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Early life trauma is associated with altered white matter integrity and affective control

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ABSTRACT

Early life trauma (ELT) has been shown to impair affective control and attention well into adulthood. Neuroimaging studies have further shown that ELT was associated with decreased white matter integrity in the prefrontal areas in children and adults. However, no study to date has looked at the relationship between white matter integrity and affective control in individuals with and without a history of ELT. To examine this, we tested 240 Veterans with (ELT N = 80) and without (NoELT N = 160) a history of childhood sexual abuse, physical abuse or family violence. Affective control was measured with the Affective Go/No-Go (AGN) and attention was indexed with the Test of Variable Attention (TOVA). White matter integrity was measured using fractional anisotropy (FA). Results showed greater number of errors on the AGN in ELT compared to NoELT. There was no difference on the TOVA. While there were no mean differences in FA, there was an interaction between FA and reaction time to positive stimuli on the AGN where the ELT group showed a positive relationship between FA and reaction time in right frontal and prefrontal areas, whereas the NoELT group showed a negative or no association between FA and reaction time. This suggests that ELT may be associated with a distinct brain-behavior relationship that could be related to other determinants of FA than those present in healthy adults.

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1. Introduction

The aim of the current study was to examine the association between white matter integrity and cognitive performance in a sample of Veterans with and without a history of early life trauma. Emerging literature has alerted researchers and clinicians to the long-term impact of exposure to early life trauma (ELT) on physical and psychological health and well being (Anda et al., 2006). While the exact definition of what constitutes ELT or childhood adversity differs between studies, most authors include childhood sexual abuse, physical abuse and family violence under the umbrella term ELT, since these three traumas share an interpersonal dimension (De Bellis and Zisk, 2014; Perry et al., 1995). Importantly, it appears that the effects of trauma are greatest during specific sensitive periods of brain development (Andersen, 2003). This increased impact of stress on the brain has already been illustrated in animal models, especially in the area of the hippocampus, amygdala and prefrontal cortex (PFC) (McEwen, 2008). Based on these animal models, studies using Magnetic Resonance Imaging (MRI) have provided evidence of the important and lasting impact of ELT on brain integrity potentially suggesting altered development. For example, ELT has been associated with alteration in the fundamental symmetry of the PFC of children exposed to ELT compared to age-matched control subjects (Carrion et al., 2001). Another important region for stress, the anterior cingulate cortex, has been shown to be smaller in children exposed to trauma (Cohen et al., 2006). Similarly, another study (Richert et al., 2006) reported smaller dorso-lateral PFC but larger ventral and middle PFC in children exposed to ELT. Altered gray matter volume within the frontal regions of children exposed to ELT have since been replicated, underscoring the consistency of these effects (Carrion and

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Wong, 2012; Hanson et al., 2010). Studies of adults reporting a history of ELT have shown altered gray matter integrity lasting into adulthood in regions overlapping the findings of studies in children, such as the PFC (Tomoda et al., 2009), dorsal anterior cingulate cortex (Thomaes et al., 2010), orbito-frontal and anterior cingulate cortices (Dannlowski et al., 2012), as well as mid-cingulate cortex (Corbo et al., 2014).

Brain development presents different windows for gray and white matter. White matter development lasts longer, with myelination in the frontal areas extending into early adulthood (Andersen, 2003). Despite what may be a larger window for the effect of stress on the white matter, studies investigating the impact of ELT on the brain have mainly focused on gray matter and our knowledge of the impact of ELT on white matter development is sparser. Recent studies have used diffusion tensor imaging to investigate the integrity of the underlying white matter tracts across the central nervous system. These studies have shown reduced fractional anisotropy (FA), a marker of white matter integrity, in the anterior and posterior sections of the corpus callosum in maltreated children compared to healthy control subjects (Jackowski et al., 2008), in the left arcuate fasciculus and cingulum bundle in adults victim of verbal abuse during childhood (Choi et al., 2009), and in the inferior longitudinal fasciculus of the occipital region (Choi et al., 2012) of adults reporting a history of domestic abuse. A recent study (Teicher et al., 2014) extended these findings by showing how ELT (verbal abuse) was associated with reduced FA in the corpus callosum and corona radiata. Similarly, one study (Benedetti et al., 2014) showed that ELT affected the white matter integrity of the bilateral superior longitudinal fasciculi and the left anterior thalamic radiation. Collectively, these studies suggest an impact of ELT on the development of white matter, though the specific localization of the impact remains largely unclear.

Brain imaging studies of ELT are critical to understanding reported behavioral impairments in victims of ELT, especially the cognitive domains of attention and affective control. Studies showed that children reporting maltreatment presented a bias in attention to threat-related stimuli, suggesting altered attention control (Gamble and Rapee, 2009; Pine et al., 2005; Roy et al., 2008; Waters et al., 2008). Beyond the attention bias, children exposed to ELT have been shown to perform more poorly on cognitive tasks involving attention and affective control compared to healthy age-matched control subjects (DePrince et al., 2009; Gould et al., 2012; Kaplow et al., 2008; Nikulina and Widom, 2013; Porter et al., 2005). Similar impairments have been shown in neutral (Navalta et al., 2006) and affective (Gould et al., 2012) Go/No-Go paradigms, suggesting that ELT may impair inhibition and affective control, in general, as well as attention. In sum, there is mounting evidence for both impaired attention in individuals with a history of ELT and decreased integrity of brain structures thought to support attention and affective control. However no study to date has investigated how ELT may influence the association between white matter integrity, especially in tracts located in the PFC (Casey et al., 2000; Manna et al., 2010; Wood and Grafman, 2003), and performance on tasks of attention/affective control, a brain region and cognitive functions that may be specifically impacted by ELT.

The objectives of the current study were to examine the impact of ELT on prefrontal white matter integrity and to evaluate a possible link between white matter structural changes and behavioral performance on tasks of affective control and attention. White matter integrity was evaluated across the whole brain using diffusion tensor imaging. Attention and affective control were measured using a continuous performance task and affective Go/No-go task, respectively. We hypothesized that individuals with ELT would show decreased FA in the corpus callosum and the PFC/anterior cingulate. We also hypothesized that individuals with ELT would evidence impaired attention performance, indexed by greater number of commission errors, on the sustained attention task and greater interference of negative emotional distracters on the affective go/no-go task, indexed by greater number of commission errors for the negative distracter (positive target).

2. Material and methods

2.1. Recruitment

Three hundred and seven service members were initially recruited from the cohort of the VA Rehabilitation Research & Development-supported Traumatic Brain Injury (TBI) National Center for TBI Research (NCR) at VA Boston Healthcare System: The Translational Research Center for TBI and Stress Disorders (TRACTS). Participants enrolled in the TRACTS NCR cohort are recruited from the Boston Metropolitan area and the surroundings. Individuals were ineligible for enrollment in TRACTS if they met any of the following criteria: (a) history of neurological illness (other than TBI); (b) history of seizures; (c) current diagnosis of schizophrenia spectrum or other psychotic disorders (not related to PTSD); (d) current active suicidal and/or homicidal ideation, intent, or plan requiring crisis intervention; or (e) cognitive disorder due to general medical condition other than TBI. The Institutional Review Board of Human Studies Research at the VA Boston Healthcare System approved all research procedures and all participants provided informed consent and were reimbursed for their time and travel expenses. From the original 307 participants, we excluded participants with missing ELT rating (N = 13), individuals with missing neuropsychological data (N = 17) and clinical data (N = 10). Additionally, to ensure that performance accurately reflected subject's abilities, the Medical Symptom Validity Test [MSVT, (Green, 2003)] was administered. Subjects who failed the MSVT were excluded from the analyses (N = 27). The final sample consisted of two hundred and forty participants, including a total of 22 women and 218 men.

2.2. Participants

History of ELT was determined using the Traumatic Life Events Questionnaire (see below). Based on this questionnaire, the ELT group (N = 80) was composed of individuals reporting a history of physical abuse, sexual abuse and/or family violence before the age of 18 coupled with an A2 reaction of fear/helplessness/horror as defined by DSM-IV-TR, (APA, 2004). The age cut-off insured that the traumatic event would be pre-deployment. The control group (NoELT, N = 160) was composed of individuals who reported no interpersonal trauma before the age of 18. This did not preclude exposure to other events not of an interpersonal nature (e.g. natural disaster, motor-vehicle accidents, witness of robbery, criterion A2 of the DSM-IV-TR), though none were diagnosed with PTSD as a result of this pre-deployment event. Effectively, this means that subjects of the ELT group all had trauma exposure before deployment, while some of the participants in the NoELT group reported a first trauma exposure before deployment (e.g. earthquake that did not result in PTSD).

2.3. Clinical assessment

All clinical assessments were conducted by a doctoral-level psychologist and reviewed by at least three doctoral-level psychologists to achieve consensus

Clinician Administered PTSD Scale (CAPS): Current PTSD Diagnosis and symptoms severity were assessed using the Clinician-