Original Investigation

Decreased Regional Cerebral Perfusion at Resting State in Acute Posttraumatic Stress Disorder Resulting From a Single, Prolonged Stress Event

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Rationale and Objectives: This study evaluated the altered regional cerebral blood flow (rCBF) in resting state in patients with acute posttraumatic stress disorder (PTSD) 3 months after trauma.

Materials and Methods: The rCBF was measured in 30 patients with acute PTSD and 36 healthy controls.

Results: Survivors with acute PTSD showed decreased rCBF, the Clinician-Administered PTSD Scale score correlated negatively with the rCBF, and rCBF at resting state decreased in acute PTSD.

Conclusions: PTSD symptom severity was associated with diminished cerebral blood flow in the right insular cortex and right orbital medial frontal gyrus. The rCBF may predict PTSD symptom severity.

Key Words: Brain; posttraumatic stress disorders; MR imaging; statistical parametric mapping; arterial spin labeling.

INTRODUCTION

Posttraumatic stress disorder (PTSD) is a condition that develops from a sudden, life-threatening, or catastrophic event causing delayed emergence and long-term persistence of mental disorders. Patients experience mental disorders in various ways, including intrusive memories, disturbing recollections, nightmares, flashbacks, distress, and physiological reactions on exposure to reminders of the traumatic event. These disorders seriously affect the patients' quality of life.

Many functional imaging studies have been performed in patients with chronic PTSD. For example, Semple et al. (1) found increased regional cerebral blood flow (rCBF) in the right amygdala, left parahippocampal gyrus, and occipital cortex when patients performed an auditory continuous performance task. Further, patients with PTSD showed decreased frontal cortex and anterior cingulate activity compared to healthy controls. In a similar study, the researchers found a significantly increased rCBF in the orbitofrontal cortex and a reduced left/right hippocampal perfusion ratio in the PTSD group (2). The subjects in the foregoing studies included veterans with combat-related PTSD and a history of substance abuse, associated with major effects on brain structure and function (3). Indeed, many patients with PTSD are often heavily medicated or have current or past alcohol and substance abuse issues (4).

Previous cerebral blood flow (CBF) research in PTSD has been performed with single-photon emission computed tomography (SPECT) and positron emission tomography (PET). Researchers have used Tc-99m hexamethyl propylene amine oxime leukocyte scintigraphy under resting conditions and found CBF abnormalities (5,6). Lucey et al. (6) found a decreased rCBF in the superior frontal cortex and the right caudate. Bonne et al. (5) found increased rCBF in the right precentral, superior temporal, and fusiform gyri.

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Activation studies of PTSD used reminders of the traumatic events to record CBF. For example, patients with PTSD were reexposed to trauma by traumatic scripts (7,8). In a study monitoring CBF changes, veterans without PTSD listened to combat sounds compared to a control group (9). Lindauer et al. showed that rCBF decreased in the medial frontal gyrus and increased in the right cuneus of the PTSD group relative to the trauma-exposed control group (7). A previous study found decreased perfusion of medial prefrontal cortex (mPFC) and increased rCBF in regions involving visuospatial processing compared to healthy controls (10). Using color Stroop and emotional Stroop conditions, one study found rCBF abnormalities in women with early childhood sexual abuse–related PTSD compared to women without PTSD but who were abused (11). Shin et al. (12) found increased rCBF in both the right amygdala and the ventral aspects of the anterior cingulate gyrus, using visual images of combat situations.

The aforementioned PTSD investigations were based on PET or SPECT studies. Although some studies have investigated arterial spin-labeling magnetic resonance imaging (ASL-MRI) of PTSD (13), the authors of these studies did not adjust for underlying gray matter (GM) atrophy in PTSD and ignored partial volume effects (PVEs) associated with white matter (WM). As SPECT does not allow absolute measurements of rCBF, values were normalized to the mean global activity. Our studies involving ASL-MRI of PTSD provided data correction for PVEs, which produced a more accurate determination of the regional pattern of rCBF in patients with PTSD by diminishing the artifacts of regional differences in tissue loss on the rCBF data. After the PVE correction, the rCBF distribution was more homogeneous throughout the brain with less intersubject variation than the original distribution.

On March 28, 2010, a coal mine was flooded in Linfen in the Shanxi province of China. Workers showed a strong social homogeneity that is more consistent with the social status, work experience, education level, and age. Most importantly, they had a single-stimulus condition and intensity. Our research group investigated recent-onset PTSD and non-PTSD 6 months after the trauma using voxel-based morphometry (VBM) method. Our data avoided many confounding factors and offered a unique advantage of correlating psychological consequences of PTSD and stress on brain structure. We found that compared to normal controls, patients with recent-onset PTSD had smaller GM volume in the left dorsal anterior cingulate cortex, and subjects without PTSD had smaller GM volume in the right pulvinar and left pallidum (14). These results showed brain structural changes in recent-onset PTSD and non-PTSD following prolonged exposure to a single trauma.

In this study, we used pulsed arterial spin labeling (PASL) to determine whether rCBF levels changed in patients with acute PTSD from the coal mine flood under resting state. This technology is a novel technique that enables quantitative measurement of CBF using magnetically labeled arterial blood water as an endogenous tracer (15). The noninvasive nature of PASL offers promise for larger scale studies (16,17). Based on the results of previous studies, we hypothesize that rCBF may be altered in different regions in patients with acute PTSD relative to normal controls. The severity of PTSD symptoms may correlate with the rCBF in patients with acute PTSD.

MATERIALS AND METHODS

Subjects

We recruited 30 survivors of a coal mine flood that occurred in March 2010 in the Shanxi province of China. During this coal mine flood disaster, 153 miners were trapped in the coal mine for 226 hours and 115 miners were ultimately rescued. As a program of psycho-aid organized by the government, the clinical evaluation and diagnosis of the members were carried out approximately 3 months after the disaster by a psychiatric team from Xijing Hospital who were experts trained to use the Diagnostic and Statistical Manual of Mental Disorders of Fourth (DSM-IV) (18). Sixty-five of the survivors and 30 survivors' wives agreed to attend an MR study. As a result, 30 of the trauma survivors were diagnosed with PTSD in the study, including 17 survivors and 13 survivors' wives. The Clinician-Administered PTSD Scale (CAPS) was administered to quantitatively characterize PTSD symptoms. Their symptoms were mild. A total of 36 age- and sex-matched controls who exhibited normal mental health based on the Prodromal Questionnaire were recruited from the health physical examination center in the Shanxi province of China (19). The elapsed time between the traumatic event and the MRI scan ranged from 90 to 93 days (mean: 91 ± 0.46 days). The study protocol was approved by the Medical Ethical Committee of Xijing Hospital of the Fourth Military Medical University. All participants provided voluntary, written, informed consent before entering the study.

Exclusion criteria for both groups included psychiatric diagnoses (schizophrenia, neurologic disorders, major depression, bipolar disorder, and organic mental disorder), head trauma with loss of consciousness, mental retardation, seizures, psychotic disorders, panic disorder, phobia, obsessive-compulsive disorder, and dissociative disorders as well as left-handedness. All subjects who had a history of treatment with psychotropic drugs or substance abuse (alcohol, smoking, or drugs) were also excluded.

Imaging Data Acquisition

Structural MRI Data

Imaging was performed using a 3.0 T MR scanner (MAGNETOM Trio, Siemens AG, Erlangen, Germany) located in the Department of Radiology, Xijing Hospital. A high-resolution three-dimensional magnetization rapid acquisition gradient echo T1-weighted sequence covering the whole brain (192 sagittal slices) was acquired. Other acquisition parameters were repetition time (TR): 1900 ms; echo time (TE): 2.26 ms; inversion time (TI): 900 ms; flip angle: 9°; field of view: 220 mm; matrix: 256 × 256; and slice thickness: 1.00 mm, with no interslice gap.