Brief Report

Neural Correlates of Traumatic Memories in Posttraumatic Stress Disorder: A Functional MRI Investigation

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Objective: The neuronal circuitry underlying posttraumatic stress disorder (PTSD) was studied in traumatized subjects with and without PTSD.

Method: Traumatized subjects with (N=9) and without (N=9) PTSD were studied by using the script-driven symptom provocation paradigm adapted to functional magnetic resonance imaging at a 4-T field strength.

Results: PTSD subjects showed significantly less activation of the thalamus, the anterior cingulate gyrus (Brodmann's area 32), and the medial frontal gyrus (Brodmann's area 10/11) than did the comparison subjects.

Conclusions: The findings suggest anterior cingulate, frontal, and thalamic involvement in the neuronal circuitry underlying PTSD.

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Previous neuroimaging studies have implicated limbic, paralimbic, and prefrontal structures in the pathophysiology of posttraumatic stress disorder (PTSD) (1–5). Paralimbic structures that are thought to be involved in PTSD include the anterior cingulate gyrus (Brodmann's areas 24, 32), the subcallosal anterior cingulate gyrus (Brodmann's area 25), and the orbitofrontal cortex. Prefrontal structures implicated in PTSD include the left inferior prefrontal cortex and Broca's area (1–5).

To our knowledge, there are no functional magnetic resonance imaging (fMRI) studies of PTSD that have used a symptom provocation paradigm involving script-driven traumatic imagery. In the fMRI study reported here, we hypothesized that PTSD patients would show less activation than comparison subjects in prefrontal regions as well as in subcortical structures such as the thalamus that are more accessible to imaging at a 4-T field strength.

Method

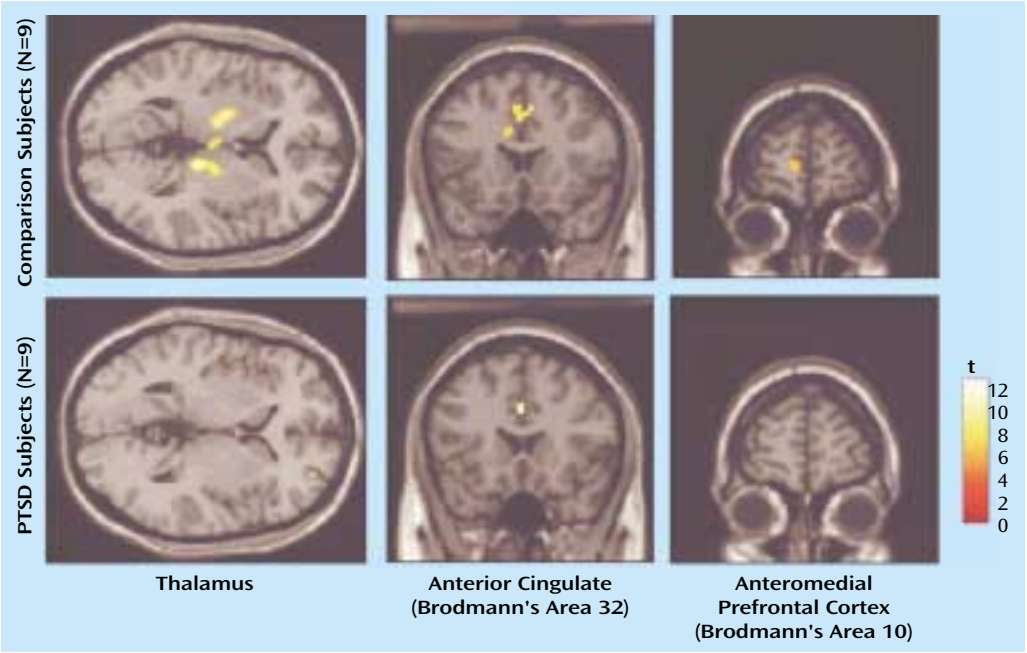
Nine subjects who had developed PTSD as a result of sexual abuse/assault (N=6) or motor vehicle accidents (N=3) were studied. Comparison subjects were nine subjects who met DSM-IV criterion A for PTSD (as a result of sexual abuse/assault [N=5] or motor vehicle accidents [N=4]) but who did not meet the full DSM-IV criteria for the disorder. Written consent was obtained from all subjects. Subjects' diagnoses were based on their responses on the Structured Clinical Interview for DSM-IV Axis I Disorders (6) and the Clinician-Administered PTSD Scale (7). The mean score on the Clinician-Administered PTSD Scale was 75 for the subjects with PTSD (SD=17) and 4 for the comparison subjects (SD=2). Comorbid disorders in the PTSD group included major depression (N=2), dysthymia (N=3), and panic disorder (N=2), lifetime history of drug abuse and dependence (N=2), lifetime history of alcohol abuse and dependence (N=4), and current nicotine abuse (N=4). The comparison subjects were similar to the PTSD subjects in age (mean=37 years, SD=12, for the PTSD group; mean=41 years, SD=10, for comparison group), sex, and race. All subjects were right-handed. The PTSD subjects had undergone a supervised drug washout for at least 2 weeks before scanning. PTSD subjects with a history of psychosis, bipolar disorder, and substance use disorder in remission for less than 6 months were excluded from the study, as were PTSD subjects with any significant medical or neurological conditions or a history of head injury.

MRI studies were performed on a 4-T whole-body Varian/Siemens imaging system with a 90-cm diameter horizontal bore and a whole-body 68-cm diameter gradient set with a maximum strength of 40 mT/m and a slew rate of 120 mT/m per second. A whole-head hybrid birdcage radio frequency coil was used for transmission and detection of signals. Before imaging, a global shimming procedure using first- and second-order shims was performed to optimize the magnetic field over the imaging volume of interest. The subject's heart rate was monitored with a fiber-optic pulse oximeter.

The radio frequency coil was placed around the subject's head. Each functional brain volume was acquired by using a navigator echo-corrected, interleaved multishot (four shots), echo-planar imaging pulse sequence with a 128×128 matrix size and a total volume acquisition time of 5 seconds (TE=15 msec, flip angle=45°, field of view=24.0 cm). The volume acquired covered the whole brain and consisted of 12 transverse slices, 6 mm thick (voxel size=1.87×1.87×6 mm).

Functional maps of the activated pixels were constructed by pixel-by-pixel comparisons of the signal intensity in the baseline and task-related images. Statistical parametric mapping methods (SPM99 software) were used. Basis functions representing epochs of interest were entered into SPM99. Variability in scans attributed to each basis function relative to SPM99's implicit baseline were revealed by using contrasts. Fixed-effects analyses were performed by modeling each group's evoked blood-oxygen-level-dependent (BOLD) response with hemodynamically convolved

FIGURE 1. Brain Activation Sites[a] in Traumatized Subjects With and Without PTSD



[a] Areas of significantly (p<0.001) increased activation during the final 30 seconds of a 60-second period of recalling a traumatic event, relative to average baseline activation 60 seconds before each recollection of the traumatic event, superimposed on T_1-weighted magnetic resonance imaging templates.

boxcar basis functions. The regions of interest were defined on the basis of T_1-weighted images and Talairach coordinates (8).

The script-driven imagery procedure was adapted to fMRI according to previously published methods (4, 9). Scanning of the traumatic imagery condition was repeated three times. Each subject was instructed to lie still, breathe through his/her nose, and allow himself/herself to begin focusing on the traumatic script as soon as the script was read. Reading of the script lasted 30 seconds. As soon as the subject heard the script, he/she was encouraged to remember all sensations that were associated with the traumatic event for 60 seconds. The subject's heart rate was measured during that time. The script was repeated after 120 seconds. Baseline brain activation was calculated on the basis of the average activation patterns 60 seconds before each recollection of the traumatic event. Brain activation during the recall of the traumatic event was calculated on the basis of the average activation patterns during the final 30 seconds of each period of recollection of the traumatic event.

Results

Figure 1 shows the brain activation sites in the PTSD and comparison groups. Areas of significantly increased BOLD response across all subjects in each group are shown. The t values are represented by the color of the activation sites. The unidirectional hypotheses stated in the introduction were based on previous studies (1–6), as well as on our own pilot data. One-tailed t tests were therefore used. Regions of activation during traumatic memory recall versus implicit baseline where the comparison group (N=9) showed greater activation than the PTSD group included the right thalamus (Talairach coordinates, x=12, y=–12, z=2) (t=8.98, df=741.5, p=0.0001), left thalamus (x=–4, y=–14, z=18) (t=6.93, df=741.5, p=0.0001), left medial frontal gyrus (Brodmann's area 10/11) (x=0, y=34, z=–12) (t=6.84, df=741.5, p=0.0001), right medial frontal gyrus (Brodmann's area 10/11) (x=0, y=34, z=–12) (t=6.84, df=741.5, p=0.0001), left anterior cingulate gyrus (Brodmann's area 32) (x=0, y=34, z=–12) (t=6.84, df=741.5, p=0.0001), right anterior cingulate gyrus (Brodmann's area 32) (x=0, y=34, z=–12) (t=6.84, df=741.5, p=0.0001), and the right occipital lobe (Brodmann's area 19) (x=28, y=–86, z=38) (t=6.06, df=741.5, p=0.0001).

Brain activation patterns during the first 30 seconds of recall were similar to those during the final 30 seconds of recall. Amygdala activation was not observed at any time during the recall of the traumatic memory. Brain activation returned to baseline during the rest periods in all brain areas studied for both the PTSD and the comparison groups. Time courses of activation showed that 60 seconds was enough time for the subjects to recover from the traumatic scripts. Baseline brain activation did not differ between the PTSD subjects and the comparison subjects (data not shown). The PTSD subjects showed a greater increase in heart rate from baseline than the comparison subjects (PTSD group: mean=12 bpm, SD=7; comparison group: mean=2 bpm, SD=2; t=4.2, df=10, p=0.0004, one-tailed).

Discussion

Subjects with PTSD showed lower levels of brain activation than comparison subjects in the thalamus, the medial frontal cortex (Brodmann's area 11), and the anterior cin-

gulate gyrus (Brodmann's area 32). Lower levels of anterior cingulate gyrus activation and medial prefrontal cortex activation (Brodmann's area 11) are consistent with previous positron emission tomography (PET) studies of subjects with PTSD related to sexual abuse and to combat (1, 2, 5). To our knowledge, no studies have reported changes in thalamic activation in subjects with PTSD. One explanation for this discrepancy may be differences in methods (PET versus fMRI).

Alterations in thalamic activation may be attributable to the high levels of arousal that can arise from recall of traumatic material. High levels of arousal during traumatic experiences have been hypothesized to lead to altered thalamic sensory processing (10), which in turn results in a disruption of transmission of sensory information to the frontal cortex, cingulate gyrus, amygdala, and hippocampus. This is one mechanism that has been hypothesized to underlie dissociative symptoms (10) and may be one of the mechanisms underlying flashbacks in PTSD. The present data showing changes in prefrontal, anterior cingulate gyrus, and thalamic activation during the recall of traumatic memories may provide some insight into the neuronal circuitry underlying the reexperience of traumatic events.

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