder, Boulder, CO, USA

<sup>g</sup> Department of Anatomical Sciences and Neurobiology, University of Louisville, Louisville, KY, USA

### ARTICLE INFO

#### Keywords:

Magnetic resonance imaging (MRI)  
Anatomy  
Post-traumatic stress disorder (PTSD)  
Mild traumatic brain injury (mTBI)  
Modified Iowa Gambling Task (mIGT)  
Veterans

### ABSTRACT

Post-traumatic stress disorder (PTSD) and mild traumatic brain injury (mTBI) are two of the most common consequences of combat deployment. Estimates of comorbidity of PTSD and mTBI are as high as 42% in combat exposed Operation Enduring Freedom, Operation Iraqi Freedom and Operation New Dawn (OEF/OIF/OND) Veterans. Combat deployed Veterans with PTSD and/or mTBI exhibit deficits in classic executive function (EF) tasks. Similarly, the extant neuroimaging literature consistently indicates abnormalities of the ventromedial prefrontal cortex (vmPFC) and amygdala/hippocampal complex in these individuals. While studies examining deficits in classical EF constructs and aberrant neural circuitry have been widely replicated, it is surprising that little research examining reward processing and decision-making has been conducted in these individuals, specifically, because the vmPFC has long been implicated in underlying such processes. Therefore, the current study employed the modified Iowa Gambling Task (mIGT) and structural neuroimaging to assess whether behavioral measures related to reward processing and decision-making were compromised and related to cortical morphometric features of OEF/OIF/OND Veterans with PTSD, mTBI, or co-occurring PTSD/mTBI. Results indicated that gray matter morphometry in the lateral prefrontal cortex (LPFC) predicted performance on the mIGT among all three groups and was significantly reduced, as compared to the control group.

### 1. Introduction

Post-traumatic stress disorder (PTSD) and mild traumatic brain injury (mTBI) are two of the most common consequences of combat deployment (Dolan et al., 2012). PTSD, a disorder mainly characterized by exposure to actual or threatened death or serious injury (American Psychiatric Association, 2013), affects estimates of 10–30% of previously deployed combat Veterans from Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn (OEF/OIF/OND; Dolan et al., 2012; Hoge et al., 2007). Similarly, a significant percent (e.g., 15–25%) of OEF/OIF/OND Veterans are also affected by mTBI (Hoge et al., 2008). Mild TBI is characterized as a traumatically induced

physiological disruption of brain function which contains at least one of the following: (i) any period of loss of consciousness, (ii) any loss of memory for events immediately before or after the accident, (iii) any alteration in mental state at the time of the accident, and (iv) focal neurological deficits that may or may not be transient (Head, 1993). Mild TBI is unique from moderate and severe traumatic brain injury in length of loss of consciousness and posttraumatic amnesia (Head, 1993). Because of the high prevalence of trauma-related events during combat exposure, estimates of comorbidity of PTSD and TBI are as high as 42% in combat exposed OEF/OIF/OND Veterans (Hoge et al., 2008; Nelson et al., 2009). Literature suggests that combat exposure, rather than deployment itself, increases the likelihood of self-reported post-

\* Corresponding author at: Department of Psychological and Brain Sciences, University of Louisville, Louisville, KY, USA.  
E-mail address: [brendan.depue@louisville.edu](mailto:brendan.depue@louisville.edu) (B.E. Depue).

traumatic symptoms or a PTSD diagnosis following deployment (Smith et al., 2008), calling for the need of specific control groups (i.e., combat deployed Veterans with no PTSD/mTBI diagnosis). Recent work suggests that an occurrence of TBI may render individuals more susceptible to PTSD (Elder and Christian, 2009; Mayou et al., 2000; Stein and McAllister, 2009; Vasterling et al., 2009). Therefore, it is paramount to investigate not only individuals with singular diagnostic PTSD or mTBI, but also individuals with co-occurring PTSD/mTBI, to associate different deficit profiles in an attempt to specialize treatment.

Behaviorally, the most consistent finding in the extant literature indicates that individuals with either PTSD or TBI show similar patterns of executive function deficits, such as attention and working memory, when compared to control individuals using standard neuropsychological assessments (Leskin and White, 2007; Uddo et al., 1993; Vasterling et al., 1998, 2002). Although neuropsychological research is less abundant among individuals with mTBI, as opposed to moderate or severe TBI, these individuals have also been shown to display deficits in executive functioning (Lipton et al., 2009). Even scarcer are studies examining individuals with co-occurring PTSD/mTBI, however individuals with these conditions have demonstrated deficits in attention and processing speed as compared to control individuals (Nelson et al., 2009). Similarly, previously deployed OEF/OIF/OND combat Veterans with co-occurring PTSD/mTBI exhibit increased behavioral impulsivity and reduced inhibitory control, as compared to combat deployed non-diagnostic Veterans (Depue et al., 2014; Swick et al., 2012).

Possibly underlying these behavioral deficits, consistent neuroimaging research indicates that individuals with either PTSD or TBI show abnormal structure and function of the prefrontal cortices (Karl et al., 2006; Lipton et al., 2009; Shin et al., 2006; Sponheim et al., 2011; Thomaes et al., 2010). Specifically, individuals diagnosed with PTSD exhibit reduced gray matter in the ventromedial prefrontal cortex (vmPFC; Karl et al., 2006; Shin et al., 2006; Sponheim et al., 2011), dorsolateral prefrontal cortex (dlPFC; Thomaes et al., 2010) and in the amygdalar/hippocampal complex, when compared to control individuals (Karl et al., 2006; Kasai et al., 2008; Kitayama et al., 2005; Rauch et al., 2003; Woodward et al., 2006). Similarly, individuals with moderate and severe TBI also exhibit volumetric reductions in the vmPFC, as compared to controls (Ariza et al., 2006; Himanen et al., 2005; Mollica et al., 2009), suggesting that mTBI may also demonstrate similar morphometric differences as PTSD, and moderate and severe TBI in the vmPFC. However, this is relatively unknown in regard to mTBI. Therefore, among these individuals it appears as though the most consistent neuroimaging findings indicate abnormalities of the vmPFC (Karl et al., 2006; Mollica et al., 2009).

Taken together, deficits in classically defined executive function (e.g., attention, memory, processing speed, response inhibition), putatively associated with IPFC function (Corbetta and Schulman, 2002; Depue et al., 2010; Depue et al., 2015), and abnormalities of the vmPFC in combat deployed Veterans with PTSD, mTBI, or both seems clear, however, less research examining reward processing and decision-making has been conducted. This is surprising as the most associated behavioral relationships with the vmPFC are reward processing and decision-making. One of the hallmark neuropsychological tests measuring reward processing and decision-making is the Iowa Gambling Task (IGT; Bechara et al., 1994). Studies indicate the direct relationship of impaired performance on the IGT and damage to the vmPFC (Bechara et al., 1994, 1996, 1999, 2000; Fellows and Farah, 2005). The IGT simulates real-life decision-making by assessing whether participants can learn to sacrifice immediate rewards in favor of long-term gain (Lawrence et al., 2009). The IGT requires a participant to select a card from one of four card decks. Two of the decks are considered 'advantageous' as choosing cards from these decks ultimately leads to gains; conversely, the other two decks are considered 'disadvantageous' as choosing cards from these decks leads to losses. Performance on the IGT is dependent upon a participant's ability to learn to identify the two 'advantageous' decks from the two 'disadvantageous' decks to inform

future decisions about whether to "play" or "pass" a card from each deck.

A compendium of neuroimaging research (Bechara et al., 2000) suggests that individuals who have vmPFC lesions perform more poorly on the IGT, as they are insensitive to positive or negative future consequences, which subsequently affects learning. Impaired performance is not limited to lesions in the vmPFC, as studies have also demonstrated that lesions to the dlPFC, a region implicated in working memory and attention (Barbey et al., 2013; Corbetta and Schulman, 2002) and decision-making, are associated with poor performance on the IGT (Clark et al., 2003; Fellows and Farah, 2005; Manes et al., 2002). Given that the vmPFC and dlPFC each appear to be uniquely involved in decision-making and reward processing, Manes et al. (2002) suggested that the ventral and dorsal regions of prefrontal cortex must interact to make rational decisions.

Although scarce, behavioral research indicates that individuals with PTSD also demonstrate difficulties with decision-making and reward processing (Killgore et al., 2008; Levine et al., 2005; Sailer et al., 2008) and suggest these individuals may have difficulty identifying positive rewards over time due to decreased task-related motivation and/or cognitive fatigue (Sailer et al., 2008). Still, there are only a few studies to date, which have used the IGT to investigate decision-making and reward processing within these populations (Levine et al., 2005; Levin et al., 2010; Pustilnik et al., 2016). Research from Levin et al. (2010) comparing previously deployed combat Veterans from OEF/OIF/OND with a history of mTBI and a comparison group without head blast exposure, indicates comparable performance on the IGT. However, it is important to note that results from Levine et al. (2005) suggest that individuals with mTBI learn at a slower rate and demonstrate lower overall performance relative to a control group.

Given the strong neuroanatomical evidence of alterations in the vmPFC and dlPFC in individuals with PTSD and mTBI and initial behavioral indications of deficits in decision-making and reward processing, the current study sought to be the first to investigate brain morphometry associated with decision-making and reward processing in previously deployed OEF/OIF/OND Veterans with co-occurring PTSD/mTBI using the modified version of the IGT (mIGT; Cauffman et al., 2010; Tanabe et al., 2013). According to Cauffman et al. (2010), the mIGT prevents participants from differentially ignoring certain decks while attending to others, and thus may be better at assessing learning rates given an equal amount of experience with all decks. As reward and punishment cannot be untangled from perseveration on the standard version of the IGT (Bechara et al., 1994), the mIGT ensures that cards are drawn equally from each of the four decks, so that any deficit that can be attributed to learning about rewards and punishment and informing future decisions will be more easily identifiable. Hence, the mIGT enables one to examine decisions and learning rates, specifically on decks that are associated with reward, punishment or a combination of both (i.e., total plays overall).

Therefore, the current study is the first, to our knowledge, to examine decision-making and reward processing, as it relates to surface-based brain morphometry. Furthermore, we examined these processes in previously deployed Veterans with either PTSD or mTBI, or both compared to deployed Veterans with no PTSD or mTBI diagnosis. The following hypotheses were posited: (i) previously deployed OEF/OIF/OND Veterans with PTSD, mTBI, or co-occurring PTSD/mTBI will demonstrate poorer performance on the mIGT when compared to unaffected previously deployed OEF/OIF/OND Veterans, (ii) previously deployed OEF/OIF/OND Veterans with PTSD, mTBI, or co-occurring PTSD/mTBI will demonstrate reduced gray matter (GM) in vmPFC and dlPFC regions involved in decision-making and reward processing when compared to unaffected OEF/OIF/OND deployed Veterans, (iii) reduced GM of prefrontal cortical regions of the vmPFC and dlPFC will also be associated with performance on the mIGT in PTSD, mTBI, PTSD/mTBI, as compared to, unaffected previously deployed OEF/OIF/OND Veterans, and (iv) previously deployed OEF/OIF/OND Veterans with

Download English Version:

<https://daneshyari.com/en/article/4933958>

Download Persian Version:

<https://daneshyari.com/article/4933958>

[Daneshyari.com](https://daneshyari.com)