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Evidence of resilience: Neuroimaging in former prisoners of war

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Abstract

In this study, single voxel proton magnetic resonance spectroscopic imaging (^{1}H-MRS) and volumetric analysis of hippocampal magnetic resonance imaging (MRI) images were used to determine if any differences in hippocampal biochemistry or volume were present between former prisoners of war (POWs) with and without posttraumatic stress disorder (PTSD) and control subjects matched for age and education. This study did not find lower hippocampal concentrations of *N*-acetylaspartate (NAA), smaller hippocampal volumes, or more impaired memory function in older veterans with PTSD compared with a group matched for traumatic experience or a nontraumatized control group.
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1. Introduction

Posttraumatic stress disorder (PTSD) has been a focus of attention for neuroimaging research over the last decade. During that time, a number of human research studies have implicated various brain regions in this condition, including portions of the frontal lobe, the amygdala, and the hippocampus (Villarreal and King, 2001). This last structure has received the most attention in structural imaging studies, due to the relationships between stress and hippocampal atrophy demonstrated in several animal studies (Sapolsky, 1996). To date, most studies of PTSD subjects using magnetic resonance imaging (MRI) have shown that these subjects have smaller hippocampal volumes than matched controls. Studies using proton magnetic resonance spectroscopy (^{1}H-MRS) have typically also revealed abnormalities in hippocampal biochemistry in PTSD subjects, commonly showing lower levels of hippocampal *N*-acetylaspartate (NAA), an excitatory neurotrans-

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mitter associated with neuronal integrity, in PTSD subjects relative to controls (Villarreal et al., 2002).

Considerable debate continues regarding the meaning of these findings in PTSD subjects. Smaller hippocampal volumes or altered hippocampal biochemistry could either precede a traumatic event and predispose individuals to PTSD or follow the traumatic event as a consequence of neurobiological changes associated with extreme stress. Evidence for both arguments has been put forward (Gilbertson et al., 2002; Bremner et al., 1995). Given the widespread prevalence of PTSD in the population, another very practical focus for investigation is the study of possible ongoing negative neurobiological and cognitive consequences associated with chronic PTSD. Most neuroimaging studies that have shown significant differences in hippocampal biochemistry or structure among PTSD subjects have been completed in individuals who have had the disorder for decades. Studies of children or more recent victims of trauma typically do not reveal similar differences in hippocampal biochemistry or structure (Bonne et al., 2001; De Bellis et al., 2001), though there are exceptions (Wignall et al., 2004). This suggests that if the smaller hippocampal volumes and altered neurochemistry associated with PTSD are not purely premorbid to the index traumatic event, the processes leading to these deleterious outcomes may continue to act over the affected individual's lifetime.

To investigate the possibility of accelerated neurobiological decline in subjects with chronic PTSD, investigators might need to construct longitudinal studies that last for decades, since longitudinal neuroimaging studies that have examined PTSD subjects over time frames of 6 months to 2 years have not shown significant changes in hippocampal structure during that time (Bonne et al., 2001; De Bellis et al., 2001). An alternative strategy that would not necessitate the logistical problems associated with longitudinal studies lasting decades would be to examine older subjects who have been exposed to significant, documented traumas earlier in life and who have met criteria for PTSD for the majority of their lives. Examining hippocampal morphometry and biochemistry in these subjects could shed light on the chronic neurobiological consequences of lifelong PTSD.

Former prisoners of war (POWs) have frequently been the focus of research efforts into the relationship of severe early adult trauma to psychopathology and cognitive functioning, though few neuroimaging studies have examined this population. Former POWs have been shown to have a high prevalence of PTSD. A number of studies suggest that 30% to 70% of former POWs meet lifetime criteria for PTSD (Sutker et al., 1993; Engdahl et al., 1997). In addition to experiencing a high rate of PTSD, former POWs have demonstrated a direct relationship between their weight loss during captivity and their current PTSD symptoms. We have found that the documented percentage weight loss during POW internment is strongly correlated with PTSD symptom severity six decades after the original trauma (Myers et al., 2005). Despite a clear research interest in this subject group, investigations of former POWs have tended to focus on issues of cognitive function (Sutker et al., 1990; Sulway et al., 1996) and reports of psychopathology (Sutker et al., 1993; Engdahl et al., 1997), with little attention paid to neuroimaging, though one early study did examine the relationship of sleep disturbances to the ventricle/brain ratio as determined by computed tomographic imaging (Peters et al., 1990) in former Japanese held POWs, and one more recent study (Brown et al., 2003) examined differences in medial temporal lobe (MTL) biochemistry between former POWs with and without PTSD using magnetic resonance spectroscopy (MRS).

Our goals in this study were to expand on our previous work by examining the ^{1}H-MRS measures of hippocampal biochemistry, hippocampal volumes, and neuropsychological findings in three groups of subjects: former POW subjects with PTSD, former POW subjects without PTSD, and control subjects matched for age and education. Our intent was to determine if the presence of chronic PTSD would be associated with decreased hippocampal *N*-acetylaspartate/creatine ratios (NAA/Cr) and smaller hippocampal volumes in subjects exposed to similar severe and well-documented traumatic experiences compared with a matched control group. Our previous work had shown a significant correlation between reported reexperiencing symptoms in PTSD subjects and medial temporal lobe (MTL) NAA/Cr ratios but had shown no significant differences in MRS-determined MTL NAA/Cr or choline/creatine ratios (CHO/Cr) between POWs divergent for PTSD diagnosis (Brown et al., 2003); however, this earlier study had not compared POW subjects with a matched control group and had not examined hippocampal volumes between POW groups.

2. Methods

A total of 26 male veteran subjects (20 former POWs and 6 control subjects) participated in the study. The Human Use Committee of the University of Arkansas for Medical Sciences approved the research