Journal of Affective Disorders 223 (2017) 130–138

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Neural differences underlying face processing in veterans with TBI and co-occurring TBI and PTSD

J. Bomyea[a,b], S.C. Matthews[a,b], M.S. Buchsbaum[b], A.D. Spadoni[a,b], I.A. Strigo[c], A.N. Simmons[a,b,*]

[a] Center of Excellence for Stress and Mental Health, San Diego Veterans Affairs Health Care System, United States
[b] Department of Psychiatry, University of California, San Diego, United States
[c] San Francisco Veterans Affairs Medical Center, United States

ARTICLE INFO

Keywords:
TBI
PTSD
Emotional processing
FMRI

ABSTRACT

Background: Traumatic brain injury (TBI) is common in military personnel and associated with high rates of posttraumatic stress disorder (PTSD). TBI impacts widely-distributed neural patterns, some of which influence affective processing. Better understanding how TBI and PTSD/TBI alters affective neural activity may improve our understanding of comorbidity mechanisms, but to date the neural correlates of emotional processing in these groups has been relatively understudied.

Methods: Military controls, military personnel with a history of TBI, and military personnel with both TBI and PTSD (N = 53) completed an emotional face processing task during fMRI. Whole-brain activation and functional connectivity during task conditions were compared between groups.

Results: Few whole-brain group differences emerged in planned pairwise contrasts, though the TBI group showed some areas of hypoactivation relative to other groups during processing of faces versus shapes. The PTSD/TBI group compared to the control and TBI groups demonstrated greater connectivity between the amygdala and insula seed regions and a number of prefrontal and posterior cingulate regions.

Limitations: Generalizability to other patient groups, including those with only PTSD, has not yet been established.

Conclusion: TBI alone was associated with hypoactivation during a condition processing faces versus shapes, but PTSD with TBI was associated altered functional connectivity between amygdala and insula regions and cingulate and prefrontal areas. Altered connectivity patterns across groups suggests that individuals with PTSD/TBI may need to increase frontal connectivity with the insulae in order to achieve similar task-based activity.

1. Introduction

Traumatic brain injury (TBI) occurs when an external force alters brain function, resulting in alteration or loss of consciousness, post-traumatic amnesia, neurological deficits, and/or intracranial lesion (Bryant et al., 2010). In military personnel deployed to recent conflicts in Iraq and Afghanistan (i.e., Operation Enduring Freedom, Operation Iraqi Freedom, Operation New Dawn [OEF/OIF/OND]), mild TBI (mTBI) occurs in a significant portion (i.e., 10–20% (Hoge et al., 2008; Polusny et al., 2011; Tanielian and Jaycox, 2008)). The high number of mTBI exposures in combat in this population has led to the designation of mTBI as the "signature injury" of these conflicts (Independent Review Group, 2007).

Individuals exposed to mTBI are at higher risk for adverse outcomes relative to unexposed counterparts. In particular, mTBI is associated with high rates of co-occurring mental health disorders, commonly including posttraumatic stress disorder (Hoge et al., 2008; Schneiderman et al., 2008; Tanielian and Jaycox, 2008). The co-morbidity of PTSD and mTBI is associated with negative outcomes such as suicide (Bryan and Clemans, 2013), and data suggest that the presence of PTSD mediates the relationship between mTBI exposure and variables including poor health outcomes, neuropsychological performance, and functional impairment (Hoge et al., 2008; Ragsdale et al., 2013; Shandera-Ochsner et al., 2013). Identification of clinical and biological factors that distinguish individuals who have experienced mTBI with and without co-occurring PTSD may provide important information about risk factors or treatment options.

Altered emotion processing has been documented in both mTBI and PTSD behaviorally, suggesting that similarities and differences in brain functioning across these conditions during such processing merits empirical study (Bomyea et al., 2017; Litz et al., 2000; Maki-Marttunen et al., 2015; Milders et al., 2008). Though brain activity specifically

* Corresponding author at: Center of Excellence for Stress and Mental Health, San Diego Veterans Affairs Health Care System, United States.
E-mail address: ansimmons@ucsd.edu (A.N. Simmons).

http://dx.doi.org/10.1016/j.jad.2017.07.003
Received 14 December 2016; Received in revised form 19 June 2017; Accepted 5 July 2017
Available online 06 July 2017
0165-0327/ Published by Elsevier B.V.

during emotional processing has been understudied in mTBI, a widely distributed network of brain structures is affected by mTBI, including superior and middle frontal gyri, superior and inferior parietal lobules, superior temporal gyri, and medial frontal cortex (Simmons and Matthews, 2012). Moreover, severe TBI has been linked to aberrant neural processing of affective social stimuli (Neumann et al., 2016). PTSD is also associated with an array of brain differences during negative emotion processing relative to healthy individuals. Research has shown greater activation in the amygdala and insula, which are responsible for emotional and arousal-related processes (Fonzo et al., 2010; Rauch et al., 2000; Shin et al., 2005), and less activation in prefrontal cortex (PFC) regions implicated in emotion regulation (Etkin and Wager, 2007). Although the neurobiological mechanisms of the development of PTSD/TBI comorbidity has not yet been established, the high degree of co-occurrence may be accounted for by shared disruption of PFC areas (e.g., dorsolateral PFC) that are responsible for modulating affective reactivity and responding (Stein and McAllister, 2009; Vasterling et al., 2009). Brain activity comparisons in patients with mTBI who do and do not have PTSD may improve our understanding of the neural mechanisms of this comorbidity, yet there is relatively little known of the impact of mTBI and co-occurring PTSD on brain functioning during affective processing.

Examination of the association *across* functional units in the brain may provide more meaningful information than examining activation in regions in isolation. One result of neural abnormalities observed in mTBI and PTSD may be that higher-level cognitive processes (e.g., complex cognitive functions, emotional regulation and processing) requiring functional integration across diverse and spatially distinct brain areas are compromised. Connectivity-based assessments, which examine potential differences in regional connections through functional pathways by quantifying temporally correlated brain activity, may provide important information regarding the sequelae of mTBI with and without co-occurring PTSD. Individuals with mTBI demonstrate aberrant connectivity across diverse brain regions at rest (Han et al., 2016; Hayes et al., 2016), but connectivity has not been sufficiently examined in the context of emotional processing. PTSD studies document attenuated neural connectivity in circuits that include the amygdala, insula, and dorsal anterior cingulate during passive processing of emotional stimuli in PTSD patients relative to controls (Fonzo et al., 2010; Stevens et al., 2013), suggesting that the presence of PTSD in individuals with TBI may impact connectivity patterns.

The current study used fMRI to evaluate differences in OEF/OIF/OND veterans with mTBI with and without co-occurring PTSD, as compared to military controls, on neural activation and connectivity patterns during emotional face processing. We hypothesized that individuals with co-occurring PTSD and mTBI (PTSD/TBI group) would show greater emotion-related amygdala and insula activity relative to mTBI only individuals (TBI group), and that the TBI group would show greater amygdala and insula activity as compared to military controls (MC group). We also tested the hypothesis that the PTSD/TBI group would show hypoconnectivity between limbic and PFC areas relative to the other groups.

2. Method

2.1. Participants

Nineteen males with a history of combat-related PTSD and co-occurring mTBI, 17 males with mTBI, and 17 military control males with no history of PTSD or mTBI completed a validated face-matching task during fMRI (Fonzo et al., 2010). Exclusion criteria included history of substance use disorder and problematic use within thirty days (based on meeting criteria for substance abuse during diagnostic interview), presence of conditions that would impact fMRI safety, or history of bipolar disorder or schizophrenia. PTSD/TBI subjects were not excluded based on other comorbid mental health disorders, so long as PTSD was determined to be the primary disorder by the assessing clinician (S.C.M.). The TBI group had a history of deployment to OEF/OIF/OND combat theaters but no current PTSD. Participants were not required to meet a threshold for post-concussive symptoms to be eligible for study entry in the TBI group. Individuals in the MC group had been deployed to OEF/OIF/OND but had minimal direct combat exposure, no history of TBI and no history of current or past psychiatric disorders. Participants were recruited from the VA San Diego Healthcare System (VASDHS) via advertisement materials (e.g., flyers posted in the hospital public areas) or through referrals from other ongoing research projects at this site. Participants were provided written informed consent to participate in the study, which included the assessments reported here and additional study procedures including paradigms and FDG-PET imaging published in prior studies (there is no redundancy in imaging data between prior published studies and the current manuscript) (Buchsbaum et al., 2015; Spadoni et al., 2015). All study procedures were approved by the University of California San Diego Human Research Protection Program and the Research and Development Committee at VASDHS.

2.2. Psychiatric measures

The Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) was used to assess diagnostic criteria for the study inclusion/exclusion criteria (e.g., substance use disorder, bipolar disorder). TBI and MC participants screened negative for PTSD using the MINI assessment. PTSD/TBI participants screened positive for PTSD using the MINI, and severity of PTSD symptoms were also assessed using the Clinician Administered PTSD Scale (CAPS) (Blake et al., 1995) in these groups. Only individuals endorsing combat-related trauma as the most distressing on the CAPS interview were included in the study. PTSD severity was also assessed using the PTSD Checklist-Military Version (Weathers et al., 1993). Depression severity was assessed using the Beck Depression Inventory-II (BDI) (Beck et al., 1961). General anxiety severity was assessed using the Spielberger State Trait Anxiety Inventory (STAI) (Spielberger et al., 1983). Level of combat trauma exposure during deployment was assessed using the Deployment Risk and Resiliency Inventory (DRRI; (King et al., 2006)).

TBI history was assessed using a set of interview and questionnaire responses. The interview and questionnaire items assessed TBI events, and were modeled on the VA's TBI screening evaluation, which included questions about characteristics of head injuries, including duration of loss of consciousness, alteration of consciousness, and posttraumatic amnesia. Participants completed the Defense and Veterans Brain Injury Center (DVBIC) questionnaire, which assessed history of head injury and associated symptoms. In addition, an interview was conducted with study staff to assess history of head injury and the following TBI criteria: All participants were required to have been free of TBI before entering the military, to have sustained their most severe TBI while in the military, and to have sustained their most severe TBI due to blast exposure (Table 1). A neuroradiologist reviewed all anatomical images to confirm that there were no significant abnormalities and to ensure that no participants met criteria for complicated mild TBI. A study psychiatrist also reviewed participant charts when necessary to collect corroborating evidence of diagnosis and medication status.

2.3. Stimuli and apparatus

Participants completed an emotional face-matching task used previously by our group (Fonzo et al., 2010), consisting of 18 consecutive 5-second trials alternating face and control conditions (Hariri et al., 2005; Matthews et al., 2008; Stein et al., 2007), interspersed with an 8 s fixation cross at the beginning of each trial. In the face condition (17.6% of total run time in each face type), each trial consisted of a target face presented on the top and two probe faces on the bottom left